Caring for the Hospitalized Child 3rd Edition

A Handbook of Inpatient Pediatrics

Author

American Academy of Pediatrics Section on Hospital Medicine

Editors

Jeffrey C. Gershel, MD, FAAP

Daniel A. Rauch, MD, FAAP, SFHM

American Academy of Pediatrics

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Preface

The care of the hospitalized child has evolved significantly since the term "hospitalist" was first used over 25 years ago. In most pediatric teaching services, hospitalists care for general pediatric inpatients, but the scope of practice often extends to comanagement of subspecialty and surgical patients, as well as coverage in intensive care units and newborn nurseries. Community hospitals are also employing hospitalists to improve the quality and efficiency of care while expediting admissions from a variety of outpatient sites whose physicians are unable to care for inpatients.

A consequence of the ongoing pressure from payers is that children must be sicker to be admitted, with an ever-increasing number who not only require complex care but may also depend on technology. Yet even as we care for a patient population with greater and more complex care needs, decreasing hospitalization days and lengths of stay have become core priorities for both hospitals and insurance companies. In addition, all stakeholders insist on care that is safe, efficient, timely, cost effective, patient centered, and equitable. The net result is that caring for the hospitalized child has become increasingly challenging.

The management of pediatric inpatients is addressed in many available resources, including textbooks, handbooks, and online resources. However, very few provide concise, specific, point-of-care recommendations about the most common diagnoses encountered, and none has relied primarily on hospitalists as contributors. This book was conceived as a resource written and edited by experts in the field of pediatric hospital medicine, whose primary focus is the care of hospitalized children. The authors are all leaders in the field and have hands-on experience with their topics. As their practice settings vary from children's hospitals to private community hospitals to general pediatric services in public hospitals, their guidance can be used in any of these settings. The clinical chapters are meant to be directive in immediate care and specific about when to either escalate care or begin discharge planning.

Written specifically for the hospitalist, this book includes chapters beyond just clinical care to address the whole of a hospitalist's work. We have included discussions about activities such as billing, cultural effectiveness, do not resuscitate orders, informed consent and assent, patient safety, surge planning, transport, and utilization management, and we have incorporated other facets of patient care beyond laboratory tests and treatments. Comprehensive care for hospitalized children must include attention to medical systems and ethics, because no sick child exists in a vacuum, and nonbedside activities can profoundly affect patient outcomes.

Every child is unique. Although this book gives specific direction for most cases, no one resource can account for every clinical possibility. We all learn very early in our careers that there are many ways to address a given clinical issue. We present the approaches of our contributors, while recognizing that there are many equally satisfactory alternatives.

This third edition includes updates to all chapters and 15 new topics, such as autism, COVID-19 and multisystem inflammatory syndrome in children (MIS-C), demyelinating disorders, syncope, and thrombocytopenia, as well as an entire new section on newborn care for hospitalists who provide newborn nursery coverage. We are very appreciative of all the comments we received on the second edition. As a result, many of the additions were based on reader feedback. Please continue to share your insights and suggestions.

Finally, we thank you for using and supporting this manual. This will be our final edition as editors, and it has been an honor and privilege to develop and refine this resource for pediatric care wherever children are hospitalized.

Jeffrey C. Gershel, MD, FAAP
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Adolescent

CHAPTER 1

Anovulatory Uterine Bleeding

Introduction

Anovulatory uterine bleeding (AUB), formerly known as "dysfunctional uterine bleeding," is a form of abnormal uterine bleeding that is painless, profuse, irregular (noncyclic), and unrelated to any structural changes of the uterus or systemic disease. Although there are many etiologies, anovulation secondary to hypothalamic-pituitary-ovarian axis immaturity is the most common cause of AUB in adolescents during the initial 1 to 2 years of menstruation.

Heavy (> 80 mL) or prolonged (> 7 days) vaginal bleeding that occurs at regular cyclic intervals is known as *menorrhagia.* Irregular (acyclic) vaginal bleeding is called *metrorrhagia.* Prolonged or heavy periods that occur at irregular intervals are termed *menometrorrhagia.*

A patient with AUB who is admitted to the hospital may have hemodynamic instability (eg, tachycardia, hypotension orthostatic vital signs), severe anemia (hemoglobin level < 7 g/dL [< 70 g/L] or with active heavy bleeding, < 10 g/dL [< 100 g/L]), symptomatic anemia (eg, lethargy, fatigue), need for intravenous (IV) conjugated estrogen due to inability to take oral medications, continued bleeding after 24 hours of estrogen-progestin combination, or very rarely need for surgical intervention.

Clinical Presentation

History

Obtain the patient's history with and without the presence of the patient's parent or legal guardian. Ask about the age at menarche and whether or not there was heavy bleeding at the first menses. Determine the menstrual cycle interval (3–6 weeks is normal) and the number of days of bleeding. Menstrual loss that requires pad or tampon changes (soaked pad or tampon) every 1 to 2 hours, with anything longer resulting in "flooding" or "accidents," is excessive, particularly if the menses lasts 8 days or longer. Ask about the effect of the bleeding on the adolescent's psychosocial well-being (eg, missed days at school and inability to participate in sporting and social activities). Use the HEADSS assessment tool (home, education, activities/employment, drug use, suicidality, sex) to screen for health risk behaviors. Focus on recent sexual activity, overall number of partners, recent partners, history of sexually transmitted infections (STIs), pregnancy, and possibility of sexual abuse or assault. Determine the method of contraception and whether condoms were used at last intercourse.

Ask about associated symptoms, such as light-headedness, syncope, abdominal or pelvic pain, nausea, vomiting, eating behaviors, heat or cold intolerance, fever, vaginal discharge, headaches, and weight change (gain or loss). Inquire about a history or family history of excessive bleeding with surgical or dental procedures, easy bruising or petechiae, frequent nose bleeds, or gingival bleeding. Review and document the patient's current medications and ask specifically about hormonal contraception, androgens, nonsteroidal anti-inflammatory drugs, anticoagulants, platelet inhibitors, chemotherapeutic agents, antipsychotics, antidepressants, corticosteroids, and spironolactone.

Physical Examination

Perform a complete physical examination. Record the patient's weight, height, vital signs, and orthostatic blood pressures. Note the body habitus (low hair line, webbed neck, shield chest, widely spaced nipples) and palpate the thyroid. For a suspected pituitary adenoma, check the optic fundi and perform visual field testing. Determine the sexual maturity rating (SMR) of the breasts and assess the patient for galactorrhea. Examine the skin for pallor, petechiae or hematomas, hypo- or hyperpigmentation, acanthosis nigricans, hirsutism, male pattern baldness, acne, or striae. Palpate the abdomen for a uterine or ovarian mass. Examine the genitalia (clitoromegaly, imperforate hymen) and note the pubertal hair SMR. Look for signs of sexual abuse/trauma (abrasions, contusions, or punctuate tears of the perineum and perianal areas) and STIs (malodorous vaginal discharge, vaginal erythema, vesicular lesions or ulcers).

If the patient is sexually active, perform a pelvic examination to obtain samples for STI testing. A pelvic examination performed with anesthesia may be necessary for a virginal adolescent with bleeding that cannot be controlled with hormone therapy, significant anemia, or pelvic and abdominal pain.

Laboratory Workup

Perform a pregnancy test and complete blood cell count with differential, platelet count, and reticulocyte count. If the patient requires a blood transfusion, obtain a type and screen, prothrombin time, partial thromboplastin time, fibrinogen level, and von Willebrand panel (plasma von Willebrand factor [VWF] antigen, plasma VWF activity, and factor VIII activity) prior to administration of blood products.

If the patient is sexually active, test for STIs, particularly *Neisseria gonorrhoeae* and chlamydia. STI testing can also be performed on a urine sample.

Arrange for a pelvic ultrasonographic examination if the pregnancy test result is positive (to rule out ectopic pregnancy) or if a mass is palpated during the pelvic examination.

Obtain follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in girls in whom diagnosis of anovulatory cycles is considered, if possible on day 3 or 5 of their cycle (when their levels are lowest and therefore the most reproducible).

Other laboratory testing is dictated by the history and findings at physical examination and may include thyroid function tests (goiter, short stature, obesity, skin dryness, excessive sweating, thinning hair, myxedema); testosterone evaluation including free testosterone, dehydroepiandrosterone sulfate, androstenedione levels, LH:FSH ratio (obesity, hirsutism, and acne suggestive of polycystic ovary syndrome [PCOS]); prolactin evaluation (galactorrhea, headaches, visual field defects, papilledema); and 17-hydroxyprogesterone evaluation (hirsutism, severe acne, clitoromegaly suggestive of late-onset congenital adrenal hyperplasia).

Differential Diagnosis

Most cases of AUB (90%) during the first 2 years after menarche are secondary to physiological anovulation from delayed maturation of the hypothalamic pituitary axis. However, AUB is a diagnosis of exclusion. The differential diagnosis primarily includes early or second trimester pregnancy loss, ectopic or molar pregnancy, and local infections. Systemic etiologies include bleeding disorders, endocrine disorders, and medications. Local causes include trauma, foreign bodies, and, rarely, benign and malignant tumors (Table 1–1).

Anovulation and vaginal bleeding can also be seen in thyroid disorders, PCOS, Turner syndrome, systemic illnesses (cystic fibrosis, inflammatory bowel disease, diabetes mellitus, renal disease, autoimmune disorders), strenuous exercise, and emotional stress (anorexia nervosa).

Treatment

For severe uterine bleeding, when the patient cannot tolerate oral medication, start IV conjugated estrogen (25 mg administered every 4–6 hours for up to 24 hours) until the bleeding stops. Then change to an oral contraceptive (eg, 30 mcg ethinylestradiol/0.3 mg norgestrel), 1 pill administered every 6 hours, until the bleeding slows (usually 24–36 hours), then taper by 1 pill every 3 days. If bleeding recurs during tapering, increase the total daily dose to the lowest dose that controls bleeding.

Table 1–1. Differential Diagnosis of Anovulatory Uterine Bleeding

Diagnosis	Clinical Features
Anovulation	Menarche within past 2 y No fever or abdominal/pelvic pain Noncyclic
Ectopic pregnancy	(+) Pregnancy test result Abdominal pain, nausea, vomiting
Endometriosis	Cyclic pain with menses that may progress to acyclic abdominal pain Pain with bowel movements, constipation or rectal bleeding, dysuria, urgency, hematuria
IUD-related bleeding	Intermenstrual (all IUDs), irregular (levonorgestrel), and heavy bleeding (copper IUD)
Missed abortion	Low back or abdominal pain Tissue or clot-like material passing from the vagina
Platelet disorders (eg, idiopathic thrombocytopenic purpura, thrombocytopenia, von Willebrand disease)	Heavy vaginal bleeding at the first menses Epistaxis and gum bleeds Family history of excessive bleeding Surgery-related bleeding or associated with dental work Malignancy or treatment for malignancy
STI/pelvic inflammatory disease, endometritis unrelated to pregnancy	Vaginal discharge Fever, abdominal or pelvic pain, nausea and vomiting Cervical motion and/or adnexal tenderness Vague, crampy abdominal pain; intrauterine foreign objects
Structural uterine problems including congenital uterine anomalies (septate, arcuate, unicornuate), polyp, adenomyosis, leiomyoma (fibroid)	Mostly asymptomatic Vague abdominal pain and/or pelvic pressure
Trauma, foreign body	Lacerations and/or abrasions Bruising of the perineum and perianal area

Abbreviations: IUD, intrauterine device; STI, sexually transmitted infection.
+ indicates a positive finding.

Start an antiemetic (ondansetron 8 mg [IV or by mouth], administered 3 times a day) to minimize nausea and vomiting caused by high-dose estrogen, and initiate iron therapy (60 mg elemental iron once or twice per day) as soon as the patient is stable and able to take pills by mouth.

A blood transfusion is indicated for a hemoglobin level less than 7 g/dL (< 70 g/L) associated with signs of hemodynamic instability (tachycardia, orthostatic hypotension) or ongoing bleeding. Consult with a gynecologist and hematologist for bleeding that persists beyond 24 hours of hormonal therapy. In the rare case in which treatment with hormones fails, consult with a hematologist and gynecologist to assess whether antifibrinolytics (tranexamic acid, aminocaproic acid, desmopressin) and/or surgical intervention (therapeutic dilation and curettage) are indicated.

Indications for Consultation

- **Gynecology or adolescent medicine specialist:** Severe vaginal bleeding that does not respond within 24 hours to IV conjugated estrogen
- **Hematology:** Bleeding that is continuing 24 hours after the initiation of hormonal therapy; suspicion of a bleeding diathesis

Disposition

- **Intensive care unit transfer:** Severe bleeding and signs of shock, with poor peripheral perfusion and/or hypotension
- **Discharge criteria:** Patient hemodynamically stable, bleeding under control, patient tolerating oral hormonal therapy

Follow-up

- **Primary care physician and/or gynecologist:** 2 weeks after discharge and then at least monthly until return to a pattern of normal menstrual cycles, hormonal treatments are stable, and hemoglobin is greater than 10 g/dL (> 100 g/L).

Pearls and Pitfalls

- AUB remains a diagnosis of exclusion. Consider pregnancy, STIs, and bleeding disorders.
- Severe AUB requiring hospitalization may be the first manifestation of a bleeding disorder, especially if it occurs with menarche.
- High-dose estrogen therapy requires the use of antiemetics.
- Maintain a menstrual calendar to monitor response to therapy (by using paper or smartphone apps).

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CHAPTER 2

Eating Disorders

Introduction

Adolescents with eating disorders are admitted to the hospital for acute medical stabilization, with much of the work of recovery done as an outpatient or in a residential eating disorder program. The admission serves to correct any electrolyte imbalances and arrhythmias (eg, prolonged corrected QT interval [QTc]), stabilize the nutritional status, and prevent refeeding syndrome (a rare event). Also, the process of admission offers the patient and family an opportunity to recognize the severity and magnitude of the problem, allowing education on nutritional needs, connection with essential mental health care resources, and the initiation of the process of recovery.

Anorexia nervosa (AN) refers to restriction of energy intake relative to energy requirements, leading to a significantly low body weight for age, sex, and expected height. AN can occur in the context of weight loss, as well as a failure to grow appropriately. There are 2 subtypes: restricting (weight loss occurs through dieting or fasting with or without hyperexercise) and binge-eating/purging (characterized by episodes of bingeing and purging via vomiting, laxative or diuretic use, or hyperexercising). *Atypical AN* refers to a patient with all of the physiology of AN but without weight loss below a critical threshold.

Bulimia nervosa (BN) is defined by binges, in which a patient eats a relatively large amount of food in a specific period of time, accompanied by a sense of loss of control over eating. These binges are then followed by some sort of compensatory behavior, including self-induced vomiting; nontherapeutic use of laxatives, diet pills, or diuretics; exercising; restricting; insulin misuse; or other unhealthy strategies. These behaviors must occur at least once weekly for 3 months to meet criteria for BN.

Avoidant/restrictive food intake disorder (ARFID) refers to a patient with a disrupted eating pattern that leads to significant weight loss and nutritional deficiency. The patient may be dependent on nutritional supplementation for growth or weight maintenance or may have marked interference with psychosocial functioning due to persistent inability to meet their expected nutritional needs. A patient with ARFID lacks the mindset found in AN, in that they want to gain weight and grow but cannot do so. ARFID may be secondary to limited intake (lack of interest in eating or low overall appetite), limited variety (extremely picky eater fears new foods or has aversions to certain foods due to sensory or texture issues), or aversive (food restriction or avoidance stems from a specific fear or anxiety, such as a fear of choking or the avoidance of

anticipated abdominal pain). A child with autism may have overlap among categories, with texture aversions, pickiness, and avoidant behavior interfering with eating. ARFID can lead to the same medical complications as AN or BN, requiring acute medical stabilization.

Clinical Presentation

The clinical presentation and physical examination findings of eating disorders result from the degree of malnutrition and the extent of any inappropriate compensatory behaviors. The patient may present with some combination of weight loss or falling off a growth curve, refusal to eat, recurrent vomiting, hematemesis, constipation, pubertal delay, irregular menses, weakness, syncope, seizure, edema, low-impact fractures, attempted suicide, and distress over their body image.

History

Obtain the patient's history with and without the presence of the family or guardian, and then interview the parents separately. Ask about the patient's minimum and maximum weight levels and corresponding height levels. Assess the patient's perception of their ideal weight and their understanding of what a healthy weight is. Note whether they feel guilt when eating and counting calories. Compile a 24-hour diet recall, with attention to portions and timing, and ask if they count calories and/or fat or carbohydrate grams. Inquire about any dietary restrictions, portion sizes, caffeine and/or fluid intake, eating rituals, and special diets (eg, vegan, vegetarian, low carb, paleo- or ketogenic diets, fat-avoidant diets, overly healthy eating).

Investigate exercise patterns, such as exercising alone in a room. A useful question to detect hyperexercisers is to ask how stressed they are if they miss a workout/practice.

Look for secretive behaviors, such as hoarding food; using diuretics, laxatives, diet pills, or enemas; and visiting pro-anorexia or bulimia websites. During the patient's social history, try to determine if there has been sexual or physical abuse, suicidality, or substance use. Elicit any family history of eating disorder, obesity, mental illness, or substance use disorder (SUD).

Ask about associated symptoms, such as fatigue, weakness, muscle cramps, dizziness, syncope, chest pain, palpitations, exercise intolerance, fullness, bloating, epigastric pain, abdominal pain, nausea, emesis, reflux, pallor, easy bruising, bleeding, poor wound healing, and intolerance to cold temperatures.

Physical Examination

Table 2–1 outlines the relevant physical examination findings. All organ systems can be affected by an eating disorder, but the patient may appear perfectly

stable despite significant electrolyte abnormalities or cardiac arrhythmias. Of note, an eating disorder may occur without obvious physical signs or symptoms, and medical consequences of eating disorders may go unrecognized. Ensure that the patient is weighed after voiding, in a hospital gown, backward on a scale (so they cannot see the weight), and at the same time each morning. The patient may have underweight, normal weight, overweight, or obesity.

Laboratory Workup

The goal of laboratory testing is to identify complications (eg, refeeding syndrome) and to exclude other diagnoses. No test is diagnostic for an eating disorder, and normal laboratory results do not exclude serious illness or

Table 2–1. Clinical Findings in Eating Disorders

Organ System	Clinical Features
Vital signs	Hypothermia Orthostatic hypotension Pulse < 50 bpm awake or < 40 bpm asleep
Skin	Cool extremities Dry skin, pallor, carotenemia, ecchymoses Raynaud syndrome, poor peripheral perfusion Russell sign: callus over knuckles (from vomiting using finger) Signs of cutting on areas such as the wrists, hips, thighs, and stomach
Hair	Dry, loss of shine, thinning Lanugo hair on trunk, face in starvation
HEENT	Cheilosis (suggests zinc deficiency) Normal thyroid Parotitis (from vomiting) Scleral hemorrhage (from vomiting)
Dental	Caries Erosions of lingual and occlusal surfaces
Cardiac	Mitral valve prolapse (occurs in one-third of patients with AN when starved) Peripheral/dependent edema Poor perfusion
GI	Constipation alternating with diarrhea Hematemesis (if excessive purging) Palpable loops of stool if constipated Scaphoid abdomen or bloating
Neuropsychiatric	Depression Flat or anxious affect Obsessive-compulsive thoughts/behaviors Poor concentration or memory loss Sciatica due to decreased fat padding

Abbreviations: AN, anorexia nervosa; bpm, beats per minute; GI, gastrointestinal; HEENT, head, ears, eyes, nose, throat

medical instability. Order a complete blood cell count to look for anemia, leukopenia, or thrombocytopenia, which can result from bone marrow hypoplasia. Assess magnesium and phosphorus levels, and obtain a comprehensive metabolic panel, paying attention to the aspartate aminotransferase, alanine aminotransferase, and albumin levels. A thyroid-stimulating hormone level is sufficient as an initial screen for thyroid pathology. Also obtain specific vitamin or mineral evaluations based on nutritional status (eg, vitamin A, vitamin D, zinc). Check a urinalysis, which can identify ketosis, proteinuria, and a low specific gravity, suggestive of a patient who is water loading to falsely increase their weight.

In the setting of laxative abuse, hyperchloremic metabolic acidosis, hyperuricemia, hypocalcemia, and elevated transaminase levels can occur. Persistent emesis can lead to a hypokalemic, hypochloremic metabolic alkalosis. Obtain an electrocardiogram (ECG) if there are any electrolyte abnormalities, cardiac symptoms, significant purging, or weight loss. Electrocardiographic findings may include bradycardia, low-voltage changes, prolonged QTc, ST depression, and T-wave inversion.

Perform a urine pregnancy test if physiologically appropriate, and, if the patient is amenorrheic, order prolactin, luteinizing hormone, follicle-stimulating hormone, and estradiol levels. If the patient has been amenorrheic for more than 6 months or if there is a history of recurrent low-impact fractures, order a bone mineral density (BMD) scan. Osteopenia is a BMD level greater than 1.0 SD below normal; osteoporosis is suggested by a density that is 2.5 SDs below normal.

Do *not* order the following studies for routine screening, although they may be helpful if the patient's history is not conclusive for an eating disorder: upper gastrointestinal (GI) series with small-bowel follow-through, neuroimaging, and celiac blood panel.

Differential Diagnosis

The differential diagnosis of eating disorders is summarized in Table 2–2.

Complications

The most frequent complications of eating disorders are summarized in Table 2–3. Heart failure and suicide are the most common causes of death.

Refeeding Syndrome

Refeeding syndrome can occur in a patient who has underweight, normal weight, or obesity. Risk factors include chronic undernourishment with little to no energy intake for more than 10 days; median body mass index

Table 2–2. Differential Diagnosis of Eating Disorders	
Vomiting	
Diagnosis	**Clinical Features**
Chronic cholecystitis	Constant right upper quadrant pain
CNS lesion	Headache, seizure, visual disturbances
Pancreatitis	Persistent, severe epigastric abdominal pain
Pregnancy	Amenorrhea, fatigue, (+) pregnancy test result
Superior mesenteric artery syndrome	Postprandial epigastric pain with early satiety, bilious emesis
Weight Loss	
Diagnosis	**Clinical Features**
Adrenal insufficiency	Postural dizziness, hypotension, hyperkalemia, hypercalcemia, hyponatremia
Celiac disease	Chronic diarrhea with foul-smelling and/or floating stools, constipation with abdominal distention
Depression	Anhedonia, ↓ appetite, sleep disturbance, feelings of worthlessness or guilt, impaired concentration
Diabetes mellitus	Polyuria, polydipsia, hyperglycemia
HIV	Fever, lymphadenopathy, sore throat, mucocutaneous ulcer, rash, myalgia, night sweats, diarrhea
Hyperthyroidism	Anxiety, emotional lability, weakness, tremor, palpitations, heat intolerance, ↑ perspiration
Inflammatory bowel disease	Bloody diarrhea, colicky abdominal pain, urgency, tenesmus, incontinence, hypotension
Substance use	Needle marks, skin infections, unexplained burns, atrophy of nasal mucosa

Abbreviation: CNS, central nervous system.
+ indicates a positive finding; ↓, decreased; ↑, increased.

(BMI) less than 75% for a patient less than 18 years of age or BMI less than 15 kg/m^2 for an older patient; precipitous or profound weight loss ($>$ 10%–15% of total body mass lost in $<$ 3–6 months); and a history of previous refeeding syndrome. Other risk factors include status post bariatric surgery, excessive alcohol intake, and misuse of diuretics, laxatives, or insulin.

Refeeding syndrome is primarily caused by total body phosphorus depletion during the starving state, leading to hypophosphatemia, hypokalemia, and hypomagnesemia. With reintroduction of carbohydrates into the diet, insulin is released, increasing the uptake of phosphorus, potassium, and magnesium, which can adversely affect cardiac and respiratory function. If refeeding syndrome is not diagnosed and managed expeditiously, it can potentially lead to fatal congestive heart failure (CHF) and respiratory failure.

The patient may present with edema, profound muscle weakness, cardiac and/or respiratory failure, GI distress, and delirium.

Table 2–3. Common Complications of Eating Disorders	
Organ System	**Complications**
Cardiac	Bradycardia Conduction abnormalities CHF Mitral valve prolapse Pericardial effusion
Electrolyte	Refeeding syndrome: ↓ potassium, phosphate, magnesium levels ↓ or ↑ sodium level ↓ potassium level
Endocrine	Anovulation Euthyroid sick syndrome Growth restriction Vitamin D deficiency
GI	Constipation Delayed gastric emptying, leading to bloating Esophagitis, Mallory-Weiss tear Rectal prolapse Superior mesenteric artery syndrome
Hematologic	Bone marrow hypoplasia
Neurologic	Peripheral neuropathy Seizures *AN*: cortical atrophy, ventriculomegaly, white/gray matter loss
Orthopedic	Osteopenia
Psychiatric	Suicidal ideation Comorbid disorders include anxiety, depression, and substance abuse
Pulmonary	*BN*: pneumomediastinum, aspiration pneumonia
Renal	Nephrolithiasis *AN*: concentrating defect (polyuria) *BN*: sodium and water retention (edema)

Abbreviations: AN, anorexia nervosa; BN, bulimia nervosa; CHF, congestive heart failure; GI, gastrointestinal.
↓ indicates decreased; ↑, increased.

Treatment

Acute medical stabilization is indicated for a patient presenting with electrolyte abnormalities, ECG abnormalities (bradycardia < 50 beats per minute or a prolonged QTc), or acute suicidal ideation with inability to contract for safety. The goals of hospitalization include vital sign and electrolyte stabilization, reversal of medical complications, monitoring for refeeding syndrome, initiation of weight gain (aim for a gain of 0.2 kg/d), and reintroducing healthy eating behaviors. This requires a multidisciplinary approach, with involvement of the medical team, nutritionist, social worker, therapist, and psychiatrist, and typically requires 7 to 10 days of inpatient treatment. Nutritional

rehabilitation is the key to managing reversible complications. Basic steps in treatment include:

- Consult with the appropriate specialists (psychiatry, nutrition, gastroenterology, adolescent medicine, and endocrinology) to develop and implement an eating disorder protocol with a behavior plan and contract.
- Search the patient's belongings for laxatives, diuretics, diet pills, chewing gum, and exercise weights. Do not allow the patient internet or cell phone access.
- Perform suicidality screening and arrange for the patient to have a one-on-one sitter or nurse. A family member is not a substitute for a sitter.
- Insert an intravenous (IV) catheter for emergency access in case of complications.
- Initially, keep the patient on bed rest. Then, upgrade the patient's activity level according to stability of vital signs, but do not permit exercise.
- As noted above, obtain the patient's weight in the morning (in a gown only), after voiding.
- Limit meals to 30 minutes, in the patient's room, with no visitors present.
- Restrict bathroom access for 1 hour after meals and instruct the patient not to flush the toilet after use, so the staff can evaluate the toilet for signs of purging.

If the patient is refusing to be fed orally, nasogastric (NG) tube placement is necessary, but avoid IV nutrition. If there is concern that the patient will dislodge the NG tube, secure it with a nasal bridle. Rarely, if the patient is not tolerating feedings, central line placement and total parenteral nutrition will be necessary. Address the patient's hydration status and monitor fluid intake. Unless medically necessary, limit rapid fluid infusions because they can cause cardiac compromise. Cardiac monitoring with telemetry is necessary for a patient with bradycardia or other dysrhythmias.

Refeeding syndrome most commonly manifests in the first week of nutritional rehabilitation and can last for up to 2 weeks. To prevent refeeding syndrome, administer a phosphorus supplement (250 mg phosphorus, 164 mg sodium phosphate, or 278 mg potassium phosphate) for the first 5 days, divided into 2 daily doses. Check the phosphorus, magnesium, and potassium levels daily; monitor strict fluid intake and output; assess the patient for edema; and order continuous cardiorespiratory monitoring.

Address other nutritional deficiencies, such as thiamine or phosphorus levels, with the appropriate supplementation. Do not routinely order pharmacotherapy, although it may be indicated for a patient with a comorbid psychiatric diagnosis. Oral contraceptives and bisphosphonates do not help to restore BMD.

Disposition

- **Intensive care unit monitoring:** Dysrhythmia, severe bradycardia, severe electrolyte abnormality, CHF.
- **Transfer to a tertiary care facility with an eating disorder service:** If the current facility does not have the staffing or expertise to care for the patient.
- **Discharge criteria:** Once the patient is medically stable, disposition is variable and depends on the appropriate resources available to the patient. Options include an intensive outpatient program, a partial hospitalization program (6 hours a day), and a residential program that provides intense therapy and nutritional counseling with an in-house physician.

Follow-up

- **Primary care:** Weekly for weight checks and monitoring for refeeding syndrome. Refer the patient to an adolescent medicine specialist if the primary care physician is not comfortable coordinating care.
- **Psychotherapy:** As recommended by the treating psychologist or psychiatrist.

Pearls and Pitfalls

- Fluid retention can occur after laxative cessation, with up to a 4.5-kg (10-lb) weight gain in 24 hours.
- Edema can last up to 3 weeks.
- Refeeding syndrome most commonly manifests in the first week of nutritional rehabilitation and can last for 2 weeks.
- Identify comorbid psychiatric illness (including suicidal ideation) or SUD.
- Heart failure and suicide are the most common causes of death.
- Avoid discharging the patient on a Friday or a weekend to ensure that adequate follow-up occurs.

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CHAPTER 3

Sexually Transmitted Infections

Introduction

Chlamydia and gonorrhea are the most common bacterial causes of sexually transmitted infections (STIs) in adolescents, with chlamydia being the leading cause. Other possible STIs include human papillomavirus, herpes simplex virus (HSV), trichomoniasis, syphilis, and HIV. Most cases of STI are managed on an outpatient basis, but these infections may coexist with, or be included in the differential diagnoses of, many conditions in hospitalized adolescents. In addition, pelvic inflammatory disease (PID) can have significant long-term consequences, including infertility, ectopic pregnancy, tubo-ovarian abscess, and chronic pelvic pain.

Clinical Presentation

History

Conversations regarding STIs and family planning are considered confidential. Without a parent or partner present, assure the patient of privacy and confidentiality and use a nonjudgmental approach to take a sexual history. Ask about sexual risk factors, including the number of sexual partners, the genders of their partners, nature of the sexual activity (eg, oral, anal, and/or vaginal), contraception use, partner history of STIs, and history of sexual assault or abuse. In a female patient, ask about vaginal discharge, lesions, odor, pruritus, irritation, dysuria, heavy bleeding, spotting, abdominal or back pain, nausea or vomiting, fever, and dyspareunia. In a male patient, ask about testicular pain, penile discharge, lesions, dysuria, and pruritus. For all patients, elicit any history of arthralgia, malaise, pharyngitis, conjunctivitis, hematochezia, and generalized or localized rashes. However, keep in mind that many STIs are asymptomatic. An asymptomatic patient requesting STI testing might be a warning sign for possible sexual abuse or trafficking.

Physical Examination

The priority is the genital examination. In the presence of a chaperone, note any external lesions or excoriations, as well as internal signs of trauma, such as bruising or lacerations in the vestibule, and observe the configuration of the hymen. In a postpubertal female, perform a bimanual examination for adnexal tenderness, cervical motion tenderness (CMT), or uterine/lower abdominal pain associated with PID. If a speculum examination is performed

(for excessive vaginal bleeding, possible retained foreign body, or need to visualize an intrauterine device [IUD]), examine the cervix for friability, as well as blood or mucopurulent material within the endocervical canal. Note the color, consistency, and malodor of any abnormal discharge. In a prepubertal or sexually naive female, anterior traction of the labia is well tolerated and will allow for good visualization of the hymenal rim and the intravaginal vault. If a speculum examination is needed due to concerns for bleeding of unknown origin or retained foreign body, an examination under anesthesia may be necessary. If sexual abuse is suspected or disclosed, involve a child protection or abuse/assault specialist.

Perform a careful external examination of the entire anogenital region for signs of trauma, such as abrasions, contusions, lacerations, ulcerations, verrucae, and vesicles. For a male, note any lesions, rashes, skin tags, urethral discharge, testicular pain, hydrocele, and swelling of the epididymis.

Examine the abdomen for pain, rebound tenderness, and right upper quadrant abdominal pain, which can occur with perihepatitis (Fitz-Hugh-Curtis syndrome). In addition, note any pustules, especially on the extensor surfaces of the extremities, or maculopapular exanthem, including the palms of the hands and soles of the feet. Look for conjunctivitis, oropharyngeal lesions, lymphadenopathy (generalized, inguinal), and osteoarticular involvement (gonococcal infection). The clinical findings of STIs are summarized in Table 3–1.

Laboratory Workup

Perform STI screening for all sexually active adolescents. Test for chlamydia and gonorrhea, order a rapid plasma reagin (RPR) or a Venereal Disease Research Laboratory (VDRL) test for syphilis, and test for HIV. The nucleic acid amplification test (NAAT) for urine (first catch) is highly sensitive and specific for chlamydia and gonorrhea and therefore obviates the need for cultures. If appropriate, perform a pregnancy test and, if positive and the patient has abdominal pain, obtain ultrasonography (US) to rule out an ectopic pregnancy.

If PID is suspected, send any abnormal vaginal discharge for NAAT, Gram stain, and microscopic analysis for white blood cells (WBCs), *Trichomonas* infection, candidiasis, and bacterial vaginosis.

For a male, send any urethral discharge for microscopic analysis, Gram stain, and NAAT. More than 5 WBCs per high-power field is consistent with urethritis.

Table 3–1. Clinical Presentation of Sexually Transmitted Infections

Sexually Transmitted Infection	Clinical Features
Condyloma acuminatum (human papillomavirus)	Flesh-colored, painless anogenital warts May be pruritic
Epididymitis	Unilateral testicular pain and swelling Dysuria, urgency
Gonorrhea (disseminated)	Petechial/pustular exanthema Asymmetrical arthralgia, tenosynovitis, septic arthritis
Herpes simplex virus	Painful/pruritic vesicles or shallow ulcerations Vaginal/penile discharge, dysuria Tender inguinal lymphadenopathy
PID	Dysmenorrhea, dyspareunia, spotting off-cycle or with intercourse Fever, nausea, vomiting Lower abdominal pain or chronic abdominal pain Excessive vaginal discharge/bleeding Cervical motion and/or adnexal tenderness
Reiter syndrome (chlamydia)	Conjunctivitis, urethritis, arthritis
Syphilis (primary)	Single painless ulcer (chancre) Nontender inguinal lymphadenopathy
Syphilis (secondary)	Fever, malaise, myalgia, pharyngitis Salmon-pink macules/copper-colored papules involving the palms of the hands and soles of the feet Condyloma lata (anogenital flesh-colored hypertrophic papules) Generalized painless adenopathy
Trichomonas	Often asymptomatic in males Malodorous, frothy, yellow-green discharge External irritation

Abbreviation: PID, pelvic inflammatory disease.

Obtain HSV polymerase chain reaction or culture the base of any unroofed vesicular lesions for HSV, but do not submit a Tzanck preparation, which lacks sufficient sensitivity and specificity. Confirm a positive RPR/VDRL result with treponemal tests (fluorescent treponemal antibody absorption, *T pallidum* particle agglutination, enzyme immunoassays).

Radiology Examinations

US is the preferred imaging study, due to better visualization of gynecologic structures and lack of radiation. Obtain a pelvic sonogram if there is abdominal tenderness or guarding. This will help rule out a tubo-ovarian abscess. An abdominal US scan may also be helpful for evaluating for gynecologic (ovarian) pathology, ectopic pregnancy, complications of PID, and suspected appendicitis.

Differential Diagnosis

The differential diagnosis can be challenging in an adolescent female with abdominal pain. See Table 3–2.

Treatment

Treatment of STIs based solely on the minor's consent is allowed, although some states set a minimum age for this. No state requires that physicians notify parents regarding STI evaluation or treatment, although 18 states allow physicians to do so if it is determined to be in the patient's best interest. The Centers for Disease Control and Prevention (CDC) provides information on

Table 3–2. Differential Diagnosis of Abdominal Pain in the Sexually Active Female

Diagnosis	Clinical Features
Appendicitis	Pain migrates from periumbilical area to right lower quadrant Vomiting follows onset of pain, anorexia Rebound, abdominal guarding, leukocytosis
Ectopic pregnancy	(+) Pregnancy test finding Missed or late menstruation Vaginal bleeding Abdominal or pelvic pain
Endometriosis	Chronic abdominopelvic or low back pain, may be associated with the menstrual cycle Dysmenorrhea, dyspareunia
Nephrolithiasis	Colicky pain (may occur in paroxysms), flank pain Nausea, vomiting, dysuria May have hematuria
Ovarian cyst	Pelvic pain Menstrual irregularities Acute pain with rupture
Ovarian torsion	Nausea, vomiting Fever uncommon, except with late presentation Severe, acute lower abdominal pain (with rebound or abdominal guarding)
PID/tubo-ovarian abscess	Nausea, vomiting, fever Cervical motion/adnexal tenderness Excessive vaginal discharge ↑ C-reactive protein level/erythrocyte sedimentation rate/WBC count
Pyelonephritis	Dysuria, urgency, frequency Costovertebral angle tenderness (+) Urinalysis and urine culture

Abbreviations: PID, pelvic inflammatory disease; WBC, white blood cell.
+ indicates a positive finding; ↑, increased.

the specific state laws that allow for a minor to provide informed consent (www.cdc.gov/hiv/policies/law/states/minors.html).

The treatment of the most common STIs encountered in the hospitalized patient is outlined in the following sections. Refer to the *Red Book: 2021 Report of the Committee on Infectious Diseases* (https://publications.aap.org/redbook) or the 2021 U.S. CDC Sexually Transmitted Diseases Treatment Guidelines for specific treatments of less prevalent infections or infections in special populations. Wait for a negative pregnancy test result before treating the patient with metronidazole or initiating HIV prophylaxis.

Pelvic Inflammatory Disease

Initiate treatment of PID as soon as a presumptive diagnosis is assigned to reduce the chances of long-term sequelae. Indications for inpatient treatment include

- Inability to exclude a surgical emergency as the cause of the symptoms
- Pregnancy
- Outpatient therapy failed or not tolerated
- Tubo-ovarian abscess
- Severe illness with high fever, nausea, and vomiting
- Lack of adequate social or financial support to begin or comply with consistent oral therapy

Treat with intravenous (IV) ceftriaxone (1 g administered every 24 hours) *plus* doxycycline (100 mg administered orally *or* IV every 12 hours) *plus* metronidazole (500 mg administered orally or IV every 12 hours). Oral doxycycline is preferred if tolerated, as IV doxycycline can be painful.

Alternative regimens are *either* IV cefotetan (2 g administered every 12 hours) *or* IV cefoxitin (2 g administered every 6 hours) *plus* doxycycline, as above. For all regimens, continue the IV therapy until the patient is improving for 24 to 48 hours, but complete a 14-day course of doxycycline and metronidazole (if being given). The results of cultures and NAAT do not affect empirical coverage, and the patient's response does not change the total of 14 days of treatment.

Typically, there is a prompt (24–72 hours) response to antibiotics (improvement in pain level, CMT, adnexal tenderness, fever). If the response is poor, consider pelvic US to look for a tubo-ovarian abscess or other causes of abdominal pain (appendicitis, ovarian torsion, cysts). Leave an IUD in place unless there are complications from the IUD placement.

Chlamydia/Gonorrhea (Uncomplicated)

Treat urethritis and cervicitis due to chlamydia with oral doxycycline (100 mg administered twice a day for 7 days). Azithromycin (1 g orally in a single dose)

is an alternative. The 2021 CDC guidelines confirm that doxycycline is effective for urogenital, rectal, and oral infections with chlamydia. Do not treat for both chlamydia and gonorrhea if there is no evidence of co-infection; however, do treat empirically for both if co-infection cannot be ruled out.

Treat urethritis and cervicitis due to gonorrhea with 1 dose of intramuscular (IM) ceftriaxone (45–150 kg, 500 mg as a single dose; > 150 kg, 1g as a single dose). Treat epididymitis with IM ceftriaxone (500 mg as a single dose) *plus* oral doxycycline (100 mg administered twice a day for 10 days). If there is a history of insertive anal sex, treat with 1 dose of IM ceftriaxone (500 mg as a single dose) *plus* oral levofloxacin (500 mg administered once a day for 10 days) to cover enteric organisms. Also provide bed rest, scrotal elevation, and analgesia with nonsteroidal anti-inflammatory medications.

Tests of cure are generally not necessary. Exceptions include chlamydia proctitis and when there is a concern of sexual abuse or assault.

Herpes Simplex Virus

Treat a first clinical episode of genital HSV orally with acyclovir (400 mg administered 3 times a day for 10 days) *or* valacyclovir (1 g administered 2 times a day for 7–10 days) *or* famciclovir (250 mg administered 3 times a day for 7–10 days). For severe infections (disseminated infection, pneumonitis, hepatitis), give IV acyclovir 5 to 10 mg/kg administered every 8 hours for 2 to 7 days or until there is clinical improvement. Continue with oral therapy (as above) to complete a minimum of 10 total days of treatment. Adjust the dose for renal impairment.

Syphilis (Primary or Secondary)

Order 1 dose of IM benzathine penicillin G (50,000 U/kg; maximum 2.4 million U).

Trichomoniasis

Give oral metronidazole 500 mg administered 2 times a day for 7 days *or* 1 dose of oral tinidazole 2 g. Advise the patient to avoid alcohol intake.

Postexposure Prophylaxis for HIV

Indications for initiation of postexposure prophylaxis (PEP) include

- Exposure where the risk of transmission is high (exposure to blood, genital secretions, or infected body fluids of a person known to be HIV positive).
- Medical care sought within 72 hours after exposure.
- Patient or parent is able to strictly adhere to a 28-day regimen.

PEP is not generally recommended without the presence of all 3 indications because the effectiveness of prophylaxis is unlikely to outweigh the risks and side effects of antiretroviral regimens. Consult a pediatric HIV specialist

or, if one is not locally available, the National Clinician Consultation Center (888/448–4011) for recommendations about PEP in specific situations. Most recent updates to the CDC PEP guidelines can be found on the CDC website (https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf). Additional information regarding pediatric and adolescent antiretroviral regimens can be found at the U.S. Department of Health and Human Services Website for HIV/AIDS (https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new-guidelines).

Indications for Consultation

- **Child abuse:** Suspicion of child abuse
- **Infectious diseases:** HIV-positive adolescents with a coexisting STI, new HIV diagnosis or suspected high-risk exposure, complicated disseminated gonococcal infection, complicated HSV
- **Obstetrics/gynecology:** Possible ectopic pregnancy, pregnant patient with PID, tubo-ovarian abscess, prolonged symptoms of PID
- **Urology:** Possible testicular torsion or abscess or epididymitis

Disposition

- **Intensive care unit transfer:** Complicated HSV infections (central nervous system or disseminated disease), syphilis with cardiac or neurologic involvement, sepsis
- **Discharge criteria:** Improved symptoms and tolerance of oral medications, social supports available, outpatient follow-up care arranged

Follow-up

Primary care: 48 hours, then 1 to 2 weeks and 3 to 6 months for repeat chlamydia and gonorrhea serology retesting

Pearls and Pitfalls

- Maintain high suspicion for PID in a sexually active female subject and treat accordingly, even if test results for chlamydia and gonorrhea are negative (to avoid possible long-term sequelae).
- Notify and treat the partner(s) of an adolescent infected with chlamydia, gonorrhea, or *Trichomonas.* More information regarding state-specific guidelines for expedited partner therapy may be found at www.cdc.gov/std/ept.
- Although all 50 states allow minors to consent to confidential STI screening and treatment, be aware of state-specific differences because reporting and insurance confidentiality measures vary.

- Review contraception options and condom use with the patient. Refer to the American Academy of Pediatrics policy statement on contraception for adolescents or the CDC (https://www.cdc.gov/reproductivehealth/contraception/usspr.htm).

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Allergy

CHAPTER 4

Anaphylaxis

Introduction

The term *anaphylaxis* applies to anaphylactic (immunoglobulin E [IgE]–mediated) and anaphylactoid (non–IgE-mediated) release of immune mediators from basophils and mast cells. It is a severe, potentially fatal, systemic allergic reaction. Therefore, it is imperative to recognize the signs and symptoms of anaphylaxis and treat it rapidly. The most common triggers are peanuts, tree nuts, and shellfish, although anaphylaxis in an inpatient may be triggered by exposure to latex, radiocontrast material, medications, or foods (Table 4–1).

As many as 15% to 20% of patients will have a biphasic response, with most episodes occurring within 6 to 12 hours after the initial reaction has abated. Risk factors for a biphasic reaction are age of 6 to 9 years, a delay of more than 90 minutes in the initial presentation of symptoms, unknown trigger, widened pulse pressure at presentation, and acute treatment that requires more than 1 dose of epinephrine. Protracted anaphylaxis (occurring for up to 72 hours) is rare and usually occurs when there is continued exposure to the trigger.

Clinical Presentation

History

The patient usually presents with some combination of flushing, pruritus, urticaria and/or angioedema, tightness of the throat, respiratory distress, vomiting and/or diarrhea, and a sense of impending doom (Table 4–2). However, severe anaphylaxis can present with involvement of just a single

Table 4–1. Agents That Can Trigger Anaphylaxis in the Inpatient Setting

Trigger	Examples
Medication	Antibiotics (β-lactam antibiotics, sulfonamides), neuromuscular blocking agents, nonsteroidal anti-inflammatory drugs, opioids
Food	Buckwheat, egg whites, fish and shellfish, milk, peanuts, sesame, soy, tree nuts (pecans, pistachios, walnuts), wheat
Hormone	Estrogen, progesterone
Infusion	Blood transfusion; dextran, monoclonal antibody, IV immunoglobulin, radiocontrast material
Latex	Balloons, gloves
Physiological factor	Cold, exercise, heat, pressure, sunlight

Abbreviation: IV, intravenous.

Table 4–2. Presentation of Anaphylaxis	
Organ System	**Presentation**
Cardiovascular	Hypotension, syncope, arrhythmias, chest pain
Central nervous	Confusion, dizziness, light-headedness, behavior changes, headache, seizures
GI	Nausea, abdominal pain, vomiting, diarrhea
Mucocutaneous	Urticaria, angioedema, flushing, pruritus without rash, diaphoresis
Respiratory	Cough, stridor, dyspnea, wheezing, rhinitis
Other	Sense of impending doom, rhinitis, metallic taste in the mouth

Abbreviation: GI, gastrointestinal.

organ system. Ask the patient about possible triggers, location and timing of events that led up to the anaphylaxis, and history of atopy or prior episodes of anaphylaxis. Also note what treatment was already administered (especially the use of an epinephrine autoinjector) and whether the patient is taking any chronic medications, particularly a β-blocker, which can worsen symptoms and decrease response to epinephrine.

Physical Examination

Perform a rapid examination to assess vital signs, airway patency, respiratory sufficiency, cardiac rhythm, and mental status. The most frequently involved organ system is the skin, followed by the respiratory system and the gastrointestinal (GI) tract (including the oral mucosa).

Differential Diagnosis

By definition, anaphylaxis is a serious systemic hypersensitivity reaction. The previous diagnostic requirement of involvement of at least 2 organ systems is no longer valid if the reaction is a severe, potentially life-threatening one of airway, breathing, and/or circulation (Table 4–3). The diagnosis is likely with onset of illness that involves urticaria and/or mucosal changes, along with any of the following conditions:

- Significant symptoms from at least one organ system
- Severe organ system involvement after a known allergen exposure
- Respiratory and/or cardiovascular compromise after an allergen exposure
- Hypotension that occurs minutes to hours after an allergen exposure

Primary Treatment

Anaphylaxis is a medical emergency and requires immediate care and attention. Initiate basic life support by addressing the circulation, airway, and breathing. Provide oxygen as needed, discontinue all ingoing intravenous

Table 4–3. Differential Diagnosis of Anaphylaxis

Diagnosis	Clinical Features
Angioedema	Swelling of the face, neck, and extremities without pruritus No acute respiratory or cardiovascular symptoms
Asthma	Patient may have had previous similar episodes No acute dermatologic, GI, or cardiovascular symptoms
Cardiac tamponade	Muffled heart sounds and presence of pericardial friction rub No acute dermatologic or GI symptoms
Cholinergic urticaria	Urticaria and wheezing occurring within 30 min of vigorous exercise
Croup	Barking cough, stridor, fever No acute dermatologic, GI, or cardiovascular symptoms
Food poisoning and scombroid poisoning	Vomiting, diarrhea, possible flushing No acute dermatologic, respiratory, or cardiovascular symptoms
Mastocytosis	Most often involves the skin Patient may have bone marrow and solid organ infiltration
Neuroendocrine tumor	Predominantly GI symptoms with intermittent flushing ↑ Catecholamine levels, vasoactive intestinal polypeptide levels, neurokinin levels
Panic attack	Feeling of impending doom No acute dermatologic symptoms
Vancomycin infusion reaction	Infusion with vancomycin may mimic anaphylaxis Slowing the rate of infusion decreases symptoms
Urticaria	No acute GI, respiratory, or cardiovascular symptoms

Abbreviation: GI, gastrointestinal.
↑ indicates increased.

(IV) antibiotics or contrast material infusions, avoid any latex products, remove any indwelling latex catheters, and begin continuous cardiorespiratory monitoring and pulse oximetry. If the patient has stridor at rest or respiratory compromise despite the administration of epinephrine (see the following section), prepare to intubate. Place a hypotensive patient in the supine position, with elevation of the lower extremities. Note that treatment may prove especially challenging if the patient is taking a β-blocker.

Epinephrine

Epinephrine is the first and most important treatment for anaphylaxis; there are no contraindications. It will reverse peripheral vasodilation and bronchoconstriction, decrease angioedema and urticaria, decrease upper airway edema, enhance myocardial contractility, and suppress further release of immune mediators from mast cells and basophils.

Normotensive patient: Administer 0.01 mL/kg of body weight (0.5 mL maximum) of *1:1,000* epinephrine *intramuscularly* into the lateral thigh. Repeat the dose every 5 to 15 minutes, as needed.

Hypotensive patient: Arrange for transfer to an intensive care unit (ICU) and administer 0.01 mg/kg (0.1 mL/kg, 10 mL maximum) of *1:10,000* epinephrine *intravenously*. Repeat every 3 to 5 minutes. In the absence of IV access, administer 0.01 mg/kg of *1:1,000* epinephrine *intramuscularly* (0.1 mL/kg, 3 mL maximum). IV administration must be in a monitored setting, under the guidance of personnel skilled with its administration, as it can cause fatal arrhythmias.

A patient who remains hypotensive is classified as being in anaphylactic shock. Initiate an IV drip of epinephrine, starting with 0.1 to 1 mcg/kg/min (5 mcg/min maximum). Start at the lowest dose and gradually titrate the infusion until the patient becomes normotensive. Continue to provide fluid and boluses as appropriate.

Vasopressor Infusion

If the patient remains hypotensive despite epinephrine administration and volume repletion, start a vasopressor infusion with dopamine drip (2–20 mcg/kg/min), norepinephrine (0.05–1 mcg/kg/min), or vasopressin (0.001–0.003 mcg/kg/min).

Secondary Treatment

Epinephrine is *always* the primary treatment, and administration should never be delayed. Secondary treatment modalities are not reliable interventions for prevention of biphasic reactions. In the hospitalized child, it is reasonable to monitor the patient with resolved symptoms without scheduled medications for 12 hours from epinephrine administration. A patient requires observation if they had a greater severity of presentation and required at least 2 doses of epinephrine. Secondary treatment may prove beneficial in the appropriate clinical context, as discussed in the following sections.

Antihistamines

Do not routinely give H_1- or H_2-antihistamines, which block the effect of circulating histamines but do not exert an immediate benefit or prevent a biphasic reaction. However, they may provide some symptomatic relief for a patient with severe cutaneous manifestations. For symptomatic relief of pruritus or urticaria, administer IV or oral diphenhydramine ([H_1-antihistamine] 1–2 mg/kg, every 6 hours; maximum, 100 mg per dose) *or* oral hydroxyzine ([H_1-antihistamine] 2 mg/kg/d, divided into doses administered every 6–8 hours, 100 mg/d maximum). Antihistamines may also be used to prevent anaphylaxis to certain chemotherapy or contrast for patients with prior contrast hypersensitivity reactions.

For a patient with GI symptoms, give IV or oral famotidine ([H_2-antihistamine] 0.5 mg/kg, 40 mg maximum).

Albuterol

If the patient continues to experience bronchospasm after epinephrine administration, treat with nebulized albuterol (0.15 mg/kg per dose, 2.5 mg minimum, 10 mg maximum), hourly or continuously.

Corticosteroids

The use of glucocorticoids for anaphylaxis is not beneficial in the acute setting, nor does it prevent a biphasic reaction. Glucocorticoid use may have some benefit in preventing anaphylaxis secondary to chemotherapy or radioactive contrast.

Glucagon

A patient taking β-blockers will have a limited response to epinephrine, which increases the risk for bronchospasm, hypotension, and paradoxical bradycardia. Administer an IV loading dose of 20 to 30 mcg/kg (1 mg maximum) over 5 minutes, followed by a continuous infusion of 5 to 15 mcg/min by titrating the dose to the ideal blood pressure. Glucagon may cause emesis, with subsequent risk of aspiration in a drowsy or obtunded patient, which necessitates airway protection.

Indications for Consultation

Allergist: First or severe episode of anaphylaxis, recurrent anaphylaxis, unknown anaphylaxis origin or allergen exposure, systemic reaction to hymenoptera venom

Disposition

- **ICU transfer:** Severe respiratory distress requiring intubation, continuous epinephrine drip needed, hypotension requiring epinephrine infusion, patient has taken a β-blocker.
- **Discharge criteria**
  - — The patient is normotensive, without respiratory distress or end-organ dysfunction, and is taking oral therapy after a 12-hour observation period.
  - — The patient and/or family has a prescription for an epinephrine auto-injector and is educated about its use (carry 2 injectors stored at room temperature, administer through the clothing at the anterolateral aspect of the thigh, and avoid holding the thumb over the tip of the applicator).

— The patient and/or family is aware of the importance of avoiding triggers, including cross-reacting substances.
— The patient and/or family has been instructed on how to order a MedicAlert bracelet (888/633–4298 or www.medicalert.org).

Discharge Management

- Provide a self-injectable epinephrine twin pack and a comprehensive, individualized anaphylaxis action plan.

Follow-up

- **Allergist:** 2 to 3 weeks
- **Primary care:** 2 to 3 days

Pearls and Pitfalls

- Resuscitation will be challenging if the patient is taking a β-blocker.
- Anaphylaxis can be triggered by exposure to foods or medications during an inpatient service.
- Response may be seen as late as 72 hours after allergen exposure.
- A biphasic response occurs most commonly within 12 hours after resolution of initial symptoms.

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Behavioral and Mental Health

CHAPTER 5

Acute Agitation

Introduction

Agitation is a state of behavioral dyscontrol that manifests as excessive motor and verbal activity. It is the final common pathway for a broad range of medical and psychiatric conditions. Early recognition and effective management of agitation can prevent escalation and potential harm to the patient, family members, and health care workers. The identification of the underlying etiology guides the choice of interventions that will diminish agitation and minimize restrictive treatment measures.

Clinical Presentation

History

The severity of agitation ranges from restlessness, irritability, crying, or confusion to loud speech, psychomotor agitation, and combative behavior. Ask how the patient's current state of behavioral control differs from baseline. Note the timing of the onset of agitation and any associated factors. Ask what happens before, during, and after the episodes to identify triggers or secondary gain.

Obtain a biopsychosocial history, including past treatments for medical, neurologic, psychiatric, and behavioral disorders. Explore the possibility of toxin exposure, ingestion, or overdose. For a patient with a developmental disorder, ask about sensory preferences, modes of communication, and what irritates and soothes them. Ask about sleep-wake cycles and identify potential iatrogenic disruptions of sleep. Before selecting a pharmacologic agent for treatment of agitation, inquire about past paradoxical reactions to benzodiazepines or antihistamines. Additionally, ask about relatives with sudden cardiac death or possible long QT syndrome (congenital hearing loss, seizures, syncope), which may affect the choice of antipsychotic medication. Identify the patient's allergies, prescribed and over-the-counter medications, and any other medications (prescription and nonprescription) in the household.

During the interview, use nonpharmacologic de-escalation strategies: introduce yourself clearly, speak in a soft tone, offer frequent reassurance, respect the patient's autonomy, honor reasonable requests, use nonthreatening body language, avoid prolonged eye contact, leave the examination door open, and conduct the interview while seated. If feasible, offer the patient any available comforts (eg, warm blankets, food, drink) and directly integrate trusted family, friends, and staff members into the discussion.

Physical Examination

Prior to conducting a physical examination, engage the patient in understanding the purpose and extent of the examination. Priorities include autonomic instability, fever, signs of inadequate perfusion consistent with shock or sepsis, and Cushing triad, suggestive of increased intracranial pressure. Perform a detailed neurologic examination and evaluate pupillary size and reflex, if possible, and note any focal neurologic deficits, muscle tone, reflexes, and abnormal movements. Screen for delirium by assessing the patient's orientation and attention, which can be assessed in a verbal adolescent by asking them to say the months of the year backward. Assess and reassess thought process and content for stigmata of mania and psychosis. A patient seeming to respond to stimuli that others do not perceive suggests visual or auditory hallucinations.

Laboratory Workup

If the patient is delirious and an underlying cause has not been determined, obtain a complete blood cell count, electrolyte and glucose levels, liver function test results, thyroid panel, ammonia level, folate level, vitamin B_{12} level, thiamine level, antinuclear antibody panel, and electroencephalogram, and perform a urinalysis. Obtain an urgent nonenhanced head computed tomography (CT) image if the patient has demonstrated recent head trauma, partial seizure, known intracranial lesion, immunosuppression, suspected subarachnoid hemorrhage, progressive headache, papilledema, visual field deficit, or other focal neurologic findings.

Perform a lumbar puncture (LP) with opening pressure, once CT is performed, if indicated (mental status changes accompanied by fever, headache, or focal neurologic deficit; physical examination signs of meningeal irritation; no reasonable alternative explanation for the agitation). Defer the LP if there are signs of increased intracranial pressure. Send the cerebrospinal fluid for cell count, glucose and protein level evaluation, Gram stain, and culture, and save an additional tube of fluid for possible serologic testing or polymerase chain reaction testing (herpes simplex virus, encephalitis panel, enterovirus).

Differential Diagnosis

In a hospitalized child, there are 6 etiologic categories for agitation: (1) toxic, (2) metabolic, (3) central nervous system (CNS) functional or traumatic/structural, (4) infectious, (5) psychiatric or developmental, and (6) behavioral (Table 5–1). Of note, the first 4 categories (toxic, metabolic, CNS, and infectious) may present as delirium. Deficits in orientation and a waxing and waning pattern differentiate delirium from primary psychiatric or behavioral

Table 5–1. Etiologies of Agitation in the Hospitalized Child

Examples	Common Causes
Toxic Etiologies	
Adverse medication effects Medication interaction Withdrawal	Anticholinergics Baclofen withdrawal Benzodiazepines Corticosteroids Intoxication with illicit drugs NMS Polypharmacy Serotonin syndrome Withdrawal from opiates or benzodiazepines
Metabolic Etiologies	
Electrolyte disturbance Endocrinopathy End-organ failure Hypoxia Inborn error of metabolism	Hepatic encephalopathy Hyper-, hypoglycemia Hyper-, hyponatremia Hypercarbia Hypertensive encephalopathy Renal failure Thyroid or parathyroid dysfunction Vitamin deficiencies (B_{12}, thiamine)
CNS Functional, Traumatic, Structural Etiologies	
CNS injury ↑ Intracranial pressure Primary neurologic disorder	Autoimmune encephalitis Confusional migraine Hematoma Hemorrhage Hydrocephalus Parenchymal injury Seizure/postictal state Stroke Tumor or space-occupying lesion
Infectious Etiologies	
CNS infection Systemic infection	Brain abscess Meningitis Sepsis Viral or bacterial encephalitis
Exacerbation of Primary Psychiatric or Developmental Disorders	
Frustration Inclination toward aggression Poor communication interfering with reporting of symptoms or needs Natural exacerbation in course of illness Noncompliance with treatment regimen	Anxiety disorder Attention-deficit/hyperactivity disorder Autism Bipolar disorder Communication disorder Intellectual disability Posttraumatic stress disorder Schizophrenia and other psychoses Untreated pain or unmet hunger in a patient with a developmental or communication disorder

Continued

Table 5–1. Etiologies of Agitation in the Hospitalized Child, continued	
Examples	**Common Causes**
Behavioral Etiologies	
Secondary gain Situational response	Avoidance (procedures, therapies) Conduct disorder Difficulty coping Disruptive behavior disorder Interpersonal or family conflict Maladaptive response to limit setting Oppositional defiant disorder Psychosocial stress

Abbreviations: CNS, central nervous system; NMS, neuroleptic malignant syndrome.
↑ indicates increased.

disturbances. The acute onset of hallucinations in a medically hospitalized patient with no past psychiatric history is delirium until proven otherwise.

Treatment

Maximize nonpharmacologic interventions for agitation before prescribing psychotropic medications. Yet, with severe agitation, physical and chemical restraints may be necessary to maintain safety.

If the patient is delirious, first aggressively pursue and treat the underlying medical condition, ensure appropriate cardiorespiratory monitoring and airway support, reduce stimulation, reorient the patient frequently, and mimic night-day light cycles. Arrange for staff members to work consistently with the patient so they can develop familiarity and rapport. Avoid anticholinergic medications and benzodiazepines in a delirious patient because they can worsen and prolong the patient's agitation. For moderate agitation in delirium, use low doses of an oral atypical antipsychotic medication (eg, risperidone, quetiapine, olanzapine) on an as-needed basis or scheduled in the evening to prevent sundowning.

If there has been an ingestion of a toxin or substance, the agitation will diminish with time in a controlled environment, but benzodiazepines are preferred as a first-line treatment, followed by antipsychotics. For a patient in withdrawal from opiates or benzodiazepines, carefully taper the medication while monitoring vital signs and symptoms of withdrawal. Treat opiate withdrawal symptomatically, with clonidine and/or opiate replacement (methadone, suboxone).

For any patient with agitation, arrange an adequate staff-to-patient ratio and remove all potentially harmful items from the room. Attempt to verbally de-escalate the episode, remove any agitating family members, decrease

stimulation, and provide distraction and comfort. Offer the patient an orally dispensed medication to help them calm. If these efforts fail and agitation has escalated to threats or overt violence, a physical or chemical restraint is indicated.

Medication

When the underlying cause of agitation is a known psychiatric disorder, whenever possible treat the patient with a medication that is indicated for that diagnosis. When the underlying cause of agitation is behavioral, consult a psychologist or social worker for further evaluation and to implement psychotherapeutic, social, and behavioral interventions.

If the patient will not accept oral medications and if intravenous (IV) access is not secured, some useful medications can be administered intramuscularly (Table 5–2). In such a case, prescribe monotherapy, followed by

Table 5–2. Medications for the Treatment of Acute Agitation

Medication	Routes	Initial Dose	Max Dose	Side Effects
α-Agonists				
Clonidine	PO	0.05–0.1 mg	0.2 mg	Hypotension Bradycardia
Antihistamines				
Diphenhydramine	PO IM IV	1.25 mg/kg	50 mg	Anticholinergic CNS and/or respiratory depression May worsen airway reactivity Worsens delirium Paradoxical disinhibition
Benzodiazepines				
Lorazepam	PO IV IM	0.02–0.10 mg/kg	2 mg	Habituation/tolerance Paradoxical disinhibition Respiratory depression Worsens delirium
	PR	0.5 mg/kg (using the IV formulation)	20 mg	
Atypical Antipsychotics (No Weight-Based Dosing)				
Risperidone	PO/ODT	0.125–0.25 mg	1 mg	Dystonic reactions[a] Least seizure threshold reduction among atypical antipsychotics Risk of NMS Sedation ↑ QTc interval

Continued

Table 5–2. Medications for the Treatment of Acute Agitation, continued

Medication	Routes	Initial Dose	Max Dose	Side Effects
Olanzapine	PO/ODT	2.5–5 mg	10 mg 30 mg/d	Hypotension (at high doses) ↑ QTc interval ↓ Risk of EPS and NMS Do not give IM within 1 hour of any benzodiazepine due to risk of respiratory depression
	IM	2.5–5 mg	10 mg 30 mg/d	

Abbreviations: CNS, central nervous system; EPS, extrapyramidal symptoms; IM, intramuscular; IV, intravenous; Max, maximum; NMS, neuroleptic malignant syndrome; ODT, orally dissolvable tablet; PO, per os (oral); PR, per rectum; QTc, corrected QT interval.
↑ indicates increased; ↓, decreased.
[a] Treat dystonia (oculogyric crisis, torticollis, opisthotonus) with IV, IM, or oral diphenhydramine (1.25 mg/kg) every 30 minutes or with IV, IM, or oral benztropine (0.02–0.05 mg/kg).

evaluation of the response, rather than administering multiple medications simultaneously.

Restraint

Restraints are interventions that restrict patient movement and are categorized into physical and chemical (or pharmacologic) methods. Consider restraints to be a last resort, and reserve them for a patient who is a clear danger to themselves or others. There is variation among the states in terms of allowed and preferred physical restraints. In addition, safety is dependent on appropriate staff training and adherence to an individual hospital's monitoring protocols.

A chemical restraint is any medication administered on an involuntary basis to sedate the patient and thus restrict movement. Do not use restraints as punishment, as a means of compensating for inadequate staff-to-patient ratio, or for convenience. The goals of restraint are to reduce further escalation, maintain safety, protect the patient and staff members from injury, and facilitate performing physical examinations, diagnostic tests, and essential medical interventions. Before initiating either method, carefully document all antecedent measures taken to calm the patient, as well as indications for escalating to restraint, and adhere to all of the institution's restraint policies and procedures.

If chemical restraint is used, start with the lowest dose necessary to calm the patient, and then titrate to the behavioral severity and urgency of the situation. Always offer the patient an oral sedative. This can give the patient a sense of control and maintains rapport, while having a lower risk of side effects than parenteral medications. Be aware of any potential drug interactions that can cause corrected QT interval prolongation or exacerbate respiratory or CNS depression. Provide continuous cardiorespiratory monitoring whenever indicated.

Therapeutic options for chemical restraint (Table 5–2) generally fall into 4 pharmacologic categories: α-agonists, antihistamines, benzodiazepines, and antipsychotics. Selection of the agent is determined by the underlying etiology (Table 5–3). For delirium, use an atypical (second-generation) antipsychotic, and avoid benzodiazepines and antihistamines. Benzodiazepines are best for a toxic or substance intoxication, or for instances in which the cause is unknown. For exacerbation of a mood, psychotic, or disruptive behavior disorder, or a developmental or autistic disorder, use an atypical antipsychotic. Treat an acute exacerbation of posttraumatic stress disorder, attention-deficit/hyperactivity disorder, or opiate withdrawal with clonidine.

Prevention

There are a number of basic measures that can lower the risk of agitation in an inpatient. Minimize the use and duration of indwelling catheters, implement venous thromboembolism prophylaxis in high-risk patients, reduce polypharmacy, and be vigilant for drug interactions. Training staff members in patient-centered preventive and de-escalation strategies effectively diminishes the need for restrictive interventions. Call for additional staff members at the earliest sign of agitation. In addition, the presence of security staff could allow the patient to take a walk or change their surrounding environment.

Indications for Consultation

- **Child life specialist:** Most cases of agitation (once stabilized)
- **Neurology:** Stroke, neuroleptic malignant syndrome (NMS), serotonin syndrome, pre- or postictal state, confusional migraine, encephalitis

Table 5–3. Selection of Chemical Restraint by the Underlying Etiology

Underlying Cause of Agitation	Recommendation
Anxiety	Antihistamine or benzodiazepine
Attention-deficit/hyperactivity disorder Autism Developmental delay Opiate withdrawal Posttraumatic stress disorder	Clonidine
Bipolar disorder Disruptive behavior Psychosis	Atypical antipsychotic
Delirium	Atypical antipsychotic
Substance intoxication Substance withdrawal	Benzodiazepine
Unknown	Benzodiazepine

- **Psychiatry:** Moderate or severe agitation, exacerbation of a primary psychiatric disorder, NMS, serotonin syndrome, psychotropic polypharmacy
- **Psychology or social work:** Interpersonal or family conflict, psychosocial stress, difficulty coping, maladaptive response to limit setting, and when agitation yields secondary gain or functions to avoid treatment engagement
- **Occupational therapy and speech therapy:** As needed, for a patient with developmental, intellectual, or communication disorders

Disposition

- **Intensive care unit transfer:** NMS, severe serotonin syndrome, moderate/severe traumatic brain injury
- **Discharge criteria:** Agitation resolved and behavior returned to baseline or the family feels competent to manage at home and there are no safety concerns

Follow-up

- **Primary care provider:** 1 week
- **Mental health professional:** If indicated by any underlying mental health diagnosis

Pearls and Pitfalls

- Identification of the underlying cause of agitation is the first step in successful management.
- Delirium is common in medically ill children and can be differentiated from a primary psychiatric disorder by evaluating orientation and attention, and whether there is a waxing/waning pattern of alertness.
- Document all de-escalation efforts, and use restraint only when these less intrusive means of intervention have failed.

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CHAPTER 6

Autism Spectrum Disorder

Introduction

A patient with autism spectrum disorder (ASD) has persistent deficits in social communication and interaction, along with restrictive, repetitive behaviors. Children with autism are more likely to be hospitalized, have longer lengths of stay, and have higher rates of medical and psychiatric comorbidities, which can complicate the hospitalization. Children with ASD may also be more likely to have aggressive behaviors when compared to their typically developing peers and children with other developmental disabilities.

The hospital environment can be challenging for a patient with ASD and their family. Issues include an unfamiliar setting, interactions with numerous new health care workers, and frequent, novel, and noxious sensory stimuli. Previous traumatic experiences within inpatient units or psychiatric hospitals can further exacerbate a patient's distress. Risk factors for agitation include a history of sensory sensitivities and a previous hospitalization with agitation.

Clinical Presentation

History

Patients with ASD can have varying levels of intellectual ability and deficits in social communications. Verbal and nonverbal communication difficulties can be highly variable and range from mutism to language delay or regression to deficits in understanding gestures or facial expressions. Restricted and repetitive behaviors can cause difficulty coping with change and switching between activities. The patient may have increased or decreased sensitivity to pain, temperature, and sounds.

Given the individuality of each patient's needs, it is important to ask the family the patient's developmental history, emotional disturbances, communication abilities, preferences, and triggers for anxiety and agitation, as well as home strategies to manage them. The family can identify changes in baseline behaviors, which can be manifestations of discomfort, and this may help to identify the cause of the current illness.

Learn the patient's unique needs regarding agitation, sensory preferences, expression of pain, baseline and abnormal activity levels, self-injurious behaviors, and barriers to communication and social interaction. The method

by which the patient demonstrates anxiety and agitation may vary, depending on their degree of communication ability. These behaviors include, but are not limited to, crying, vocalization, self-injury (head banging, biting, hitting self), hyperactivity, and aggression. Also ask about the common comorbid conditions (Table 6–1).

There are limited validated tools for rating anxiety and pain for a patient with abnormal receptive language ability. At the same time, exercise caution when using pain rating scales validated for neurotypical patients. A patient's preferred means for identifying and soothing anxiety and pain is best performed in partnership with a caretaker, as they may know best whether the child is in pain. In a verbal child, it can be helpful to assess anxiety with closed-ended questions or with the use of visual-analog scales.

Be sure to use the patient's communication assist devices or comfort items.

Physical Examination

Although a complete physical examination is indicated, because a patient with ASD is still at risk for the full range of pathology, it may be necessary to tailor the examination to the history that was obtained and the patient's current status. If the presenting complaint is related to pain or agitation, pay specific attention to the organ systems that may be involved.

Table 6–1. Common Comorbidities Requiring Hospitalization in Patients With Autism

Comorbidity	Findings
Dental issues	Poor dentition including caries and dental abscesses
Epilepsy	Altered mental state, abnormal movements, staring episodes
Feeding dysfunction	Weight loss, rumination, vitamin/mineral deficiencies Risk for refeeding syndrome
Gastrointestinal issues	Withholding behaviors, constipation, encopresis, GERD, behavioral vomiting
Hydrocephalus	Headaches, agitation, altered mental status, vomiting
Motor disorders	Tics, catatonia, loss of motor skills
Pica	Toxic ingestions, lead intoxication
Psychiatric and behavioral conditions	Anxiety Attention-deficit/hyperactivity disorder Bipolar disorder Depression Irritability and aggression Obsessive-compulsive disorder Sleep disturbance

Abbreviation: GERD, gastroesophageal reflux

Difficulties with social communication, sensory sensitivity, and adherence to routines can make the physical examination stressful to the patient. Among potential strategies to minimize anxiety and agitation are to

- Encourage parental participation and presence at the bedside
- Assess the patient's needs, as described above, prior to beginning the examination
- Limit the number of people in the room, especially during the invasive portions of the examination
- Explain and demonstrate portions of the examination in a stepwise manner prior to physical contact with a patient
- Use patient-preferred communication, including picture tools, assisted communication devices, sign language, or verbal communication
- Use concrete and easy-to-understand language and avoid figurative language when describing the examination
- Allow the patient choice in determining the order of examination components, when possible, to promote a routine
- Allow the patient to engage in self-soothing behaviors without interruption
- Discontinue the examination if the patient becomes distressed

Laboratory Workup and Radiology Examinations

Tailor the laboratory evaluation to the clinical presentation, particularly if the patient is nonverbal and presents for evaluation of agitation or pain. Try to batch blood draws, with minimum frequency, to minimize distress.

If the patient presents for agitation or altered mental status, obtain levels of chronic antiepileptic drugs to determine if sub- or supratherapeutic levels may be impacting the behavior.

ASD is associated with higher risk of congenital hydrocephalus and epilepsy. It may be difficult to interpret whether agitation, aggression, altered mental state, and stereotyped behaviors are related to a patient's baseline or concerning signs for seizure or increased intracranial pressure. If there is reasonable suspicion, obtain an electroencephalogram, neuroimaging (magnetic resonance imaging or computed tomography), and shunt series (if applicable).

Treatment

Effective treatment requires consideration of social and communication deficits, sensory needs, and restrictive/repetitive behaviors. This is best accomplished with a combination of lifestyle interventions and pharmacologic management. It is most successful when applied with the assistance of consultants, including child life specialists, art and music therapists, occupational and physical therapists, and speech and language pathology specialists. These

consultants can help identify preferred communication style and tools, as well as sensory triggers and modifications to reduce sensory stimuli. They also can provide soothing devices (eg, weighted blankets) and assist with organizing daily routines. An informed approach to these patients by the whole staff, including nursing, aides, and other floor staff, can likewise benefit in the care of other patients with behavioral challenges.

For acute anxiety and agitation, implement environmental and behavior interventions before pharmacologic management. Treat underlying causes of anxiety such as gastrointestinal disorders, sleep disturbances, or localized pain before using pharmacologic interventions. Involve the patient's primary physician or psychiatrist to address chronic anxiety.

Sleep disturbance may be ameliorated by giving melatonin 30 minutes before bedtime (infant, 1 mg; older child, 2.5–3 mg; adolescent, 5 mg). Treat aggression and behavioral disturbances that are unresponsive to behavioral and environmental interventions with an α-2 agonist such as clonidine (> 5 years old and < 45 kg, 0.05 mg/d; over 45 kg, 0.1 mg/d; with slow titrated increases every 4 days) or guanfacine (> 5 years old and < 25 kg, 0.25 mg/d; > 25 kg, 0.5 mg/d; with slow titrated increases every 4 days). For more severe behaviors, contact a behavioral health specialist, who may recommend a second-generation antipsychotic. Whenever possible, also consult with the patient's primary psychiatrist if alterations are being made in the home psychotropic medications.

Invasive procedures, prolonged imaging, and surgery can be highly stressful. Provide expectations to the patient and family in advance of procedures, minimize the duration of preprocedural fasting state, encourage caregivers to remain with the patient until the procedure start time, and maintain the usual routines leading to the procedure. Postprocedure, pay close attention to analgesia needs.

Disposition

- Discharge criteria are dependent on the primary diagnosis and not specific to the underlying diagnosis of ASD. Try to identify a safe disposition destination early in the hospitalization.
- The combination of the primary inpatient diagnosis and ASD may lead to the need for outpatient services not otherwise required by the primary diagnosis, such as continuation of IV antibiotics via a peripherally inserted central catheter for a child who cannot take oral antibiotics.

Follow-up

- **Primary care:** Depending on specific deficits and comorbid conditions addressed during the hospitalization

- **Therapists (early intervention, physical therapy, occupational therapy, speech language pathology):** Depending on the specific treatment plan
- **Psychiatrist:** 1 to 2 weeks, if the patient was admitted for a behavioral disturbance, especially if new psychotropic medications were initiated

Pearls and Pitfalls

- Understanding baseline behaviors, communication, and routines can provide insight into the underlying diagnosis.
- Partner with the parents to optimize compassionate care and avoid generalizing when considering sensory and communication needs.
- Consult other services such as child life, art and music therapy, physical and occupational therapy, and speech and language pathology to help with communication and environment and to provide coping mechanisms for the patient.
- Avoid physical restraints during times of agitation and anxiety, as this can be a traumatic sensory experience.

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CHAPTER 7

Depression

Introduction

Depression is a psychiatric disorder with a wide spectrum of severity that affects up to 2% of children and about 10% of adolescents. A severe sequela of depression is suicide (see Chapter 8, Suicide and Self-Harm), which is the third-leading cause of death among adolescents in the United States. Risk factors for depression are both genetic and environmental and include a family history of depression and/or anxiety in a first-degree relative, personal history of anxiety disorders or attention-deficit/hyperactivity disorder, adverse childhood events (eg, a history of physical and/or sexual abuse, substance use), family dysfunction, and chronic illness. Others who may be at risk include patients facing racial, gender-based, or orientation-based discrimination, as well as high-achieving children with overinvolved parents. In addition, a hospital stay itself can promote depressive symptoms, and some medications are also risk factors (eg, steroids).

Clinical Presentation

History

A patient with depression may present with recurrent somatic complaints (abdominal pain, headaches, myalgia) for which no organic cause can be found. Conversely, chronic medical conditions and/or pain may be reported. The patient may have recently developed a loss of interest in friends or activities once found to be enjoyable. There may be a history of irritability, oppositional behavior, aggression, running away, stealing, fire setting, being accident-prone, substance use, and gender identity or sexual orientation issues. Ask about suicidal ideation and whether the patient has formulated a plan. The parents or caregivers may be concerned about a loss of appetite, poor school performance, increased isolation, or change in sleep pattern. Inquire about a family history of mood disorder or suicide. A useful mnemonic for the signs of depression is SIGE-CAPS: changes in **S**leep, loss of **I**nterest in activities, **G**uilt, decreased **E**nergy, reduced **C**oncentration, loss of **A**ppetite, **P**sychomotor (agitation or lethargy), and **S**uicidal ideation.

As a part of the review of systems, perform a mental health screening for any adolescent admitted to the hospital, regardless of the admitting diagnosis. In addition, a chronically ill patient will often have a psychological overlay to their illness, even if it does not meet the *DSM-5* threshold for inpatient hospitalization or medical therapy.

Physical Examination

Use the physical examination to screen for abnormalities associated with organic causes of depression. In a patient with depressive symptoms, poor hygiene and eye contact, flattened affect, and psychomotor depression or agitation may be present. Often, there are significant abnormalities in mood, thought content, and quality of speech. In addition, look for any signs of self-harm (eg, old or current scarring or burns) and atypical bruising, which suggest abuse or intimate partner violence.

Laboratory Workup

The goal of laboratory testing is to attempt to rule out organic causes of depression in a patient who is presenting with the disorder for the first time. Obtain blood for a complete blood cell count, comprehensive metabolic panel, thyroid function tests, and syphilis serology, as well as urine for a pregnancy test (if appropriate) and toxicologic evaluation.

Differential Diagnosis

Except for an acutely suicidal patient, the priority is to exclude medical conditions that can mimic the clinical presentation of depression (Table 7–1). In addition, consider recent stressors (procedures, prolonged clinical course, "bad news") that may be contributing to the patient's depressive symptoms.

The definitive diagnosis of depression requires the input of a psychologist or psychiatrist, on the basis of a carefully assembled clinical history and mental status examination finding. Screening tools, such as the PHQ-9: Modified for Teens, the Beck Depression Inventory, and the Children's Depression Inventory are helpful adjuncts for the evaluation of depressive symptoms.

Table 7–1. Psychiatric Conditions That Can Be Confused With Depression

Diagnosis	Clinical Features
Adjustment disorder with depressed mood	Depressive symptoms start within 3 mo of significant stressor(s) and resolve within 6 mo Stressor can be chronic (ongoing abuse), leading to symptoms lasting > 6 mo
Bipolar disorder	Episodes of mania/hypomania alternating with depression At presentation, manic episodes may appear with decreased need for sleep, flight of ideas/distractibility, increased interest in pleasurable activities, or pressured speech
Medication- or substance-related mood disorder	Clinical findings of a preexisting medical condition May not fulfill all *DSM-5* depressive disorder criteria Higher risk of suicide with chronic or terminal illness
Posttraumatic stress disorder	Depressive symptoms follow a traumatic event Flashbacks, recurrent dreams, reliving the event

Treatment

Consult a child psychiatrist to develop a comprehensive treatment plan in collaboration with the patient and family. After assessing the degree of depression and underlying medical conditions, the psychiatrist may recommend a regimen of pharmacologic intervention, psychotherapy, or a combination of both. Selective serotonin reuptake inhibitors are first-line pharmacologic treatments, but the only antidepressants approved by the U.S. Food and Drug Administration for use in children are fluoxetine (patients > 8 years of age) and escitalopram (patients > 12 years of age). Defer initiating pharmacologic treatment, including "off-label" uses of other common antidepressants (citalopram, sertraline, venlafaxine, bupropion), to the psychiatrist.

Because inpatient mental health resources for pediatric patients are limited, a patient who requires inpatient psychiatric care may be admitted to a general pediatric ward until an appropriate inpatient psychiatric bed becomes available. The most frequent such indication is a suicide attempt, in which case the patient must be placed under continuous (one-on-one) observation by a sitter. Remove any safety hazards that are commonly found in a hospital room (eg, sharp objects, unnecessary cords/cables) or belong to the patient (eg, belts, razors, cell phone charging cords, shoelaces). Take the patient's clothing and have them wear a hospital gown/pants. Ensure that all members of the care team are trained in the identification of agitation and de-escalation techniques. Involve the child life and/or behavioral health teams to engage the patient while they are restricted to the room.

Indications for Consultation

- **Psychiatrist, clinical psychologist, or therapeutic social worker:** All patients

Disposition

- **Inpatient psychiatric service transfer:** Active suicidal ideation, suicide attempt, or the patient's symptoms are having a severe effect on daily life
- **Discharge criteria:** A care plan is in place, with medication being tolerated, outpatient management arranged, and no active suicidal or homicidal ideation; potentially lethal items (firearms, medications) have been removed from the home

Follow-up

- **Mental health professional:** 1 week
- **Primary care provider:** 1 week

Pearls and Pitfalls

- Depression may appear with psychotic features at presentation (eg, auditory and/or visual hallucinations and delusions).
- Little evidence exists that "contracting for safety" reduces suicide.
- In most states, adolescents who are actively suicidal can receive treatment without parental or guardian consent, and the resulting treatment plan can remain confidential (see Chapter 8, Suicide and Self-Harm).
- Discharge planning can be challenging in view of the relative paucity of inpatient and outpatient pediatric psychiatry services.

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CHAPTER 8

Suicide and Self-Harm

Introduction

Suicide is the second leading cause of death among 10- to 24-year-olds. Adolescents who experience suicidal ideation (SI), compared to those without SI, are 12 times more likely to attempt suicide by young adulthood. It is estimated that there are 50 suicide attempts for every 1 that is completed. Females are twice as likely to attempt suicide as males, but males are 3 times more likely to succeed because they often choose more violent means of death (eg, guns, suffocation, hanging). There is room for ongoing understanding and prevention given that about 40% of adolescents who die by suicide were previously treated for a mental health concern.

Self-harm or self-injurious behavior is the intentional destruction of one's body tissue (eg, scratching, pinching, hitting, biting, carving, burning). It is also referred to as nonsuicidal self-injury, as it may not accompany SI. However, evidence suggests that nonsuicidal self-injury is a predictor of future suicide attempts.

Clinical Presentation

There is no one-size-fits-all presentation for youth at risk for suicide and self-harm, as it affects young people from all races and socioeconomic groups. However, clinicians must appreciate patients' risk factors in order to be vigilant and astute in caring for adolescents. Risk factors include a wide range of issues: history of psychological or mental health disorder (particularly depression, eating disorders, schizophrenia, or anxiety); American Indian/Alaska Native ethnicity; bias, discrimination, or violence experienced by lesbian, gay, bisexual, or transgender identity; history of trauma or abuse; history of substance use (including alcohol and marijuana); impulsive or aggressive tendencies; access to firearms; family history of suicide; exposure to suicidal behavior of peers or in the media; bullying; and previous suicide attempts. Environmental stressors, such as the COVID-19 pandemic, may also worsen the risk of suicide attempts due to decreased social connectedness, limited access to mental health treatment, increased substance use, and anxiety about family health and/or financial hardship. Patients with SI often have feelings of hopelessness and are more likely to have a comorbid psychiatric condition and/or a chronic medical condition.

As a part of the review of systems, perform a depression screening for any child or adolescent admitted to the hospital, regardless of the admitting

diagnosis. Screen for personal or family history of suicide and access to firearms, medications, and drugs or alcohol.

Expressions of SI or suicidal threats must be taken seriously. "Red flags" or warning signs include:

- Expressing SI
  - — Talking about suicide
  - — Making statements such as "I'm going to kill myself," "I wish I were dead," "I wish I hadn't been born," or "it would be easier if I didn't wake up"
  - — Mood changes (eg, dysphoria, irritability, self-reports of feeling "numb"), although some patients, particularly younger children, may present as irritable or cranky, rather than sad or dejected
  - — Preoccupation with death, dying, or violence
  - — Feeling trapped or expressing hopelessness, helplessness, or worthlessness
  - — Searching the internet or social media about suicide
- Demonstrating at-risk behaviors
  - — Social withdrawal
  - — Change in normal routine, including self-care and eating or sleeping habits
  - — Risky or self-destructive behaviors, such as substance use or reckless driving
  - — Giving away belongings, cleaning up a messy room, or discarding cherished items when there is no other logical explanation for doing this
  - — Change in school performance, refusal to go to school, or refusal to participate in previously enjoyed extracurricular activities
  - — Excessive crying spells, somatic complaints, decreased energy, or extreme sensitivity within the peer group, family, and/or academic setting
  - — Escalating self-harm frequency or intensity

Mental Status Assessment

The following screening tools and questions can be used (by the hospitalist team or the psychiatry/psychology/social work team) when assessing the patient:

- Clinical interview
- Patient Health Questionnaire 9 (PHQ-9, ages 11–17)
- ASQ Suicide Risk Screening Toolkit (ages 8+)
- Children's Depression Inventory II (ages 7–17)
- Columbia Suicide Severity Rating Scale

Assessing the Patient for Self-Harm and Suicidal Ideation

- "Do you have any thoughts of hurting yourself? Have you had a plan of what you would do to hurt yourself?"
- "Do you self-harm? If so, where on your body?"
- "What do you use to self-harm? How frequently does it happen?"
- "What is your intent when you self-harm?"
- "Do you have thoughts of wanting to die when you self-harm?"
- "Do you sometimes wish you could cut more deeply and end your life?"
- "Have you considered ending your life?"
- "Do you want to die?"

Assessing Risk Factors

- "Have you ever attempted suicide or self-harm?"
- "Do you have a family history of mental illness?"
- "Do you have a family history of suicide attempts?"
- "Have you ever received a diagnosis of mental illness?"
- "Do you use alcohol or other substances?"
- "Have you recently started a new medication?" (eg, antidepressants may increase the patient's risk of SI)
- "Do you have any other stressors in your life?" (eg, bullying, changes in the home environment, peer pressure, medical conditions, recent loss, trauma)
- "Have you had any friends or acquaintances with recent attempts or completions?"
- Assess for substance abuse with a screening tool, such as the Brief Screener for Alcohol, Tobacco, and other Drugs (BSTAD) or the Screening to Brief Intervention (S2BI).

Assessing the Patient for a Suicide Plan

- "Do you have a plan, or have you considered how you would hurt/harm/kill yourself?"
- If yes, assess lethality:
  - "How, when, and where would you carry out this plan? What did you think would happen to you? Would there be anybody else physically with you when you started this plan?"
  - "Do you have the means to take your own life?" (eg, hoarding of medications or gaining access to firearms or other lethal means, such as cleaning products)

Assessing Protective Factors

- Individual strengths, such as coping skills
- Psychosocial situation for support (eg, friends, family, religion)

- Reasons for living
- Motivation and hopefulness
- Future-oriented thinking and planning

Physical Examination

There may not be any physical signs of SI. In a patient with depression or other mood disorder, there may be signs of poor hygiene, poor eye contact, flattened affect, weight change, lack of energy, or disturbances in mood, thought, or speech. Use the physical examination to screen the patient for abnormalities associated with organic causes of depression, such as hypothyroidism, diabetes, active substance use, neurologic disorders, and infections. During the physical examination, there may be signs of self-injury or cutting behavior. These may be hidden under clothes in the groin, upper thigh, abdomen, and forearm areas. Be aware of escalating behaviors in self-injury (eg, if cutting frequency, depth, or amount is increasing), as this may correlate with a higher risk for future attempts of self-harm or accidental suicide.

Laboratory Workup

The goal of laboratory testing is to determine if there were any toxic ingestions (see Chapter 68, Toxic Exposures), organic causes of depression (see Chapter 7, Depression), or altered mental status (see Chapter 78, Altered Mental Status). Otherwise, routine tests are not indicated, with the exception of a pregnancy test in a postpubertal female patient.

Treatment

The safety of the patient is the priority, and the level of SI, suicidal intent, or self-injurious behavior determines the best course of action. Every situation and every patient presents unique factors that must be taken into consideration, including the patient's potential discharge environment and social determinants that would impede a plan of care.

If the patient is suicidal with a detailed plan and intent to kill themself, urgently consult a mental health professional for further evaluation and to develop a course of treatment. Arrange for one-on-one supervision and monitoring. If the patient remains suicidal but is medically stable for discharge, the psychiatrist must conduct a thorough suicide/risk assessment to determine if admission (involuntarily or voluntarily) to an inpatient psychiatric unit/hospital is warranted.

If the patient is expressing SI but does not have a clear plan or intent, consider developing a safety plan, ideally with the psychiatrist or psychologist. Although this is not a safety contract or legal document, it can help

patients and parents develop a clear plan of action for hospital discharge. This safety plan often includes a list of coping strategies, reasons to live, and people or resources the patient would contact during times of crisis or if feeling suicidal. The plan is often a structured document written in outline form in the patient's own words (but with family input). Coping skills can include activities the patient can do alone or with others, such as going for a walk, listening to music, journaling, or engaging in relaxation exercises (eg, diaphragmatic breathing). Additional coping skills may include the support of friends or family, such as calling a friend, watching a movie, or going out for a snack with others. A safety plan also includes precautions that the caregiver will take at home, such as locking up medications and sharp objects, and increasing supervision. A safety plan does not replace treatment or continued assessment, which is a necessity if the patient is expressing any plans or intent to self-harm.

A patient engaging in nonsuicidal self-injury may be trying to achieve emotional relief via physical pain. It is therefore important to arrange an evaluation for depression or other psychiatric illness, as it could possibly lead to future suicide attempts. Conduct this assessment during hospitalization to help determine disposition and the appropriate outpatient plan. Bring harmful behavior (eg, cutting) to the parents' attention, as it indicates a high degree of emotional distress and could accidentally result in death. Remove any items in the patient's room that could be used for self-injury (eg, needles, hard eating utensils, ropes/belts/shoestrings), as well as cell phones and other connections to the internet, and limit visitation. In the hospital, this may require a daily room search of the patient's belongings.

Indications for Consultation

Arrange a consultation with a psychiatrist, psychologist, or clinical social worker. It is important to communicate with the family any level of risk of harm. Discuss these concerns and obtain collateral information that can be used to develop a safe and appropriate discharge plan. Before discharge, review the safety plan with the parents so they understand what coping skills the patient may find useful, individuals the patient feels comfortable talking to in times of crisis, and how to access additional resources. This will also help the family understand the severity of the symptoms, identify warning signs indicating that the patient is in distress, ensure outpatient follow-up, and understand how and when to escalate care, if the need arises. Breaching confidentiality is permitted if the patient is suicidal, although expressing SI is not necessarily sufficient to warrant a breach. Use the consultative service to help make this determination.

Disposition

- **Transfer to an inpatient psychiatric facility:** The patient has active SI with a feasible plan or is experiencing severe symptoms that are affecting daily life.
- **Discharge criteria:** The patient is deemed safe (no active suicidal or homicidal ideation, no active plans for suicide) by the psychiatry or psychology team, with appropriate outpatient psychiatry/psychology follow-up arranged; safety planning has been conducted with the psychiatry/psychology team, and the parents/caregivers are aware of this plan.

Follow-up

- **Mental health professional:** As soon as possible, ideally within 1 to 3 days (up to 1 week maximum)
- **Provide additional referrals for the patient/family to use if needed:**
  — 911 or a local emergency service that can be called in an emergency
  — The U.S. Suicide and Crisis Lifeline number: 988
  — Text the Crisis Text Line: Text "HOME" to 741741
  — A specific crisis line for the local county
- **Primary care provider:** 1 week

Pearls and Pitfalls

- Establish rapport by starting the conversation with the patient in a manner that encourages their participation and provides a confidentiality statement to demonstrate that you care about their safety.
- Developing a safety plan does not guarantee that the patient will not initiate another suicide attempt in the future.
- Assessing for a suicidal plan or ideation will not cause a patient to want to commit suicide. These questions are key to determining the seriousness of the situation.
- Discharge planning can be challenging because of the lack of pediatric psychiatric and psychological resources in the community. Start this process at admission with the help of the psychiatry/psychology/social work team.
- Appropriate family involvement, patient protective factors, and good communication between the treatment team and family/patient are keys for safe discharge planning and transition to an outpatient team of providers.

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Cardiology

CHAPTER 9

Arrhythmias and Electrocardiogram Interpretation

Introduction

An electrocardiogram (ECG) is a graphic representation of the progression of electric activity through the heart. It is often used as a screening test in situations such as suspected congenital heart disease, arrhythmias, chest pain, syncope, acquired heart disease, hypertension, and medication monitoring. See Table 9–1 for ECG reference values.

Common ECG Patterns in Clinical Diseases

Innocent Murmurs

No abnormal ECG changes.

Structural Heart Disease

See Table 9–2.

Chest Pain/Ischemia

The etiology of the vast majority of pediatric chest pain is noncardiac, so most ECG findings will be normal. Clinical manifestations that are concerning for underlying cardiac chest pain include chest pain with exertion; diaphoresis; pallor; anxiety; shortness of breath; nausea and/or vomiting; radiation of pain to the arm, jaw, neck, or back; and syncope.

The adult pattern of ECG changes of ST segment elevation with deep, wide Q waves evolving to wide Q waves with T wave inversion is not always seen. Frequent findings in pediatric ischemia include wide Q waves ($>$ 0.035 seconds), ST segment elevation greater than 2 mm, and a prolonged corrected QT (QTc) interval with pathologic Q waves.

Serial ECGs are important when ischemia is suspected, as about half of initial ECGs in the setting of myocardial infarction are normal.

Myocarditis

ECG findings are variable in myocarditis. Any of the following may be seen: low-voltage QRS; nonspecific ST segment changes, T wave inversion possible; long QT interval; and arrhythmias, especially premature atrial or ventricular contractions.

Table 9–1. Age-Related Normal ECG Parameters in Children

Age	Heart Rate (bpm)	QRS Axis (degrees)	PR Interval (ms)	QRS duration (ms)	R Wave (mm)	S Wave (mm)	R/S Ratio	R Wave (mm)	S Wave (mm)	R/S Ratio
					Lead V1			Lead V6		
< 1 d	94–155 (122)	58–168 (+135)	79–160 (107)	5 (0.7)	5–27 (14)	0.5–23 (9)	0.2–9.8 (2.3)	0–12 (5)	0.2–10 (4)	0.5–9 (2.5)
2–3 d	91–158 (124)	65–171 (+134)	81–139 (108)	5 (0.7)	5–27 (15)	0.5–21 (10)	0.2–6.0 (2.0)	0.1–12 (5)	0.2–10 (3)	0.5–11 (3)
4–7 d	90–166 (128)	76–168 (+133)	75–137 (104)	5 (0.7)	3–25 (13)	0.5–17 (7)	0.2–9.8 (2.8)	0.5–12 (5)	0.4–10 (4)	0.5–10 (2.5)
8–30 d	106–182 (148)	65–159 (110)	73–138 (101)	5 (0.7)	3–22 (11)	0.5–12 (4)	1.0–7.0 (2.9)	3–17 (8)	0.2–10 (3)	0.5–12 (4)
1–3 mo	120–179 (149)	31–115 (75)	73–130 (98)	5 (0.7)	3–19 (10)	0.5–13 (5)	0.3–7.5 (2.3)	5–22 (12)	0.3–7 (3)	0.5–12 (4.5)
4–6 mo	105–185 (142)	7–105 (60)	74–145 (106)	5 (0.7)	3–20 (10)	0.5–17 (6)	0.2–6.0 (2.4)	6–23 (14)	0.2–10 (3)	0.5–18 (6.5)
7–12 mo	107–168 (132)	7–98 (54)	73–156 (156)	5 (0.7)	2–20 (9)	0.5–18 (7)	0.1–3.9 (1.8)	6–23 (13)	0.2–8 (2)	0.5–22 (8)
1–3 y	90–151 (119)	8–100 (55)	82–148 (114)	6 (0.7)	3–18 (9)	1–21 (9)	0.1–4.2 (1.4)	6–23 (14)	0.1–7 (2)	0.5–28 (9.5)
4–5 y	73–137 (108)	7–104 (55)	85–161 (118)	7 (0.8)	2–18 (8)	2–22 (10)	0–2.8 (0.9)	9–25 (15)	0.1–6 (2)	0.8–30 (11)
6–8 y	65–133 (100)	10–140 (66)	90–164 (124)	7 (0.8)	1–13 (7)	3–24 (12)	0–2.0 (0.8)	9–27 (17)	0.1–4 (1)	1–30 (12)
9–12 y	63–129 (92)	9–115 (61)	87–171 (128)	7 (0.9)	0.5–10 (6)	3–26 (12)	0–1.9 (0.6)	10–26 (17)	0.0–4 (1)	2–33 (14)
13–16 y	66–120 (86)	11–133 (58)	92–175 (135)	7 (1.0)	0.5–10 (5)	3–22 (11)	0–1.8 (0.5)	7–23 (15)	0–4 (1)	2–39 (15)

+ indicates positive.

Data are electrocardiographic normal ranges (2%–98%), with mean values given in parentheses.

Data are from Davignon A, Rautaharju P, Boisselle E, Soumis F, Mégélas M, Choquette A. Normal ECG standards for infants and children. *Pediatr Cardiol.* 1980;1(2):123–131; and Deal B, Johnsrude C, Buck S. *Pediatric ECG Interpretation: An Illustrative Guide.* Blackwell; 2004.

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Table 9–2. ECG Findings in Structural Heart Disease	
Heart Condition	**ECG Findings**
Aortic regurgitation	Normal to LVH, LAH
Aortic valve stenosis	Normal to LVH; strain pattern
Atrial septal defect	RAD, RVH, RBBB
Coarctation of the aorta	LVH; infants may have RBBB or RVH
Endocardial cushion defect	Superior QRS axis, LVH or BVH
Hypertrophic obstructive cardiomyopathy	LVH, deep Q waves in leads V_5 and V_6
Patent ductus arteriosus	Normal to LVH or BVH
Pulmonary stenosis	Normal to RAD, RVH (RAH in severe cases)
Tetralogy of Fallot	RAD, RVH or BVH, possibly RAH
Ventricular septal defect	Normal to LVH or BVH

Abbreviations: BVH, biventricular hypertrophy; ECG, electrocardiogram; LAH, left atrial hypertrophy; LVH, left ventricular hypertrophy; RAD, right axis deviation; RAH, right atrial hypertrophy; RBBB, right bundle branch block; RVH, right ventricular hypertrophy.

Pericarditis

Pericardial effusion causes a low-voltage QRS.

ST-T changes follow a time-dependent progression: initially, ST segment elevation, which returns to normal levels over 2 to 3 days. Then, T wave inversion occurs 2 to 4 weeks after the onset of disease.

Long QT Syndrome

The QTc interval varies with age, but in general, any QTc interval greater than 0.45 is abnormal and requires evaluation by a cardiologist. In addition, the following can also be seen: abnormal T wave morphology, bradycardia, second-degree atrioventricular (AV) block, multifocal premature ventricular contractions, and ventricular tachycardia (VT).

Screen all first-degree relatives of the patient to look for a familial long QT syndrome (LQTS), such as Jervell and Lange-Nielsen syndrome (congenital deafness, syncope, and family history of sudden death); Romano-Ward syndrome (same findings as Jervell and Lange-Nielsen syndrome, but with normal hearing); Timothy syndrome (webbed fingers and toes); and Andersen-Tawil syndrome (muscle weakness, periodic paralysis, ventricular arrhythmias, and developmental delays).

Electrolyte Disorders

Hyperkalemia

ECG changes vary with the level of hyperkalemia:

- Potassium level greater than 6 mEq/L (6 mmol/L): tall, peaked T waves

- Potassium level greater than 7.5 mEq/L (7.5 mmol/L): widened QRS complex, PR prolongation, tall T waves
- Potassium level greater than 9 mEq/L (9 mmol/L): disappearance of P waves and sinusoidal QRS; ultimately leads to asystole

Hypokalemia

No changes until potassium level is 2.5 mEq/L (2.5 mmol/L). Findings then include depressed ST segments, biphasic T waves, prolonged QTc interval, and the possible appearance of U waves.

Hypercalcemia

Serum calcium level greater than 11 mg/dL (2.75 mmol/L) or ionized calcium level greater than 5 mg/dL (1.25 mmol/L) cause shortened ST segment, without changing the T wave morphologic appearance, and a shortened QTc interval.

Hypocalcemia

A prolonged ST segment without changing T wave morphologic appearance and a prolonged QTc interval are seen when an infant's serum calcium level is less than 7.5 mg/dL (1.88 mmol/L) or ionized calcium level less than 3.5 mg/dL (0.88 mmol/L); or a child's serum calcium level is less than 8.5 mg/dL (2.13 mmol/L) or ionized calcium level less than 4.5 mg/dL (1.13 mmol/L).

Kawasaki Disease

Up to 60% of patients have prolonged PR interval during acute presentation, with arrhythmias, nonspecific ST-T wave changes, or ischemic changes with severe disease.

Lyme Carditis

PR interval prolongation is the most frequent finding.

Acute Rheumatic Fever

PR interval prolongation is the most frequent finding.

Acute COVID-19 Disease/Multisystem Inflammatory Syndrome in Children

No specific ECG findings.

Arrhythmias

Introduction

Arrhythmias are encountered in 2 types of inpatients. One is the patient with a history of known or recently diagnosed heart disease who is admitted for

medical or surgical treatment or for management of a complication from the heart disease or its treatment. In the second type of patient, the arrhythmia either is an incidental finding or is related to a non–cardiac disease process, such as hyperthyroidism, fever, electrolyte abnormality, toxic ingestion, or medication side effect.

Clinical Presentation

When a child presents with a suspected arrhythmia (Table 9–3), it is critical to focus on the history and physical examination findings. The amount of detail obtained depends on how stable the patient is. In an unstable patient, perform a directed history and examination, so as not to delay the administration of lifesaving treatment.

History

A patient with an arrhythmia can present in a variety of ways, depending on age and underlying heart rhythm and/or heart disease. An infant may have nonspecific signs and symptoms, such as tachypnea, diaphoresis and/or cyanosis during feeding, irritability, and inconsolability. An older patient may report chest pain, nausea, palpitations, syncope or near syncope, or shortness of breath. A patient of any age may present with cardiovascular collapse.

Have the patient or family describe the current episode and any previous similar episodes. Assess the patient for other symptoms, including chest pain, light-headedness, dyspnea, palpitations, fatigue, irritability, and altered mental status. Ask about recent illnesses and review any medications or possible ingestions. Determine the patient's medical history, especially if there are any chronic illnesses or a family history of heart disease or sudden or unexplained death.

Physical Examination

Perform a directed physical examination, focusing on the vital signs, to determine if the patient is hemodynamically stable. A stable patient has a maintainable airway, minimal to no respiratory distress, and adequate perfusion. *Adequate perfusion* is defined as appropriate mental status, capillary refill test time of less than 2 seconds, appropriate blood pressure for the patient's age, normal oxygen saturation, and adequate urine output. Auscultate for breath sounds, as well as heart rate, rhythm, murmur, and additional sounds, such as clicks or gallops. Check for hepatosplenomegaly, jugular venous distention, and peripheral edema.

Treatment of Specific Arrhythmias

If the patient is stable, there is time to systematically evaluate the situation. Many arrhythmias have underlying reversible causes, for which the American

Table 9–3. Electrocardiographic Findings in Arrhythmias

Heart Rate (bpm)	Heart Rhythm	PR Interval	QRS Interval	Causes
Asystole				
0	None	Absent	Absent	See Box 9–1
Atrial Fibrillation				
Atrial: 350–600 Ventricular: variable	Irregularly irregular	Absent Fibrillation waves present	Normal	Cardiac surgery, valvular or ischemic disease, idiopathic origin, WPW
Atrial Flutter				
Atrial, 240–360; ventricular, depends on degree of block (2:1–4:1)	Saw-toothed flutter waves with regular ventricular conduction at a fixed ratio (2:1–4:1)	Absent	Normal	Same as atrial fibrillation
First-degree AV Block				
Normal for age	Regular	Prolonged for age	Normal	Normal variant, ARF, CM, CHD, digitalis toxicity, CTD
Second-degree AV Block Type I				
Normal for age	Progressive lengthening of PR interval until nonconduction of a QRS	Progressively lengthening	Normal	Normal variant, myocarditis, CM, CHD, AMI, SLE, Lyme disease, digitalis or β-blocker toxicity
Second-degree AV Block Type II				
Normal to bradycardic for age	AV conduction cycles between normal and complete block, resulting in dropped QRS (blocked P wave)	Normal, fixed duration	Normal	Same as type I
Third-degree AV Block				
Dissociation between atrial and ventricular heart rates, heart rate of P wave > QRS	Heart rate of P waves and QRSs are regular but independent of each other	Variable	Normal in congenital cases; prolonged in acquired cases	Congenital causes: maternal SLE or CTD and CHD Acquired causes: ARF, myocarditis, Lyme disease, CM, AMI, and digitalis toxicity

Table 9–3. Electrocardiographic Findings in Arrhythmias, continued				
Heart Rate (bpm)	**Heart Rhythm**	**PR Interval**	**QRS Interval**	**Causes**
Long QT Syndrome				
Normal for age	Regular; prolonged QTc interval > 0.45; can lead to ventricular ectopy or TdP	Normal	Normal	Acquired causes include drug toxicity, and ↓ potassium, ↓ calcium, and ↓ magnesium levels; congenital causes include JLNS, RWS, various channelopathies
Sinus Arrhythmia				
Normal for age	Regularly irregular Rhythm changes with respirations	Normal	Normal	Normal respiration
Sinus Bradycardia				
Infant, < 80; Child, < 60	Regular	Normal	Normal	Normal in athletes ↑ ICP; see Box 9–1
Sinus Tachycardia				
Infant, 140–200; Child, 120–180	Regular	Normal	Normal	Shock, sepsis, pain, fever, anxiety, AMI, drug toxicity
Supraventricular Tachycardia				
Infant, > 220; Child, > 180	Regular Does not vary	Masked by tachycardia	Normal	Idiopathic origin, CHD, postoperative origin
Ventricular Fibrillation				
150–300	Chaotic, no organized electric activity	Absent	Absent	See Box 9–1
Ventricular Tachycardia				
120–200, with ≥ 3 consecutive PVCs	Regular, beat-to-beat variability	Masked by tachycardia	Widened	Myocarditis, AMI, CM, LQTS, CHD, drug toxicity; see Box 9–1

Abbreviations: AMI, acute myocardial infarction; ARF, acute rheumatic fever; AV, atrioventricular; bpm, beats per minute; CHD, congenital heart disease; CM, cardiomyopathy; CTD, connective tissue disease; ICP, intracranial pressure; JLNS, Jervell and Lange-Nielsen syndrome; LQTS, long QT syndrome; PVC, premature ventricular contractions; QTc, corrected QT; RWS, Romano-Ward syndrome; SLE, systemic lupus erythematosus; TdP, torsades de pointes; WPW, Wolff-Parkinson-White syndrome.
↑ indicates increased level; ↓, decreased level.

Heart Association has coined the mnemonic of "*H*'s and *T*'s" (Box 9–1). It is imperative that these conditions are diagnosed and treated.

Asystole

Confirm that the monitor leads are properly attached to the patient's chest and the monitor; then, change the monitor lead setting and confirm asystole with a second lead. Initiate cardiopulmonary resuscitation (CPR), secure an airway, obtain intravenous (IV) or intraosseous (IO) access, and provide oxygen and adequate ventilation.

Administer 0.01 mg/kg (1-mg maximum) of epinephrine 0.1 mg/mL concentration intravenously or via IO infusion, followed by 5 to 10 mL of normal saline. If there is no IV or IO access, use 0.1 mg/kg (3-mg maximum) of epinephrine 1 mg/mL concentration, followed by 5 to 10 mL of physiological (normal) saline solution via the endotracheal tube every 3 to 5 minutes until vascular access is achieved.

Atrial Fibrillation and Atrial Flutter

Investigate whether underlying medical conditions are present. The goals are to convert the atrial rhythm, control the ventricular response, and prevent recurrences. The approach varies, depending on the patient's clinical status.

In an acute, life-threatening situation, attempt cardioversion (0.5–1.0 J/kg). Consult with a pediatric cardiologist to initiate anticoagulation with heparin and ventricular rate control with digoxin, a β-blocker, or a calcium channel blocker. If the patient is stable with atrial fibrillation or flutter of unknown duration, consult with a pediatric cardiologist and delay cardioversion until adequate anticoagulation has been achieved.

First-degree Atrioventricular Block

In cases of first-degree AV block, no treatment is needed except in the setting of structural heart disease and drug toxicity.

Box 9–1. The "*H*'s and *T*'s" of the Reversible Causes of Arrhythmias

Hypovolemia	**T**ension pneumothorax
Hypoxia	**T**amponade (cardiac)
Hydrogen ion (acidosis)	**T**oxins
Hypoglycemia	**T**hrombosis, pulmonary
Hypokalemia, **H**yperkalemia	**T**hrombosis, coronary
Hypothermia	

From American Heart Association. Highlights of the 2020 AHA Guidelines Update for CPR and ECC. Accessed May 12, 2021. https://cpr.heart.org/en/resuscitation-science/cpr-and-ecc-guidelines.

Second-degree AV Block, Type I

In cases of second-degree AV block, type I, treat the underlying disease that is causing the arrhythmia.

Second-degree AV Block, Type II

In cases of second-degree AV block, type II, treat the underlying disorder. Be aware that this arrhythmia has a high risk for progression to third-degree AV block. Consult a pediatric cardiologist for potential pacemaker placement.

Third-degree AV Block

In cases of third-degree AV block, treat the patient with IV atropine at a dose of 0.02 mg/kg every 5 minutes for 2 to 3 doses (minimum single dose, 0.1 mg; maximum single dose, 0.5 mg in children and 1 mg in adolescents; maximum total dose, 1 mg for children and 2 mg for adolescents). Use this intervention to increase the heart rate while arranging for transcutaneous or transvenous cardiac pacing until a permanent pacemaker can be placed.

Indications for pacemaker therapy include signs and symptoms of congestive heart failure; an infant with a structurally normal heart and a ventricular rate less than 50 beats per minute (bpm); an infant with structural heart disease and a ventricular rate less than 70 bpm; and a patient with a wide QRS escape rhythm, ventricular ectopy, or ventricular dysfunction.

Long QT Syndrome and Torsades de Pointes

If the patient presents with ventricular ectopy or torsades de pointes, begin basic life support, evaluate serum electrolyte levels, and begin administration of IV magnesium sulfate at a dose of 25 to 50 mg/kg (2-g maximum). Contact a pediatric cardiologist and monitor the patient closely, because further resuscitation may be required.

If the long QT interval is an incidental finding or is discovered during the evaluation for syncope, investigate reversible causes, such as medications (most commonly macrolides, azole antifungal agents, antipsychotic agents, or fluoroquinolones). A comprehensive list can be found at www.crediblemeds.org. Refer the patient to a pediatric cardiologist if the QT interval does not normalize.

If congenital LQTS is suspected, refer the patient to a pediatric cardiologist and arrange for all first-degree relatives to undergo screening. Coordinate long-term therapies with the cardiology staff.

Symptomatic Sinus Bradycardia

Initiate basic life support, obtain IV or IO access, provide oxygen, and place the patient on a monitor. Assess the patient for reversible causes (*H*'s and *T*'s) and treat the underlying disease. Start transcutaneous pacing, if readily

available. Otherwise, treat the patient with epinephrine, as described for asystole.

If there is increased vagal tone or if the patient has an AV block, administer atropine, as described earlier for third-degree AV block. Situations where increased vagal tone is encountered include myocardial disease, hypoglycemia, hypothyroidism, increased intracranial pressure, sick sinus syndrome, and potassium abnormalities. Numerous drugs, such as digoxin and β-blockers, can also cause increased vagal tone.

Supraventricular Tachycardia

In the event of supraventricular tachycardia (SVT), initiate basic life support, obtain IV or IO access, provide oxygen, and place the patient on a monitor. Assess the patient for reversible causes (*H*'s and *T*'s) and treat the underlying disease. Initial treatment depends on whether or not the patient is well perfused.

If the patient is well perfused, initially attempt vagal maneuvers, such as covering the face with a bag of slushy ice water or attempting a Valsalva maneuver. If unsuccessful, administer adenosine as a 0.1-mg/kg rapid IV push (6-mg maximum), with the syringe as close to the IV site as possible, followed by a rapid IV push of 5 to 10 mL of normal saline. A stopcock can be used to facilitate the rapid infusion of the adenosine and the flush. If the first dose is not successful, repeat as a 0.2-mg/kg rapid IV push (12-mg maximum). If the SVT persists, consult a pediatric cardiologist to discuss the next step (administration of additional antiarrhythmic agents or synchronized cardioversion).

If the patient is poorly perfused, perform synchronized cardioversion at 0.5 to 1.0 J/kg. If unsuccessful, increase to 2.0 J/kg. If cardioversion is unsuccessful or if SVT recurs, consult with a cardiologist whenever possible and administer either IV amiodarone at 5 mg/kg over 20 to 60 minutes or IV procainamide at 15 mg/kg over 30 to 60 minutes. Be prepared to treat bradycardia or other dysrhythmias that may result after amiodarone or procainamide administration.

Ventricular Fibrillation

In the event of ventricular fibrillation (VF), initiate basic life support, obtain IV or IO access, provide oxygen, ensure adequate ventilation, and place the patient on a monitor. Once VF is noted, proceed to immediate defibrillation. Administer a single shock of 2 J/kg, followed by 2 minutes of CPR; a second shock of 4 J/kg should be followed by 2 minutes of CPR; subsequent shocks of 4 J/kg or greater to a maximum of 10 J/kg or adult levels of energy can be further administered. After the second defibrillation attempt, administer

epinephrine every 3 to 5 minutes, as for asystole. After the third defibrillation attempt, start administration of an antiarrhythmic agent, either amiodarone (5-mg/kg IV or IO bolus; may be repeated twice for refractory VF or pulseless VT) or lidocaine as a 1-mg/kg IV or IO bolus. Continue cycles of "CPR-shock-drug" until there is return of spontaneous circulation, a rhythm change, or termination of resuscitative efforts.

Ventricular Tachycardia

If VT occurs, initiate basic life support, obtain IV or IO access, provide oxygen, ensure adequate ventilation, and place the patient on a monitor. If the patient is pulseless, treat with an approach identical to that used for VF. If the patient has a pulse and poor perfusion, use synchronized cardioversion, as for SVT. Consult a pediatric cardiologist or intensivist to assist with further management (including possible procainamide infusion or synchronized cardioversion).

If the patient has a pulse and good perfusion, administer IV amiodarone (5 mg/kg over 20 minutes) or consult a pediatric cardiologist to assist with further management (including possible procainamide infusion or synchronized cardioversion).

Ambulatory Monitoring

Ambulatory Monitors

Ambulatory monitors can be initiated either in the inpatient setting or at the time of discharge. They are indicated to determine if chest pain, palpitation, or syncope are arrhythmic in origin; evaluate the effectiveness of antiarrhythmic therapy; screen high-risk cardiac patients (with cardiomyopathies or postoperative status); evaluate implanted pacemaker dysfunction; and determine the effects of sleep on arrhythmias.

Holter Monitors

Holter monitors are for short-duration use (24–72 hours).

Event Recorders

Event recorders can be used to monitor the patient for longer periods. When the patient senses the onset of symptoms, they are expected to press a button. This records the current ECG activity, as well as a time-limited amount of the ECG activity that precedes and follows the event trigger.

Disposition

- **Intensive care unit transfer:** Life-threatening arrhythmias (VF, VT, sustained SVT, symptomatic bradycardia, AV block of second-degree type II and higher, atrial flutter or fibrillation, asystole)

- **Discharge criteria:** Hemodynamically stable and placed on a regimen that can be managed at home

Indications for Consultation

- **Pediatric cardiology:** Life-threatening arrhythmias (as discussed earlier), long QT interval, SVT, heart block

Pearls and Pitfalls

- The only way to interpret an ECG correctly is within the context of the clinical history, medical factors, and age-appropriate reference values.
- Verify that the correct settings are used: paper speed of 25 mm/s and voltage at full standard.
- If something doesn't seem right, discuss it with a pediatric cardiologist.
- The clinical status of the patient determines how rapidly the arrhythmia should be treated.
- Always confirm asystole with 2 different leads.
- Symptomatic bradycardia of less than 60 bpm in any age group requires initiation of CPR.
- Suspect SVT when age-specific rate criteria are exceeded and there is no beat-to-beat variability of the rhythm. Signs and symptoms of SVT can be very nonspecific in infants.
- Second-degree AV block, type II, has a high risk of progression to complete AV block. Be prepared to pace the patient's heart, should this deterioration occur.

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CHAPTER 10

Carditis: Endocarditis, Myocarditis, and Pericarditis

Introduction

Infective Endocarditis

Infective endocarditis (IE) is an infection of the endothelium of the heart, most often caused by *Staphylococcus aureus* (especially for acute IE), *Streptococcus viridans*, coagulase-negative staphylococci, pneumococcus, "HACEK" organisms (*Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*), enterococcus, and *Candida* spp (especially in a newborn). The incidence rate is increasing as a result of the survival of children with congenital heart disease (CHD) and the more frequent use of indwelling central venous catheters (CVCs), especially in premature infants. Although IE is rare in children, there is significant morbidity and mortality associated with the condition.

Acute Myocarditis

Acute myocarditis is inflammation of the muscular wall of the heart, which may also extend to involve the endocardium and pericardium. Most cases in the United States are caused by viruses—historically, coxsackievirus and adenovirus. Recently, parvovirus B19, human herpesvirus 6, cytomegalovirus (CMV), Epstein-Barr virus (EBV), and novel H1N1 influenza have been diagnosed more frequently. In addition, myocarditis after acute COVID-19 disease can occur as part of the multisystem inflammatory syndrome in children (see Chapter 65). Other, less common infectious causes include *Meningococcus, Streptococcus, Staphylococcus, Listeria, Mycobacterium* species, and *Borrelia burgdorferi*. However, the specific causative agent is often not identified.

Medications can also cause myocardial inflammation by means of direct toxic effect (chemotherapeutic agents) or by inducing hypersensitivity reactions (anticonvulsants, antipsychotics, antibiotics). Acute myocarditis has also been reported in adolescents within several days after receiving a COVID-19 mRNA vaccine, more frequently after the second dose of the vaccine, and more often in males.

Acute Pericarditis

Acute pericarditis is an inflammatory condition of the fibrous pericardium that surrounds the heart, often accompanied by an effusion in the pericardial cavity. It may be isolated or a feature of a systemic disease, although most

cases in children are idiopathic. Specific etiologies include viral infection (most often enteroviruses), bacterial infection (purulent pericarditis), tuberculosis, connective tissue or collagen vascular diseases, metabolic diseases, uremia, neoplasms, drug reactions, trauma, and postpericardiotomy syndrome. Recently, acute COVID-19 disease has been implicated as a cause of pericarditis, occasionally in the absence of respiratory or other associated symptoms.

Purulent pericarditis is often associated with infection at another site, with hematogenous or direct spread. The most common causative organisms are *S aureus*, group A β-hemolytic streptococcus, pneumococcus, and meningococcus.

Complications of pericarditis include pericardial constriction and cardiac tamponade (acute compression of the heart from increased intrapericardial pressure caused by pericardial effusion).

Clinical Presentation

History

Infective Endocarditis

IE can be an acute or subacute process. Acute IE is a fulminant disease that presents with high fever, shock, and a toxic-appearing patient. *S aureus* is more often associated with acute IE. There can be a history of CHD (especially cyanotic), cardiac surgery, indwelling catheter placement, prematurity, or previous endocarditis. Subacute IE is caused by less virulent organisms and usually presents with nonspecific signs and symptoms, such as prolonged fever, fatigue, weakness, arthralgia, myalgia, and weight loss.

Acute Myocarditis

Clinical presentation varies according to age and severity of disease. An infant often presents with nonspecific symptoms, including poor feeding, fever, tachypnea, irritability, listlessness, pallor, diaphoresis, vomiting without diarrhea, and episodic cyanosis. Additionally, infants are more likely to have a fulminant presentation that requires early, advanced cardiorespiratory support. An older child can present with a nonspecific flulike illness or gastroenteritis. In more severe cases, there may be symptoms of congestive heart failure (CHF), including malaise, decreased appetite, shortness of breath, and exercise intolerance.

An adolescent may complain of chest pain similar to ischemia, with anterior chest pressure radiating to the neck and arms, in addition to other symptoms noted previously. An older patient may also present with

palpitations, syncope, and, rarely, sudden death. Pancarditis (myocarditis with pericarditis) presents with precordial pain that varies with respiration and position.

Acute Pericarditis

The classic presentation of acute pericarditis is sudden onset of chest pain that is pleuritic in nature (exacerbated by inspiration), worse when recumbent, and alleviated by sitting upright and leaning forward. The pain can radiate to the neck, arms, back, or shoulders. A young child may present solely with tachycardia, tachypnea, and fever, without chest pain. A patient with viral pericarditis may have a history of a recent upper respiratory infection or gastroenteritis. Bacterial pericarditis is generally more acute in onset, with symptoms developing over a few days.

Physical Examination

Infective Endocarditis

There are rarely any abnormal physical findings in subacute IE, so a new heart murmur is neither necessary nor sufficient to assign the diagnosis. Extracardiac manifestations (Osler nodes, Roth spots, Janeway lesions, petechiae, hemorrhages, splenomegaly, glomerulonephritis) are unusual in children, although emboli to the abdominal viscera, lung, or brain can occur.

Acute IE can present with shock, including hypotension, tachycardia, tachypnea, and low oxygen saturation (in CHD graft infection), along with high fever and signs of CHF.

Acute Myocarditis

Look for signs of heart failure or cardiogenic shock, including hypotension, tachypnea, hepatomegaly, abnormal heart sounds (including an S_3 or S_4 gallop), a murmur consistent with mitral or tricuspid insufficiency, abnormal lung examination findings with evidence of pulmonary venous congestion (rales), and poor perfusion (weak pulse and prolonged capillary refill time). Tachycardia out of proportion to the fever or the hydration status is a frequent, but not universal, finding.

Acute Pericarditis

A pericardial friction rub is diagnostic but not always present. Auscultate while the patient is leaning forward. The heart sounds may be muffled with a large effusion.

A patient with cardiac tamponade has an ill appearance, with signs of right-sided heart failure (lower-extremity edema, hepatomegaly) and poor systemic perfusion (weak pulse, cool extremities, delayed capillary refill) because of the decreased cardiac output. Other findings suggestive of tamponade include

pulsus paradoxus (a decrease in systolic blood pressure of > 10 mm Hg with inspiration) and Beck triad (systemic hypotension, increased jugular venous pressure, and muffled heart sounds).

Laboratory Workup and Radiology Examinations

Infective Endocarditis

If IE is suspected, obtain a complete blood cell count (CBC; the patient may be anemic secondary to hemolysis or chronic disease), erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level (usually increased), rheumatoid factor level (often increased), and a urinalysis (an associated immune complex glomerulonephritis can lead to red blood cell casts and proteinuria).

Perform 3 blood cultures from 3 separate venipunctures over a 1- to 2-hour time span, and then perform 2 to 3 more cultures if the first ones have no growth at 48 hours. Ensure that the sample size is sufficient (1–3 mL in an infant; 5–7 mL in a young child). If there is difficulty obtaining an adequate sample, inoculate the aerobic culture only. Culture of arterial blood does not increase yield, but it is an acceptable sample.

Obtain a transthoracic echocardiogram (TTE) when IE is suspected. Although a TTE is sufficient for most patients younger than 10 years of age and less than 60 kg, obtain a transesophageal echocardiogram for a patient with obesity, previous heart surgery, anomalies of the thoracic cage, or chronic lung disease.

Acute Myocarditis

Obtain a CBC and either a CRP level or ESR, which are often increased in acute myocarditis. To identify a possible pathogen, perform a blood culture, a polymerase chain reaction (PCR) of nasal or tracheal aspirates for viruses, and further viral testing as suggested by the clinical picture (viral titers [CMV, EBV, parvovirus, SARS-CoV-2], nasal and rectal viral cultures, Lyme titer). Evaluate cardiac enzyme levels, cardiac troponin T (cTnT) levels, and B-type natriuretic peptide levels, which are often increased at the time of acute presentation. Increased troponin levels help confirm the diagnosis, and in a patient without preexisting cardiac disease, a cTnT cutoff value of 0.01 ng/mL (0.01 mcg/L) has a high sensitivity and negative predictive value. In a patient with viral myocarditis, elevated troponin levels early in hospitalization have been associated with a more severe course, including receiving intravenous immunoglobulin and requiring extracorporeal membrane oxygenation (ECMO).

Obtain a chest radiograph, which frequently demonstrates cardiomegaly. Other findings include pulmonary venous congestion, interstitial infiltrates,

and pleural effusions. Also obtain a 12-lead electrocardiogram (ECG), which most commonly shows sinus tachycardia, low-voltage QRS complexes, and nonspecific T wave changes. Other ECG changes can mimic those of myocardial infarction or pericarditis, including ST segment changes and pathologic Q waves. Arrhythmias, such as supraventricular or ventricular tachycardia or varying degrees of atrioventricular block, can also be present.

Obtain a TTE to help rule out other causes of cardiac dysfunction, including vegetation (endocarditis) and pericardial effusion (pericarditis). Findings in myocarditis are variable and can include left ventricular or biventricular dysfunction, dilatation, wall motion abnormalities, and mitral and tricuspid valve regurgitation. Pericardial effusion, if present, is typically limited.

Cardiac magnetic resonance (CMR) imaging can localize the affected areas of the myocardium. The specificity is increased by using gadolinium-based contrast material. CMR imaging is also useful as a noninvasive means to follow a patient's progress over time.

Acute Pericarditis

Obtain a CBC and either a CRP level or ESR, which are often increased in acute pericarditis. A markedly increased white blood cell (WBC) count can suggest bacterial pericarditis. Perform a blood culture when sepsis is suspected (fever, tachycardia, toxic appearance). Order serologic testing, including antinuclear antibody and rheumatoid factor, in a patient with suggestive signs and symptoms for a connective tissue or collagen vascular disease, such as arthritis, rash, or weight loss. Evaluate cardiac enzyme levels when the diagnosis is unclear. Cardiac troponin T levels may be mildly increased in pericarditis, while creatine kinase–MB increase occurs in myopericarditis.

Obtain a chest radiograph, which may have normal findings or show an enlarged cardiac silhouette with a characteristic globular ("water bottle") appearance if there is a large effusion.

Obtain a 12-lead ECG, which may progress through 4 stages: diffuse ST elevation and PR depression (the classic finding), normalization of ST and PR segments, diffuse T wave inversion, and normalization of T waves.

If pericardial tamponade is suspected, obtain an urgent TTE. The presence of a pericardial effusion on an echocardiogram can support the diagnosis, although the absence of an effusion does not exclude pericarditis.

Differential Diagnosis

The diagnosis of IE can be challenging, but the modified Duke criteria have been validated for use in children (Table 10–1). Consider the diagnosis of IE for a patient with fever of unknown origin, new murmur, history of cardiac disease (especially after cardiac surgery), or history of CVC placement (Table 10–2).

Table 10–1. Modified Duke Criteria for Infective Endocarditis

Major Criteria	
(+) Blood culture finding	> 2 blood cultures with a microorganism consistent with IE (*Streptococcus viridans, Streptococcus bovis, Staphylococcus aureus,* HACEK organisms, enterococci) ≥ 2 (+) blood cultures performed > 12 h apart ≥ 3 (+) blood cultures performed > 1 h apart (+) Blood culture finding for *Coxiella burnetii* or anti–phase I IgG antibody titer > 1:800
Endocardial involvement	(+) Echocardiographic findings: oscillating mass (vegetation), abscess, new dehiscence of prosthetic valve, new valvular regurgitation
Minor Criteria	
Vascular phenomena	Arterial emboli, intracranial or conjunctival hemorrhages, septic pulmonary infarcts, mycotic aneurysms, Janeway lesions
Immunologic phenomena	Glomerulonephritis, Osler nodes, Roth spots, (+) rheumatoid factor test result
Microbiological evidence	(+) Blood culture finding not meeting major criteria *or* Serologic evidence of infection
Predisposition	Heart condition IV drug use
Fever	≥ 38.0 °C (≥ 100.4 °F)
Diagnostic Decisions	
Definite diagnosis	Pathologic criteria: microorganism detection according to culture or histologic finding of vegetation or abscess 2 major criteria 1 major criterion and 3 minor criteria 5 minor criteria
Possible diagnosis	Findings consistent with IE that fall short of "definite" but are not "rejected"
Rejected diagnosis	Resolution in ≤ 4 d of treatment with antibiotics No pathologic evidence of IE at surgery or autopsy with ≤ 4 d of treatment with antibiotics Firm alternate diagnosis

Abbreviations: HACEK, *Haemophilus* species, *Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella kingae;* IE, infective endocarditis; IgG, immunoglobulin G; IV, intravenous.
+ indicates a positive finding.
Derived from Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Inf Dis*. 2000;30:633–638.

The presentation of myocarditis is variable, depending on disease severity. Because it can be subtle, a high index of suspicion is needed to diagnose a nonfulminant case. Consider myocarditis in any patient with unopposed vomiting (without diarrhea), respiratory distress, tachycardia out of proportion to the fever or hydration status, new-onset CHF or arrhythmia, or ischemic chest pain. Myocarditis can be initially mistaken for an acute viral illness or a respiratory disorder. Other entities to consider include myocardial ischemia or infarction, pericarditis with or without myocarditis, endocarditis, other causes of CHF (see Chapter 11, Congestive Heart Failure), dilated cardiomyopathy,

Table 10–2. Differential Diagnosis of Infective Endocarditis

Sign/Symptom	Diagnoses
Prolonged fever	Infection caused by *Bartonella* species Collagen vascular disease Inflammatory bowel disease Kawasaki disease Malignancy Occult abscess Osteoarticular infections
New murmur	Anemia Fever Innocent murmur Previously undiagnosed cardiac anomaly
(+) Blood culture finding	Bacteremia or sepsis without IE Contaminated specimen

Abbreviation: IE, infective endocarditis.
+ indicates a positive finding.

and pulmonary embolism. Inflammatory processes, such as systemic lupus erythematosus, acute rheumatic fever, and Kawasaki disease, can also have myocarditis at presentation.

Pediatric chest pain is usually a benign complaint. The most common etiologies are either idiopathic or musculoskeletal (Table 10–3).

Treatment

Infective Endocarditis

Consult both a cardiologist and an infectious diseases specialist. While antibiotics are the mainstay of treatment for IE, they can be withheld for 48 hours until culture findings are positive in a patient with stable, subacute IE. The antibiotic regimens for IE are complex. Consider the organism, sensitivities, and minimum inhibitory concentration, and whether the patient has native or prosthetic cardiac material. Treat intravenously (IV) rather than intramuscularly, with bactericidal rather than bacteriostatic antibiotics.

In general, treat streptococcal IE with penicillin G or ampicillin IV for 4 weeks. Extend treatment to 6 weeks if the patient has a prosthetic valve, and add gentamicin IV for synergy for 1 to 2 weeks. For staphylococcal IE secondary to a methicillin-susceptible strain, use nafcillin or oxacillin IV for 4 to 6 weeks and add gentamicin IV for the first 3 to 5 days. For methicillin-resistant *Staphylococcus*, use vancomycin IV for 6 weeks and evaluate whether surgical intervention is warranted. Treat HACEK organisms with ceftriaxone IV or ampicillin IV for 4 weeks. Fungal infections often require surgery in addition to amphotericin B treatment.

Table 10–3. Differential Diagnosis of Pericarditis

Diagnosis	Clinical Features
Costochondritis	Chest pain reproducible by palpation at the costochondral junction Chest radiography and ECG findings normal
Endocarditis	Chest pain rare Echocardiogram findings may be (+) Osler nodes, Janeway lesions, Roth spots, splinter hemorrhages
Myocardial ischemia or infarction	Nonpleuritic chest pain Friction rub absent PR depression rare T wave inversion accompanies localized ST elevation
Myocarditis	Chest pain rare Friction rub absent Signs of CHF Low QRS voltages and occasional dysrhythmias Enlarged chambers, impaired left ventricular function on echocardiogram
Pneumonia	Decreased breath sounds or other focal findings (rales) ECG findings normal Chest radiography findings are usually diagnostic
Pneumothorax	Decreased breath sounds on the affected side Decreased QRS voltages, possible right shift of QRS axis Chest radiography findings are usually diagnostic
Pulmonary embolism	Nonpleuritic chest pain Friction rub rare No PR depression ST elevation, with T wave inversion only in leads III, aVF, and V_1

Abbreviations: CHF, congestive heart failure; ECG, electrocardiogram.
+ indicates a positive finding.

If the patient is unstable and antibiotics cannot be withheld for 48 hours or if antibiotics are being initiated for a case of culture-negative endocarditis at 48 hours, treat empirically with ampicillin/sulbactam IV plus gentamicin IV, with or without vancomycin IV. If a prosthetic valve is in place, add rifampin IV.

Indications for surgery for IE include large vegetations (> 1 cm), anterior mitral valve leaflet vegetation, growing vegetation after therapy, extension of abscess after therapy, valvular dysfunction, heart failure, heart block, embolic events after therapy, fungal endocarditis, and mycotic aneurysm.

Acute Myocarditis

If myocarditis is suspected, immediately consult a cardiologist, who can direct further workup and management. However, the treatment for myocarditis remains largely supportive, unless a treatable infectious pathogen is identified. Closely monitor the hemodynamic status for signs of worsening cardiac function or shock. Observe a patient who presents with mild disease for developing signs of CHF.

With the guidance of a pediatric cardiologist, treat CHF with traditional therapy, such as diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and β-blockers (see Chapter 11, Congestive Heart Failure). Manage arrhythmias with appropriate medications (see Chapter 9, Arrhythmias and Electrocardiogram Interpretation), although a persistent arrhythmia may require temporary or permanent pacing and possibly an implantable cardioverter-defibrillator.

Defer the decision about administering steroids and/or intravenous immunoglobulins to the cardiologist.

Acute Pericarditis

Closely monitor the patient's hemodynamic status. If tamponade is suspected, administer volume resuscitation (a 20-mL/kg bolus of normal saline delivered over 15 minutes) until the diagnosis is confirmed with an echocardiogram and/or an urgent pericardiocentesis can be performed. Other indications for pericardiocentesis include suspected purulent, tuberculous, or neoplastic pericarditis, or a large pericardial effusion. Send the fluid for a blood cell count, evaluation of glucose and protein levels, Gram stain and cultures, acid-fast bacilli stain, viral PCR (most commonly for enterovirus), triglyceride levels (to evaluate the presence of chylous effusion in a patient with a history of cardiac surgery), and, if indicated, cytologic examination.

If the clinical picture suggests purulent pericarditis, start empirical parenteral antibiotic therapy and transfer to an intensive care unit (ICU) or cardiac center for drainage via pericardiocentesis, a pericardial catheter, or an open procedure. Start with vancomycin (60 mg/kg/d divided into doses administered every 8 hours, with a 4-g/d maximum) combined with a third-generation cephalosporin (ceftriaxone, 100 mg/kg/d divided into doses administered every 12 hours with a 4-g/d maximum) until an organism is identified. Consult with an infectious diseases specialist to tailor the duration of antibiotic therapy, which averages 3 to 4 weeks. At a minimum, continue antibiotics until there is clinical resolution (no effusion present, patient is afebrile, WBC count has normalized).

If the patient is well appearing with an idiopathic or presumed viral pericarditis and a limited or midsized effusion, treat with rest and a nonsteroidal anti-inflammatory agent for relief of chest pain and inflammation. Administer high-dose ibuprofen (30–50 mg/kg/d divided into doses delivered every 8 hours, with a 2.4-g/d maximum) until symptoms resolve, typically within 1 to 2 weeks. Add cimetidine (20–40 mg/kg/d orally, divided into doses administered every 6 hours, with a 800-mg/d maximum) or famotidine (0.5 mg/kg/d orally or IV, divided into doses administered twice a day, with a 40-mg/d maximum) for gastroprotection while ibuprofen is administered.

Add colchicine for recurrent pericarditis (< 5 years of age, 0.5 mg/d; > 5 years of age, 1.0–1.5 mg/d administered in 2–3 divided doses). Do not administer steroids routinely; prescribe only for a patient with collagen vascular disease, an immune-mediated process, or an idiopathic effusion that is refractory to treatment with ibuprofen. If steroids are indicated, then use low-dose prednisone (0.2–0.5 mg/kg/d, with a 60-mg/d maximum for 4 weeks with subsequent taper).

Indications for Consultation

- **Cardiology:** Possible IE, myocarditis, or pericarditis
- **Infectious disease:** IE; myocarditis secondary to sepsis, spirochetes, or protozoa; purulent or tuberculous pericarditis
- **Rheumatology:** Pericarditis in a patient with known or suspected collagen vascular disease, recurrent pericarditis

Disposition

- **ICU transfer:** Shock, extracardiac embolic events (especially with organ dysfunction), unstable valvular vegetation, CHF, cardiothoracic surgery required, symptomatic myocarditis, purulent pericarditis, suspected or confirmed cardiac tamponade
- **Interinstitutional transfer:** Patient requires technology or management options not available locally (echocardiogram, pediatric ICU, CMR, ECMO, ventricular assist device, transplantation), or a pediatric cardiologist is not immediately available
- **Discharge criteria:**
  - **IE**: Afebrile, negative blood culture findings, completed IV antibiotic course, or patient is a suitable candidate for outpatient antibiotics (condition is stable, afebrile, at low risk for embolism; peripherally inserted central catheter is placed; home nursing is arranged; family is willing; there is prompt access to medical/surgical care if complications arise)
  - **Acute myocarditis:** Stable or improving cardiac function, managed with oral medication; advise the patient to refrain from competitive sports and vigorous exercise until cleared by a pediatric cardiologist
  - **Acute pericarditis:** Asymptomatic (no fever or chest pain), pericardial effusion is resolved or stable, no fluid reaccumulation during 1 week of observation after a drainage procedure

Follow-up

- **Primary care:** 5 to 7 days
- **Cardiology:** 2 days to 2 weeks, depending on the severity of the illness

- **Repeat echocardiogram:** Clinical deterioration during treatment, at the completion of treatment for IE, 1 week after an effusion was diagnosed (to document resolution)

Pearls and Pitfalls

- Include IE in the differential diagnosis of fever of unknown origin.
- Antibiotic therapy can be delayed until cultures are positive in a stable patient with subacute IE.
- IE can be diagnosed in the setting of negative blood culture findings and/or negative echocardiographic findings.
- Given the often subtle, nonspecific, and variable presentations of a patient with myocarditis, prompt diagnosis requires a high index of suspicion.
- Suspect myocarditis when there is unexplained CHF or arrhythmia, or when a patient with presumed gastroenteritis and/or dehydration with unopposed vomiting worsens after the administration of fluid boluses.
- A patient with pericarditis may not have the "classic" signs and symptoms of pericarditis, such as a friction rub and pleuritic chest pain that change with position.
- A chest radiograph and echocardiogram can be normal if no effusion accompanies pericardial inflammation.
- The most reliable study for assigning the diagnosis of pericarditis is an ECG with characteristic ST and PR segment changes.

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CHAPTER 11

Congestive Heart Failure

Introduction

Congestive heart failure (CHF) is the inability of the heart to meet the metabolic demands of the body. Rather than a single disease entity, CHF represents a constellation of signs and symptoms that arise from a number of processes. The most common causes of CHF in children are congenital heart disease (CHD), cardiomyopathies (genetic, acquired, and inherited metabolic or muscle disorders; infectious diseases; drugs; toxins; Kawasaki disease; and autoimmune diseases), myocardial dysfunction after surgical repair of heart defects, and multisystem inflammatory syndrome in children (MIS-C). Other etiologies include arrhythmias and valvular disease. Regardless of the cause of CHF, the resulting pathophysiological syndrome requires immediate attention, supportive care, and prompt cardiologist consultation.

Clinical Presentation

History

Infants

Feeding difficulty, with sweating on the forehead and upper lip, is the most prominent symptom and is often associated with tachycardia, tachypnea, and diaphoresis. Poor feeding ultimately leads to failure to thrive, which may be the presenting complaint.

Children/Adolescents

Toddlers and older children often exhibit fatigue, exercise intolerance, poor appetite, nausea, vomiting, and growth failure. Adolescents may have additional symptoms that are similar to those of adults, including shortness of breath, orthopnea, nocturnal dyspnea, abdominal pain, and chronic cough. A patient may present with primarily abdominal symptoms (nausea, vomiting, abdominal pain) without respiratory complaints. This may then be mistaken for acute gastroenteritis or another gastrointestinal (GI) process, potentially leading to excessive fluid administration to a fluid-overloaded patient.

Physical Examination

The patient typically presents with tachycardia and tachypnea. Hepatomegaly is an early finding, and if the enlargement is relatively acute, there may be flank pain or tenderness due to stretching of the liver capsule. Mild to moderate disease may appear with no distress at presentation, while a patient

with severe disease may be dyspneic at rest. With an acute onset, the patient may appear anxious but well nourished, versus calm yet malnourished with chronic CHF.

An infant with severe disease may have nasal flaring, retractions, grunting, and occasionally, wheezing. Rales are rare in an infant unless there is coexisting pneumonia. An infant with low cardiac output may have cool and/or mottled extremities, weak pulses, a narrow pulse pressure, and delayed capillary refill.

While uncommon in an infant, signs of increased systemic venous pressure may be exhibited in an older child, including distention of neck veins (venous pulsations visible above the clavicle while the patient is sitting) and peripheral edema (particularly in the face and dependent parts of the body). Low cardiac output may cause peripheral vasoconstriction that leads to cool extremities, pallor, cyanosis, and delayed capillary refill. With more advanced disease, pulmonary edema and rales are more likely.

The cardiac examination findings can be variable, depending on the etiology of disease. In cardiomyopathy, there is usually a quiet precordium. Shunt lesions (ventricular septal defect, patent ductus arteriosus) usually cause a hyperdynamic precordium. Obstructive lesions (aortic stenosis, coarctation of the aorta) may have a systolic thrill. A third heart sound in mid-diastole can be a normal finding in children but is noted more frequently in those with heart disease. Regardless of the etiology of CHF, a holosystolic murmur of mitral regurgitation is often present with advanced disease.

Laboratory Workup and Radiology Examinations

Standard testing to determine the etiology of CHF includes chest radiography, electrocardiography (ECG), and echocardiography. Chest radiographs will usually show cardiac enlargement, with or without evidence of pulmonary venous congestion, which depends on the etiology of the disease. It is less likely in early cardiomyopathy but more common with a left-to-right shunt or advanced disease. Echocardiography is the primary diagnostic modality for confirming the etiology of CHF (ie, ventricular dysfunction, anatomic abnormality). In contrast, ECG, while almost always abnormal, is generally not useful in the diagnosis of heart failure but may provide clues to the etiology.

If it is difficult to distinguish between a primary respiratory process and cardiac-induced respiratory symptoms, obtain a B-type natriuretic peptide level (BNP). BNP is a sensitive marker of cardiac filling pressure and diastolic dysfunction and will be increased in heart failure but normal in respiratory diseases.

Once the diagnosis of CHF has been established, the remainder of the laboratory testing depends on the age of the patient, the presence or absence of

CHD, and any coexistent systemic disorders. Obtain a complete blood cell count (CBC), electrolyte levels, liver function tests, renal function tests, a blood gas assessment, and a lactate level. The CBC may reveal leukocytosis secondary to infection, anemia, thrombocytopenia in disseminated intravascular coagulation, or pancytopenia caused by viral suppression. A patient with CHF may have electrolyte abnormalities, including hyponatremia (fluid overload) and metabolic acidosis (poor perfusion). Renal failure may be a consequence or a cause of CHF, and increased transaminase levels occur with end-organ damage or a viral illness. The blood gas assessment provides objective evidence of impending respiratory failure, while an abnormal lactate level can be a sign of poor tissue perfusion or a clue to a metabolic cause of the illness.

Differential Diagnosis

It is important to differentiate CHF from possible respiratory and/or infectious illnesses, in which case the patient is unlikely to have hepatomegaly, cardiomegaly, or failure to thrive (Table 11–1). If a patient has a history of structural heart disease and presents with new signs and symptoms of CHF, it may be caused by an aggravating condition, such as fever, anemia, or arrhythmia. In a patient without structural heart disease, there are many possible etiologies of CHF, some of which are listed in Box 11–1.

Treatment

If CHF is suspected, immediately consult with a cardiologist for recommendations regarding appropriate management. Initial stabilization includes intravenous or intraosseous access (essential), cardiorespiratory monitoring (with

Table 11–1. Differential Diagnosis of Congestive Heart Failure

Diagnosis	Clinical Features[a]
Asthma	Previous episodes Wheezing, tachypnea, retractions Chest radiograph: hyperinflation without cardiomegaly or pulmonary congestion
Bronchiolitis	Rales with or without wheezing, tachypnea, retractions Chest radiograph: atelectasis and hyperinflation without cardiomegaly
Pneumonia	Fever, rales, tachypnea Chest radiograph: focal consolidation
Gastroenteritis or other GI process	Abdominal pain, nausea, vomiting, diarrhea Dehydration causing tachycardia/tachypnea, +/− fever
Sepsis	Fever, ill appearance, poor perfusion Tachypnea, tachycardia

Abbreviation: GI, gastrointestinal.

[a] Note the absence of hepatomegaly, cardiomegaly, failure to thrive, and increased brain natriuretic peptide level in all these diagnoses.

Box 11–1. Etiologies of Heart Failure in a Previously Structurally Normal Heart

Acquired valvular disease (rheumatic heart disease)	Kawasaki disease
Anemia	Malignancy
Arrhythmia (bradycardia or tachycardia)	MIS-C
Atrioventricular fistula	Muscular dystrophy
Cardiomyopathy (acquired or genetic)	Myocardial infarction
Chemotherapy (anthracyclines)	Myocarditis (usually viral: adenovirus, coxsackievirus, HIV, parvovirus, SARS-CoV-2)
Collagen vascular disease	Pulmonary disease
Eating disorders or caloric deficiency	Renal failure
Hematologic disorders	Sepsis
Hypertension (systemic or pulmonary)	Systemic lupus erythematosus
Hypocalcemia	Thyroid disease (hypothyroidism, thyrotoxicosis)
Hypoglycemia	
Inborn errors of metabolism (disorders of fatty acid oxidation, mitochondria, glycogen storage)	

Abbreviation: MIS-C, multisystem inflammatory syndrome in children.

telemetry if available), and judicious fluid administration. Volume overload is almost always present, so use smaller 5- to 10-mL/kg boluses in place of the typical 20-mL/kg bolus, as well as a slower administration rate, while continuously monitoring the patient for signs of pulmonary and hepatic congestion.

The overall goals of medical management are decreasing afterload, increasing contractility, and reducing preload. Provide a combination of vasodilators, inotropes, and diuretics, tailored to the patient, based on the pathophysiology. Also treat (antibiotics, antiarrhythmics, etc) any underlying etiologies. If MIS-C is likely (see Chapter 65, Multisystem Inflammatory Syndrome in Children), consult with an infectious disease specialist and follow the most current treatment algorithm.

If structural heart disease is suspected, use oxygen cautiously and only in consultation with a cardiologist. This is critical because oxygen, by lowering pulmonary vascular resistance, shunts blood from the systemic circulation to the pulmonary circulation, potentially causing rapid deterioration in certain ductal-dependent or mixing lesions. Once these etiologies have been ruled out, it is safe to administer oxygen to supplement tissue oxygenation and alleviate respiratory distress.

Once a cardiac etiology is identified, treatment options may also include cardiac catheterization and/or surgical intervention. Transfer a patient with severe or unresponsive heart failure to an intensive care unit (ICU), where additional modalities, such as extracorporeal membrane oxygenation or left ventricular assist devices, are available.

Regardless of the interventions or severity of the disease, proper nutrition and growth must be addressed, along with general health measures, such as

vaccinations and exercise parameters. Consult with a nutritionist: an infant will have a significantly higher caloric need, while an older child requires a salt-restricted diet.

Disposition

- **ICU transfer:** Impending respiratory failure, poor perfusion, hypotension, severe electrolyte abnormalities, metabolic acidosis, lethargy, or any other evidence of severe cardiovascular compromise or end-organ damage.
- **Interinstitutional transfer:** Diagnostic and treatment modalities or a pediatric cardiologist and/or intensivist are not immediately available at the current location.
- **Discharge criteria:** Breathing easily without respiratory distress, maintaining adequate fluid and nutritional intake and normal electrolyte levels, and, usually, requiring no supplemental oxygen. Discharge ultimately depends on the specific etiology of disease and the cardiologist's plan of care.

Follow-up

- **Primary care:** 1 week
- **Cardiology:** 2 to 3 days, depending on etiology and severity

Pearls and Pitfalls

- Family members or caretakers who see a patient on a regular basis may not notice subtle changes in the patient's appearance or behavior in the presence of CHF. For example, edema may be mistaken for normal weight gain, and exercise intolerance may be excused as a lack of interest in activities.
- The presenting signs and symptoms of CHF can be mistaken for more common illnesses, which can delay the diagnosis.
- Supplemental oxygen may worsen the status of a patient with structural disease and a left-to-right shunt.
- Early recognition and aggressive early management are crucial for survival of a patient with CHF.
- Maintain a high level of suspicion for a cardiac etiology/CHF in a patient presenting with acute GI symptoms who does not respond or worsens with initial fluid management.

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CHAPTER 12

Hypertension

Introduction

Pediatric hypertension is the persistent elevation of blood pressure (BP) above the 95th percentile, when compared to the BP distribution of healthy children of the same age, sex, and height (Table 12–1) or, for children older than 12 years, BP greater than 130/80 mm Hg. Elevated BP is often an incidental and transient finding in hospitalized patients, as the result of pain, anxiety, or medication side effects. However, acute severe hypertension may be the primary reason for admission. In addition, a previously undiagnosed case of chronic hypertension, severe enough to warrant treatment, may be discovered in a patient admitted for some other issue.

Primary hypertension (previously termed *essential hypertension*) is more common than secondary hypertension among pediatric patients, especially in older children, and its prevalence continues to rise along with the increase in pediatric obesity. Secondary hypertension is caused by a variety of renal, cardiac, genetic, and endocrine disorders.

Hypertensive crisis is defined as a BP above the 99th percentile in both upper extremities, on at least 2 manual readings, 10 minutes apart. A BP

Table 12–1. Definition of Hypertension

Description of BP	Criteria for Description
Age 1–13 Years	
Normal	SBP and DBP < 90th percentile
Elevated BP	SBP and/or DBP between 90th and < 95th percentile *or* SBP and/or DBP between 120/80 mm Hg and < 95th percentile
Stage 1 hypertension	SBP and/or DBP between ≥ 95th percentile and 95th + 12 mm Hg *or* BP between 130/80 and 139/89 mm Hg
Stage 2 hypertension	SBP and/or DBP ≥ 95th percentile + 12 mm Hg *or* ≥ 140/90 mm Hg
Age ≥ 13 Years	
Normal	< 120/80 mm Hg
Elevated BP	SBP between 120 and 129, DBP < 80 mm Hg
Stage 1 hypertension	BP between 130/80 and 139/89 mm Hg
Stage 2 hypertension	≥ 140/90 mm Hg

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

greater than 30 mm Hg above the 95th percentile is a risk for complications, including hypertensive encephalopathy, acute kidney injury, and congestive heart failure (CHF).

Clinical Presentation

History

Review the primary reason for admission, potential sources of pain or anxiety, the patient's current medications, and any missed medications. Ask about any preexisting medical conditions, particularly obesity, diabetes mellitus, and renal or urologic abnormalities. If primary hypertension is suspected, inquire about the patient's typical diet, physical activity, and medication or illicit drug use, as well as a family history of hypertension or cardiovascular disease.

Note any risk factors for a renal or renovascular etiology, including a history of recurrent urinary tract infections or unexplained fevers, extreme prematurity requiring extensive resuscitation or umbilical artery catheterization, or a family history of renal disease or hearing loss. An endocrinological etiology might present with palpitations, sweating, and flushing from thyrotoxicosis or catecholamine excess.

Ask about the use of recreational drugs, including anabolic steroids and stimulants such as pseudoephedrine, cocaine, and methamphetamines. Inquire about the patient's sleep, as a history of snoring, daytime sleepiness, or conversely hyperactivity in a younger child may be a sign of sleep apnea.

Complaints of confusion or lethargy, vomiting, visual disturbance, seizure, chest pain, palpitations, or shortness of breath, in the context of hypertension, are indications for an urgent evaluation for hypertensive emergency.

Physical Examination

First, confirm that the patient's BP has been measured accurately. Use the appropriate cuff size for the patient and take the measurement from the right arm with the arm at the same level as the heart. Oscillometric (automatic) BP measurements are 5 to 10 mm Hg higher than those taken manually by auscultation, so confirm elevated values by repeating a manual BP twice and averaging the result. In addition, measure the BP in both arms and one leg. With coarctation of the aorta, the BP will be higher in the right arm compared to the left and higher in the upper extremities compared to the lower.

Review the patient's weight, height, and vital signs. A high body mass index (BMI) increases the risk for primary hypertension, while growth restriction can be seen in chronic kidney disease and various endocrine disorders. Tachycardia can be due to pain or anxiety but may also be a symptom of thyrotoxicosis or catecholamine excess.

Priorities on the physical examination are funduscopy (retinal vascular changes or papilledema), cardiac auscultation (murmur, gallop), abdominal palpation for a mass (kidneys), abdominal bruit (renal artery stenosis), femoral pulses (delayed or diminished with coarctation), and the presence of edema (glomerulonephritis).

Findings in endocrine hypertension include acne, hirsutism, or striae (Cushing syndrome or anabolic steroid use), goiter or exophthalmos (hyperthyroidism), proptosis, abdominal mass (neuroblastoma or pheochromocytoma), and ambiguous genitalia (congenital adrenal hyperplasia).

Signs of hypertensive emergency include altered mental status or disorientation, headache, visual changes, ataxia, seizure, and focal neurologic deficits.

Laboratory Workup

If a patient's hypertension appears to be transient, then no laboratory workup is indicated. Otherwise, order a basic metabolic panel and a urinalysis. If the patient is obese (BMI > 95th percentile), also obtain hemoglobin A_{1c}, aspartate transaminase, and alanine transaminase levels, and a lipid profile to screen for diabetes, fatty liver disease, and dyslipidemia.

If renal function is abnormal (elevated creatinine) or the patient has a history of poor growth, check a complete blood cell count. If hypokalemia and metabolic alkalosis suggesting mineralocorticoid excess are found on the basic metabolic panel, send renin and aldosterone levels. If the clinical presentation is consistent with hyperthyroidism or catecholamine excess, obtain thyrotropin, free thyroxine, and plasma metanephrine levels. If Cushing syndrome is suspected, screen with a 24-hour urinary free cortisol. Send a urine drug screen if the patient appears intoxicated.

Radiology Examinations

Obtain a renal ultrasonographic (US) examination for any hypertensive patient who either is under 6 years of age or has abnormal renal function. If there is a discrepancy in kidney size of greater than 1 cm or a history of recurrent urinary tract infections, then order a dimercaptosuccinic acid scan to look for cortical scarring. Also obtain a US examination with Doppler if renal artery stenosis is suspected, although renal angiography is the gold standard test.

Coarctation of the aorta can be confirmed or ruled out by echocardiography, which is also indicated to evaluate for left ventricular hypertrophy (LVH) in a patient with chronic hypertension requiring pharmacologic treatment. Electrocardiography is not sensitive enough to effectively screen for LVH in pediatric patients.

Obtain computed tomography of the head in a hypertensive patient with altered mental status or focal neurologic deficits.

Differential Diagnosis

The differential diagnosis is summarized in Table 12–2. In a patient admitted for a primary problem other than hypertension, first consider how pain, anxiety, and any medication side effects may be contributing to the patient's elevated BP. High-dose steroids, oral contraceptives, and stimulant medications, as well as anabolic steroids or stimulants taken recreationally, can all raise the BP. Alternatively, a patient prescribed clonidine admitted with vomiting is at risk for rebound hypertension due to clonidine withdrawal.

Suspect primary hypertension in an obese or overweight patient over 6 years of age who does not have a history or physical examination findings suggestive of a secondary cause. A personal history of diabetes, high cholesterol, smoking, or high salt intake, and a family history of hypertension and cardiovascular disease further suggest primary hypertension.

Renal disease is a common cause of secondary hypertension, especially in a young child. Renal scarring may result from recurrent urinary tract infections, chronic vesicoureteral reflux, prolonged obstruction from renal or urologic anomalies, prior episodes of acute kidney injury, or hypoperfusion from perinatal hypoxic injury. Glomerulonephritis may be isolated or part of a systemic disease such as systemic lupus erythematosus and Henoch-Schönlein purpura. A family history of renal disease is concerning for polycystic kidney disease or other hereditary renal disorders.

A higher BP in the right arm compared to the left arm, and in the upper extremities compared to the lower extremities, raises a concern for coarctation of the aorta.

Sleep apnea is suggested by a history of snoring, daytime sleepiness, or hyperactivity (in young children).

Endocrine hypertension is rare in pediatric patients. Tachycardia associated with proptosis or goiter suggests hyperthyroidism, while paroxysmal tachycardia with palpitations, sweating, and headache may reflect symptoms of catecholamine excess from pheochromocytoma or neuroblastoma. Hypokalemia and metabolic alkalosis are consistent with mineralocorticoid excess, including familial hyperaldosteronism and congenital adrenal hyperplasia.

While any neurologic symptom, including altered mental status, seizure, visual disturbance, or focal neurologic deficits, may be a sign of a hypertensive emergency, it may also point to an intracranial process as the source of the patient's hypertension, including stroke and increased intracranial pressure.

Table 12–2. Differential Diagnosis of Hypertension	
Diagnosis	**Clinical Features**
Incidental Finding	
Anxiety	Improves as patient acclimates to the hospital setting
Error in measurement	Automatic measurement Extremity below the level of the heart Too-small cuff size
Medication side effect	Use of steroids, oral contraceptive pills, or stimulant medications
Pain	Associated tachycardia Resolves with analgesia
Reason for Admission	
Chronic kidney disease	Abnormal renal US findings Elevated creatinine Growth failure
Coarctation of the aorta	Blood pressure differential between right and left arm, and between upper and lower extremities Delayed or diminished femoral pulses
Congenital adrenal hyperplasia	Ambiguous genitalia Hypokalemia Metabolic alkalosis
Cushing syndrome	Hirsutism Moon facies Striae
Familial hyperaldosteronism	Hypokalemia Metabolic alkalosis Muscle weakness
Glomerulonephritis	Abnormal urinalysis Edema
Hyperthyroidism	Goiter Proptosis Tachycardia, palpitations
Pheochromocytoma or neuroblastoma	Headache Sweating, flushing Tachycardia
Polycystic kidney disease	Family history of kidney disease Palpable kidneys
Primary hypertension	Age > 6 years Family history of cardiovascular disease Obesity
Recreational drug use	Signs of intoxication
Renal artery stenosis	Abdominal bruit History of umbilical artery catheterization
Sleep apnea	Adenotonsillar hypertrophy History of snoring

Continued

Table 12–2. Differential Diagnosis of Hypertension, continued	
Diagnosis	**Clinical Features**
Systemic lupus erythematosus	Arthritis/arthralgia Fever Rash

Abbreviation: US, ultrasonographic.

Treatment

Incidental Hypertension

Manage incidental hypertension with pain control, efforts to calm the patient, and monitoring of serial BPs.

Primary Hypertension

The first-line treatment is counseling regarding dietary changes, including decreasing salt intake, and increasing physical activity to at least 30 minutes 3 to 5 days per week. However, pharmacologic treatment is indicated for a patient with symptomatic hypertension, stage 2 hypertension, or hypertension associated with chronic kidney disease or diabetes mellitus. Prescribe a calcium channel blocker such as oral amlodipine (0.1–0.6 mg/kg daily, 10-mg maximum [approved for patients 6 years and older]). For obese patients, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers, or diuretics are often used. The long-term goal is reduction of the BP to below the 90th percentile or less than 130/80 mm Hg, whichever is lower.

Secondary Hypertension

Identify and treat any underlying causes of the patient's hypertension, and consult with the appropriate specialist (cardiologist, endocrinologist, nephrologist). Options for a patient with renal disease include ACEIs, β-blockers, and diuretics. An esmolol infusion (100–500 mcg/kg/min) is the treatment of choice for a patient with coarctation of the aorta. The treatment for endocrine hypertension varies with the primary diagnosis.

Stage 2 Hypertension

Acute treatment to lower the BP is indicated if the patient meets criteria for stage 2 hypertension (BP hypertension ≥ 95th percentile + 12 mm Hg or ≥ 140/90 mm Hg). Give intravenous (IV) hydralazine (start at 0.1 mg/kg administered every 4 hours, then titrate to the desired BP with 0.2–0.4 mg/kg per dose, 20-mg maximum) or IV labetalol (0.2–1.0 mg/kg per dose, 40-mg

maximum; avoid use if the patient has asthma or overt heart failure). If the patient has not yet developed signs of life-threatening complications, then oral hydralazine can be given instead (0.25 mg/kg administered every 6–8 hours, 25-mg per dose maximum). To avoid organ hypoperfusion, aim to lower the BP by 25% in the first 8 hours, then to the final goal of below the 95th percentile in the next 12 to 24 hours. If these measures fail to adequately lower the BP, transfer the patient to an intensive care unit (ICU) for a continuous infusion of labetalol, nitroprusside, or nicardipine.

Indications for Consultation

- **Nephrology:** Abnormal renal function, urinalysis, or renal imaging; postinfectious glomerulonephritis, hypertensive urgency, and pheochromocytoma
- **Cardiology:** Coarctation of the aorta, LVH from chronic hypertension, or hypertensive emergency with CHF
- **Endocrinology:** Abnormal thyroid function tests, positive urinary catecholamines, laboratory findings of mineralocorticoid excess (hypokalemia and metabolic alkalosis), suspicion of Cushing syndrome

Disposition

- **ICU transfer:** Refractory hypertension requiring continuous infusion of antihypertensive medications; hypertensive emergency with signs of end-organ damage
- **Discharge criteria:** Blood pressure adequately controlled, evaluation for underlying causes completed, ongoing treatment plan established, and follow-up care secured

Follow-up

- **Primary care:** 1 to 2 weeks
- **Nephrology, cardiology, endocrinology:** 2 to 4 weeks, if applicable

Pearls and Pitfalls

- For a patient with a new finding of hypertension, first confirm that the BP measurement was taken accurately and account for any pain, anxiety, or medication side effects related to the hospitalization.
- Interpret pediatric BPs in relation to the normal BP distribution for patients of the same age, sex, and height.
- A patient with a BP greater than 30 mm Hg above the 95th percentile is at high risk for complications including hypertensive encephalopathy, acute kidney injury, and CHF.

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CHAPTER 13

Shock

Introduction

Shock is a state of systemic hypoperfusion. It represents a final common pathway for several derangements in volume status, vascular tone, venous return to the heart, and cardiac pump physiology. Septic shock, which is the most common type in children, often has a progression through signs and symptoms of compensation until hypotension and ultimately cardiovascular collapse ensue (*decompensated shock*). Other types of shock are classified by etiology (anaphylactic, neurogenic, cardiogenic) or physiology (distributive, low cardiac output, obstructive, hypovolemic), with considerable overlap in clinical presentation. The key to successful shock treatment is early recognition of shock in its *compensated* stages.

The identification of shock can be expedited by noting historical risk factors and recognizing vital sign changes. The management of shock (along with respiratory failure, cardiac dysrhythmia, and arrest) is a core portion of the American Heart Association's Pediatric Advanced Life Support (PALS) program. The American College of Critical Care Medicine's (ACCM) frequently updated pediatric septic shock guidelines have become the standard evidence-based practice regarding shock management. The ACCM septic shock algorithm has become a part of PALS and is featured on the PALS pocket reference card.

Clinical Presentation

There are a number of validated measures that facilitate screening for patients at risk of decompensation. For example, early warning scoring systems, like the Bedside Pediatric Early Warning System (PEWS), can decrease the frequency of significant deterioration events (eg, cardiac arrests, unexpected intensive care unit [ICU] transfers).

History

Ask about fever, difficulty breathing, skin color (from the caregiver's knowledge of baseline appearance), changes in mental status and behavior, and urine output, as well as history of trauma and potential sources of infection and fluid loss (cough, congestion, vomiting, diarrhea, abdominal pain, bleeding). In addition, confirm that the patient has normal immune status and no history of hemodynamically significant heart disease. If the child is currently an inpatient, review the vital signs from the prior 6 to 12 hours, intake-output flow sheets, and observations made by bedside nurses, respiratory therapists, and parents.

Physical Examination

The patient typically presents in compensated shock with fever (or hypothermia), tachycardia (persistent and out of proportion to the fever), widened pulse pressure (indicating low systemic vascular resistance), orthostatic vital sign changes, difficulty breathing, and signs of altered perfusion (pallor, mottled skin, delayed capillary refill, weak pulse, altered mental status, oliguria), but with a *normal, age-appropriate blood pressure*.

Laboratory Workup

Obtain a bedside glucose level, complete blood cell count with differential, comprehensive chemistry panel (end-organ hypoperfusion leads to acute renal and hepatic injury, as well as electrolyte abnormalities), and blood culture. If sepsis is of particular concern, order a disseminated intravascular coagulation panel, inflammatory markers (C-reactive protein and/or procalcitonin), blood type and screen, and additional cultures (eg, urine, spinal fluid, cutaneous abscess, joint), depending on the patient's history, physical examination findings, and ability to tolerate the procedure.

Perform blood gas analysis with measurement of serum lactate levels (variably increased with tissue hypoperfusion) and ionized calcium levels (decreased in some cases of sepsis, can lead to refractory shock). In general, venous specimens are adequate. Obtain a chest radiograph, which may reveal infiltrates, cardiomegaly, or findings of acute respiratory distress syndrome.

Differential Diagnosis

The priority is recognizing shock early, while it is in the compensated stage. Viral, bacterial, and other infectious agents may cause fever and tachycardia in the absence of actual shock. In general, the pulse increases by approximately 9 beats per degree Celsius of temperature increase. The differential diagnosis for categories of shock is summarized in Table 13–1.

Volume Loss

Vomiting and diarrhea, along with inadequate oral intake, are common symptoms of hypovolemic shock (hypovolemia is a component of other forms of shock, as well). Hemorrhage, including hemorrhage from accidental or inflicted trauma, is another important etiology. Typical signs include decreased pulse, dry mucosal surfaces, delayed capillary refill time, decreased skin turgor, decreased urine output, and late tachycardia and hypotension.

Table 13–1. Differential Diagnosis for Types of Shock	
Diagnosis	**Clinical Features**
Sepsis	Fever Poor response to fluid administration Widened pulse pressure (warm shock)
Hypovolemia	Delayed capillary refill time Dry mucosal surfaces History of fluid loss, poor oral intake, bleeding (including internal intravascular loss) Vital signs responsive to fluid bolus(es)
Cardiogenic shock	Cardiac gallop Cardiomegaly on radiographs Hepatomegaly Rales, worsening with fluid bolus(es)
Other shock types (ie, neurogenic, obstructive, anaphylactic)	History of blunt trauma with dyspnea: obstructive shock History of exposure with rash: anaphylactic shock History of trauma with paralysis: neurogenic shock

Sepsis

Sepsis is the most commonly encountered form of shock in pediatrics. The patient may present with fever (or hypothermia) and signs and symptoms of infection (eg, cough, congestion, vomiting, diarrhea, rash). Because sepsis may manifest hypovolemic and distributive components (low vascular tone), as well as myocardial depression, a mixed clinical picture is often seen.

Cardiogenic Shock

The typical findings of cardiogenic shock are tachypnea, dyspnea, tachycardia, rales, hepatomegaly, jugular venous distention, and cardiac murmurs and gallops. Cardiomegaly and poor or delayed pulse may also be seen. Causes include congenital heart lesions, myocarditis, persistent dysrhythmias, and high-outflow conditions (anemia, vascular malformations).

Anaphylactic Shock

A patient with anaphylactic shock presents with a multisystem disturbance (ie, difficulty breathing, adventitious sounds, poor aeration, vomiting, hypotension), with or without an urticarial eruption, often in the setting of exposure to a suspected trigger.

Neurogenic Shock

Neurogenic shock involves a spinal cord injury, which leads to sympathetic denervation of the vascular bed. Warm extremities from vasodilation and relative or absolute bradycardia accompany hypotension refractory to the delivery of fluid boluses. If seen, start vasopressor support early.

Obstructive Shock

Obstructive shock is caused by impeded venous return secondary to pneumothorax, hemothorax, pericardial tamponade, or right ventricular outflow obstructive lesions. Heart and/or lung sounds may be diminished, low voltages may be seen on the electrocardiogram, and pulsus paradoxus may be noted. Distended neck veins and tracheal deviation away from the side of tension pneumothorax may also be seen.

Treatment

Early in the care process, consult with a critical care specialist or initiate transfer of the patient to a tertiary care center. For all forms of shock, initial management includes the CABs (chest compressions, airway, and breathing), including establishing and maintaining an airway, providing oxygen and ventilatory support, and securing 2 sites of vascular access (peripheral venous, intraosseous [IO], central venous). If there is concern for sepsis, administer broad-spectrum intravenous (IV) antibiotics, such as vancomycin (15 mg/kg every 8 hours or every 6 hours if meningitis is suspected, with a 4-g/d maximum) *and* ceftriaxone (50 mg/kg, or 75 mg/kg if meningitis is suspected, by administering a dose every 8 to 12 hours, with a 12-g/d maximum). However, do not delay the administration of antibiotics if the patient is too unstable to have all indicated cultures obtained (ie, lumbar puncture) or if there is difficulty obtaining vascular access for blood culture. See Chapter 66, Sepsis, for the antibiotic coverage for an immunocompromised patient. Narrow the antimicrobial coverage after culture and susceptibility data are available.

Hypovolemic, Septic, and Other Etiologies With the Component of Hypovolemia

Immediately begin rapid volume resuscitation using a balanced crystalloid solution (lactated Ringer). Deliver boluses of 20 mL/kg over 10 to 15 minutes by using a push-pull technique or rapid infuser systems, because IV infusion pumps cannot provide the crucial rate for a patient in shock. If critical care–level support is available (positive pressure ventilation, inotropes), strive to achieve resuscitation by using a "golden hour" approach, which minimizes delays between fluid boluses and reassessments. This is associated with decreased mortality and involves the delivery of rapid volume boluses, followed by rapid reassessments. Attempt to normalize capillary refill time, pulse, mental status, and blood pressure, but maintain ongoing monitoring for signs of volume overload (rales, jugular venous distention, hepatomegaly). Control the patient's temperature with antipyretics, when possible. If critical care is not

readily available, be judicious with fluid administration to prevent morbidity secondary to volume overload.

If hypotension persists or develops in the absence of ongoing losses, despite the infusion of 60 mL/kg of crystalloid fluids, the patient may benefit from further crystalloid resuscitation. As much as 80 to 100 mL/kg is at times necessary to reverse shock, particularly in a patient with septic shock. After 3 boluses, consult with an intensivist, if not already done, to discuss the initiation of vasopressor support. Also, consider the need for steroids, even in a patient without chronic steroid use or history of adrenal insufficiency. Administer IV hydrocortisone as follows for fluid refractory shock: 0 to 3 years of age, 25 mg; > 3 to 12 years of age, 50 mg; and 12 years and older, 100 mg (100-mg maximum).

When pressors are necessary, administer epinephrine via a peripheral or central line, but do not delay administration pending central access. Start at 0.04 mcg/kg/min and titrate upward in increments of 0.02 mcg/kg/min every 5 minutes (1 mcg/kg/min maximum).

If the hemoglobin level is lower than 7 g/dL (70 g/L), consider blood product transfusion support to increase the oxygen-carrying capacity. Indications for intubation and mechanical ventilation include respiratory failure, poor airway protection in an obtunded patient, and unreversed shock despite the administration of fluid boluses and peripheral epinephrine infusion. Correct hypoglycemia, hypocalcemia, and disturbances in the patient's temperature.

Cardiogenic Shock

See Chapter 9, Arrhythmias and Electrocardiogram Interpretation; Chapter 10, Carditis: Endocarditis, Myocarditis, and Pericarditis; and Chapter 11, Congestive Heart Failure, for specific therapies for cardiogenic shock. Consult with a cardiologist or intensivist, who may recommend afterload-reducing inotropic support, such as milrinone (50–75 mcg/kg infused over 10–60 minutes, followed by delivery of 0.50–0.75 mcg/kg/min) or dobutamine (initial dose, 0.5–1 mcg/kg/min). For a neonate with a ductal-dependent congenital heart lesion or undifferentiated shock, administer a prostaglandin E infusion (alprostadil, 0.05–0.10 mcg/kg/min initially, followed by 0.01–0.05 mcg/kg/min). The patient is at risk for apnea, so prepare for potential intubation.

Anaphylactic Shock

If anaphylaxis is suspected, immediately administer intramuscular epinephrine (see Chapter 4, Anaphylaxis) into the lateral quadriceps. Repeat the dose every 10 to 15 minutes, as needed. If the response is inadequate, initiate a continuous epinephrine infusion (0.1–1 mcg/kg/min, 1 mcg/min maximum),

starting with the lowest dose and gradually titrating the infusion rate until the patient becomes normotensive. Continue to provide fluid and boluses as appropriate.

Obstructive Shock

Do not delay therapy while awaiting chest radiography. Perform lifesaving needle thoracentesis, evacuation of pericardial tamponade, or prostaglandin E infusion. Treat a pneumothorax with placement of an 18- or 20-gauge angiocatheter in the midclavicular line, second intercostal space (over the top of the third rib), followed by tube thoracostomy. Treat pericardial tamponade with volume support to increase preload, and if the patient is unresponsive to fluid administration, arrange for pericardiocentesis to be performed by a qualified physician.

Indications for Consultation

- **Cardiology:** Cardiogenic shock or obstructive shock from cardiac tamponade and need for urgent pericardiocentesis
- **Critical care specialist:** Fluid refractory shock
- **Infectious diseases:** Resistant or complex infections
- **Surgeon, intensivist, other qualified physician:** If central venous access is needed or if reliable IV access cannot be obtained promptly

Disposition

- **ICU transfer:** Fluid refractory shock, ongoing increased early warning score
- **Institutional transfer:** Need for ICU or specialist consultation not available locally
- **Discharge criteria:** Normal vital signs and adequate oral intake

Follow-up

- **Primary care:** 2 to 3 days
- **Infectious diseases:** 1 week if long-term antibiotic therapy is initiated

Pearls and Pitfalls

- Inadequate recognition of compensated forms of shock (persistent tachycardia being a prime example) is associated with time-dependent mortality. Early goal-directed therapy saves lives.
- Remain vigilant for tachycardia that is persistent and out of proportion to the patient's fever/temperature as a sign of continued shock and need for prompt treatment.

- A patient with persistently abnormal vital signs (tachycardia, wide pulse pressure) or impaired perfusion, even in the absence of hypotension or vasoactive infusion requirement, may require ICU transfer for close monitoring and additional resuscitation.
- Resuscitations that require multiple boluses of 20 mL/kg of crystalloid IV fluids are common. Do not hesitate to provide adequate resuscitation (even to 80–100 mL/kg) when critical care support is available, but reevaluate the vital signs and repeat the physical examination between boluses.
- Fluid bolus rates may exceed the volume capacity of existing IV access, necessitating additional line placement or IO access.
- Administer hydrocortisone with or without pressors for fluid refractory shock.
- Promptly attempt IO line placement if securing IV access is a problem.

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Syncope

Introduction

Syncope is the sudden, but brief, loss of consciousness and postural tone, which is then followed by a spontaneous recovery to baseline. It is relatively common in the pediatric setting, especially among female adolescents.

While syncope in children and adolescents is most often due to a benign etiology, careful attention is required to exclude potentially life-threatening causes, especially cardiac disease. However, the diagnostic yield of broad laboratory and imaging in pediatric syncope is relatively low, so use a thorough history and physical examination to guide testing.

Clinical Presentation

History

Obtain a detailed history of the syncopal event, including preceding events. A history of syncope that occurs during exercise or exertion is most concerning. Other preceding events that may be pertinent include abrupt postural changes, emotional incidents, startling incidents, significant pain, loud noises, chest pain, palpitations, light-headedness, dizziness, visual changes, nausea, pallor, diaphoresis, chronic or acute medications (and any recent dose changes), and whether the room was spinning. Note whether the patient was back to baseline when emergency medical services arrived or upon triage at the hospital.

A thorough past medical history (seizure disorder, diabetes, pregnancy, eating disorder) and family history can help guide the evaluation of a syncopal episode. Ask about any previous cardiac history, including congenital or acquired heart disease and arrhythmias. Note a family history of sudden or unexplained death, early cardiac death (at age < 50 years), heart disease (including arrhythmias), and epilepsy.

Inquire whether the syncopal episode was sudden, so that the patient abruptly fell to the ground, versus "melting," in which the patient knew they were going down.

Physical Examination

Perform a thorough physical examination, including orthostatic vital signs, cardiac auscultation, and a complete neurological examination.

Laboratory Testing

Most patients who are admitted either have not returned to baseline or have a worrisome history suggestive of cardiac disease (eg, episode occurred during physical activity). In such cases, obtain a serum glucose, hematocrit, urine pregnancy test (if relevant), and urine toxicology testing. If there is a concern for cardiac pathology, obtain an electrocardiogram and arrange for an echocardiogram. Obtain neurological imaging (head computed tomography) if the syncope resulted in significant head injury or if focal findings or signs of intracranial hypertension are noted on the neurological examination. An electroencephalogram is indicated only if a seizure disorder is likely.

Differential Diagnosis

Most causes of syncope are benign (eg, vasovagal, breath-holding spells, orthostatic). Signs and symptoms suggesting a serious disease include presentation during exercise, prolonged episode (> 30 minutes), hemodynamic instability, and seizure activity (more than a few myoclonic jerks that can occur with any loss of consciousness). The differential diagnosis is summarized in Table 14–1.

Table 14–1. Differential Diagnosis of Syncope

Diagnosis	Clinical Features
Cardiac Arrhythmias	
Arrhythmogenic right ventricular cardiomyopathy	Age > 10 y Palpitations
Brugada syndrome	Pseudo–right bundle branch block Persistent ST segment elevation in leads V1 to V3 Uncommon arrhythmic events (more likely with fever)
Congenital short QT syndrome	QT interval ≤ 0.30 s May present with atrial fibrillation
Long QT syndrome	Acquired: eating disorders Congenital: other family members affected May be associated with congenital deafness Prolongation of QTc > 450 ms May present as an afebrile seizure
Structural Heart Disease	
Coronary artery anomalies	Presents with exertion
Dilated cardiomyopathy	Causes: viral myocarditis, severe anemia, muscular dystrophy
Hypertrophic cardiomyopathy	Most common cause of sudden death during exercise Autosomal dominant Presents with exertion

Table 14–1. Differential Diagnosis of Syncope, continued	
Diagnosis	**Clinical Features**
Neurologic	
Migraine syndrome	Headache May be associated with nausea, ataxia, vertigo
Seizure	Loss of consciousness and postural tone Can last longer than a typical syncopal episode May have an aura and postictal phase May have prolonged tonic-clonic activity May have incontinence
Vasovagal syncope	Most common cause Precipitating events include standing and stress Prodrome: light-headedness, dizziness, visual changes, nausea, pallor, and diaphoresis
Psychogenic/Situational	
Breath-holding spells	Age: 6–24 mo Preceding emotional event (eg, pain, anger, fear) May be cyanotic or pallid Brief posturing or tonic-clonic activity may occur
Heat illness	Usually associated with exercise (long-distance race or workout) Febrile and diaphoretic
Hyperventilation	Associated with emotional stress Chest pain, chest tightness, shortness of breath Light-headedness, paresthesias of distal extremities
Hysteria/conversion disorder	Most common among adolescents Usually an audience is present No hemodynamic or autonomic changes Can be prolonged
Reflex	
Orthostatic hypotension	Occurs upon standing or change in posture Causes: volume depletion, anemia, anorexia nervosa, pregnancy, medications
Postural tachycardia syndrome	Most common in female adolescents Excessive increase in heart rate occurring on standing without hypotension Anxiety, palpitations, dizziness, tremulousness
Other	
Hypoglycemia	Most commonly occurs in insulin-dependent patients with diabetes Pallor, diaphoresis Agitation, confusion, altered mental status

Treatment

Focus the treatment on the underlying pathologic etiology, if any. For the most common cause of syncope in children (ie, vasovagal syncope), advise the patient and family to increase oral hydration, add salt-based snacks, avoid caffeinated drinks, and practice venous pooling prevention techniques (eg, slightly bending knees with prolonged standing, folding of arms, crossing legs).

Indications for Consultation

- **Cardiology:** Concern for cardiovascular disease, persistence of syncopal episodes even after adherence to nonpharmacological treatment
- **Neurology:** Findings or history concerning for seizure, prolonged episode

Disposition

- **Intensive care or subspecialty unit transfer:** Hemodynamic instability, concern for serious cardiovascular disease, persistent abnormal neurologic findings
- **Discharge criteria:** Baseline mental status and neurological examination findings

Follow-Up

- **Primary care:** 4 to 7 days
- **Subspecialists involved in care during hospitalization:** 1 to 2 weeks

Pearls and Pitfalls

Cardiac etiology for syncopal events should always be at the top of the differential list as it can be life-threatening if not diagnosed and treated promptly. Syncopal events that occur with exertion should be especially concerning for a cardiac etiology.

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Dermatology

CHAPTER 15

Erythema Multiforme, Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, and *Mycoplasma pneumonia*–Induced Rash and Mucositis

Introduction

Erythema multiforme (EM), Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), and *Mycoplasma*-induced rash and mucositis (MIRM) are relatively uncommon, distinct disorders of the skin and mucous membranes. Classic EM involves the skin only, whereas SJS/TEN always affects the skin and mucous membranes. MIRM is now the proper terminology when a *Mycoplasma* infection causes a mucocutaneous eruption, as the clinical features are distinct from SJS/TEN. MIRM always involves the mucous membranes and may occur with or without skin involvement. EM is thought to be a postinfectious process, with herpes simplex virus (HSV) being the most well-documented trigger. Both SJS and TEN are considered variants of the same hypersensitivity disorder, with epidermal detachment of less than 10% of the body surface area (BSA) defined as SJS, more than 30% of the BSA defined as TEN, and between 10% and 30% of the BSA defined as SJS/TEN. MIRM involves immune complex deposition, which is a notably different mechanism from that of SJS/TEN. MIRM tends to involve less than 10% of BSA.

Drugs are the cause of most cases of SJS/TEN, although infections and autoimmune diseases may also be triggers. Many drugs have been implicated, but the most common are sulfonamides, anticonvulsants, β-lactam antibiotics, and nonsteroidal anti-inflammatory drugs (NSAIDs).

SJS/TEN typically resolves over a 4- to 6-week period, but the mortality rate remains high at 5% to 30%, with many more patients experiencing long-term morbidities. Early recognition and prompt withdrawal of the causative agent increases patient survival. Generally, the course of MIRM tends to be shorter and less severe than that of EM and SJS/TEN, although recurrent disease can occur in up to 20% of patients, and there may be long-term mucosal morbidity.

Clinical Presentation

History

A patient with EM typically presents with a mildly pruritic rash in association with a prodrome of mild, nonspecific systemic symptoms, such as fever, cough, and rhinorrhea.

SJS/TEN presents with pronounced constitutional symptoms, such as high fever and malaise, along with cutaneous rash and discomfort or poor oral intake related to mucous membrane lesions. The disease typically develops within 2 to 8 weeks of exposure to the offending agent.

A patient with MIRM will present with severe mucositis of multiple sites, resulting in poor oral intake and pain. Prodromal symptoms of cough, fever, and malaise precede mucocutaneous symptoms by approximately 1 week.

Physical Examination

The prototypic EM lesion is a 1- to 3-cm erythematous, edematous plaque that develops a dusky vesicular, purpuric, or necrotic center. Often there is also an edematous ring of pallor surrounded by an erythematous outer ring (the target lesion). In many cases the typical target is not seen, and only the first 2 zones are present. The lesions are typically distributed symmetrically and acrally, predominantly on extensor surfaces. They may also be present on the trunk, palms, soles, and face. The patient may have a low-grade fever, as well as mild extremity and/or facial edema.

A patient with SJS/TEN typically has a high fever and appears ill. The cutaneous lesions are more likely to occur on the face and trunk than in classic EM, and they are more often reported as painful or burning. They also tend to be macular, predominate on the trunk, may be coalescent, and often exhibit the Nikolsky sign, which is positive when slight rubbing of the skin causes exfoliation of the outermost layer. Epidermal detachment may occur but does not typically involve more than 10% of the BSA. If more than 10% of the BSA is involved, then SJS/TEN is likely. Mucosal lesions (≥ 2 sites) are requisite for a diagnosis of SJS/TEN and are characterized by erythema and bullae that become confluent with pseudomembrane formation. The mucous membrane lesions are typically hemorrhagic in appearance, which is not the case in EM. Oral lesions may extend to the respiratory mucosa, and complications may include pneumonitis and respiratory failure. Ophthalmologic findings include conjunctivitis, keratitis, and uveitis. Less commonly, urethritis or diarrhea can occur.

MIRM is characterized by more prominent mucositis than SJS/TEN. Cutaneous involvement is sparse and tends to be acral. When a rash is present,

Nikolsky sign and desquamation are typically absent. Mucosal lesions are usually hemorrhagic or ulcerative and are often painful.

Laboratory Workup

EM, SJS/TEN, and MIRM are clinical diagnoses. If SJS/TEN or MIRM is suspected, obtain a complete blood cell count, comprehensive metabolic panel, and urinalysis. The patient may have a leukocytosis or leukopenia and thrombocytosis, while eosinophilia is common in drug-related cases. There may be associated hypoalbuminemia, increased liver transaminase levels, electrolyte imbalances (hypernatremia, hyponatremia, acidosis), and increased blood urea nitrogen and creatinine levels. Pyuria indicates urethritis. The clinical picture is usually clear, but if there is diagnostic uncertainty, a skin biopsy can rule out other diagnoses. In EM, there is more dermal inflammation and individual keratinocyte necrosis when compared to SJS/TEN or MIRM, which have minimal inflammation and sheets of epidermal necrosis. If MIRM is suspected, obtain polymerase chain reaction for *Mycoplasma*.

Differential Diagnosis

EM is most often confused with urticaria. Other common diagnostic possibilities include drug eruptions, urticarial vasculitis, and viral exanthems. The diagnosis of SJS/TEN or MIRM is usually evident but may be confused with DRESS (drug reaction with eosinophilia and systemic symptoms). However, a patient with DRESS often has dramatic facial edema and more internal organ involvement (liver, kidney, lungs), without significant mucous membrane involvement. Other entities to consider include Kawasaki disease, bullous pemphigoid, bullous drug eruption, linear immunoglobulin A dermatosis, erythema annulare centrifugum, staphylococcal scalded skin syndrome, serum sickness, herpetic gingivostomatitis, and Behçet syndrome (Table 15–1).

Treatment

Treatment of EM is supportive, and its course is usually self-limited over 1 to 2 weeks. Treat the underlying cause (if identified) and discontinue nonessential medications. Topical treatments are typically not helpful. There may be recurrences, particularly of HSV-associated EM.

The treatment of SJS/TEN and MIRM is also primarily supportive, including meticulous skin care, intravenous (IV) hydration and nutrition, provision of adequate analgesia, and monitoring for complications, such as fluid or

Table 15–1. Differential Diagnosis of Stevens-Johnson Syndrome

Diagnosis	Clinical Features
Behçet syndrome	Uncommon in children Discrete genital ulcers Recurrences common
Bullous drug eruption	No systemic symptoms
DRESS	Facial edema Limited mucous membrane involvement Eosinophilia Lesions predominate on extremities and face
Herpetic gingivostomatitis	Fever and oral lesions only No cutaneous eruption
Kawasaki disease	Discrete oral lesions uncommon Nonexudative conjunctivitis, strawberry tongue Edema of the hands and feet
Serum sickness	Arthralgia common No bullae or Nikolsky sign
Staphylococcal scalded skin syndrome	Diffuse, painful erythroderma No discrete oral lesions Fissuring and crusting of the perioral area

Abbreviation: DRESS, drug reaction with eosinophilia and systemic symptoms.

electrolyte abnormalities, secondary bacterial infection, severe hepatitis, and ocular and/or airway involvement. Ocular involvement requires ophthalmology consultation, and a Foley catheter may be necessary if there is urethral involvement. Provision of adequate nutrition in the form of enteral feedings and/or total parenteral nutrition can prevent a catabolic state and may improve outcome. While clear treatment guidelines are lacking, rapid withdrawal of the offending agent(s) and optimal management of nutrition and denuded skin areas improve outcomes. Therefore, early recognition of the disease is critical. Systemic corticosteroids, IV immunoglobulin, plasmapheresis, cyclosporine, immunomodulators, and biologics have all been tried, but their effectiveness has not been proven, and their use remains controversial. Consult a dermatologist to determine if any immunomodulating treatment is indicated. Give appropriate antibiotics for specific identified infections, such as *Mycoplasma*.

Indications for Consultation

- **Dermatology:** Suspected SJS, SJS/TEN, TEN, or MIRM
- **Ophthalmology:** Suspected SJS, SJS/TEN, TEN, or MIRM
- **Urology:** Suspected urethral/meatal involvement
- **Burn specialist:** Extensive disease or more than 10% epidermal detachment

Disposition

- **Intensive care unit transfer:** Extensive amount of BSA affected, respiratory mucosa involvement (risk of respiratory failure and loss of airway)
- **Burn unit:** Extensive disease or more than 10% BSA epidermal detachment
- **Discharge criteria:** Improving clinical condition, adequate oral intake

Follow-up

- **Dermatology:** 3 to 5 days
- **Primary care:** 1 to 2 weeks
- **Ophthalmology:** 3 to 5 days (if ocular involvement present)

Pearls and Pitfalls

- Discontinue any suspected etiologic agent immediately and avoid known precipitants while the patient is hospitalized (eg, NSAIDs).
- Use of specific treatment agents remains controversial and must be done in consultation with a dermatologist.
- Consult a burn specialist and/or pediatric intensivist for severe disease.
- A patient with SJS/TEN or MIRM is at risk for long-term, severe ophthalmic sequelae (corneal ulceration and blindness). Involve an ophthalmologist at the time of admission for such all patients.

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CHAPTER 16

Rashes Associated With Serious Underlying Disease

Introduction

Rashes associated with acute illnesses are common in children. However, there are a few that can be associated with serious diseases that can have significant morbidity and mortality. These include erythroderma, some cases of cellulitis, petechiae/purpura, target lesions, and vesicles/bullae.

Clinical Presentation

History

Obtain a thorough description of the evolution of the rash. Determine when and where it started, the initial appearance and any change, and the pattern of spread (eg, from head to trunk or from hands to trunk). Note if the rash is painful or pruritic.

Ask about associated symptoms, such as the duration and intensity of any fever, fatigue, irritability, headache, sore throat, myalgia, arthralgia, abdominal pain, vomiting, and diarrhea. Document the patient's immunization status and whether they are currently taking or were recently taking any medication and whether there has been any travel, exposure to animals, bites, or contact with sick persons.

Physical Examination

Determine the size and morphology of the rash. Flat lesions smaller than 0.5 cm are called *macules;* raised lesions of similar size are *papules.* Vesicles are lesions filled with fluid; if the fluid is purulent, the lesions are *pustules.* Lesions that do not blanch suggest bleeding into the skin and are called *petechiae, purpura,* or *ecchymoses,* depending on the size.

Document the distribution of the rash. Assess the patient for desquamation and the Nikolsky sign (separation of the epidermis from the dermis with light pressure), which occurs in staphylococcal scalded skin syndrome (SSSS), toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and various bullous disorders.

Examine all of the mucous membranes (throat, lips, buccal mucosa, conjunctiva, urethra, and anus) and look for vesicles, crusting, erythema, or other abnormalities. Note if there is any eye involvement, such as conjunctival injection, purulent discharge, and abnormalities of the cornea or iris.

Look for edema of the face and/or extremities and check for lymphadenopathy and hepatosplenomegaly.

Laboratory Workup

Obtain a complete blood cell count (CBC) with differential, as well as a complete metabolic panel to assess renal and liver function. If vasculitis is suspected, order a urinalysis to look for hematuria, pyuria, and proteinuria. If the patient is ill appearing, also obtain a C-reactive protein level and/or procalcitonin, blood culture, coagulation panel, D-dimer level, and fibrinogen level. In addition, collect cultures from any suspected sites of infection, such as skin, cerebrospinal fluid, and urine. Further bacterial or viral testing may be necessary, depending on the clinical picture. If lupus is suspected, order a rheumatologic panel that includes antinuclear antibodies, anti–double-stranded DNA, anti-Smith antibodies, and antiphospholipid antibodies. In some cases, a skin biopsy can be diagnostic.

Radiology Examinations

If Kawasaki disease (see Chapter 59) or multisystem inflammatory syndrome in children (see Chapter 65) is suspected, order an echocardiogram.

Differential Diagnosis

Classify the rash according to its morphologic appearance and distribution (Table 16–1).

The differential diagnosis includes infectious exanthems, which often have characteristic features. For example, measles typically presents with a red maculopapular rash that begins on the face and moves down the body, becoming confluent (or *morbilliform,* ie, measles-like), in association with fever, cough, coryza, and conjunctivitis. Scarlet fever is characterized by a red, diffuse, sandpapery rash with accentuation in the flexion creases (Pastia lines), fever, and pharyngitis. Epstein-Barr virus may cause a maculopapular rash that is predominantly truncal, along with fever, lymphadenopathy, pharyngitis, and splenomegaly. The differential diagnosis is summarized in Table 16–2.

Treatment

Institute airborne, contact, and/or droplet precautions, as appropriate, if an infectious etiology is being considered in an ill-appearing patient.

The treatment of erythema multiforme (Chapter 15), Henoch-Schönlein purpura (HSP) (Chapter 57), Kawasaki disease (Chapter 59), and SJS (Chapter 15) is detailed elsewhere.

Table 16–1. Serious Rash Morphologic Appearances

Rash Type	Description	Possible Diagnoses
Erythema: Areas of Significant Redness		
Erythroderma	Diffuse erythema (looks like sunburn) Pruritus, desquamation Large percentage of body surface involved	Drug reaction Kawasaki disease MIS-C TSS Viral or bacterial sepsis
Painful erythema	Localized erythema that spreads rapidly Severe pain, may be out of proportion to physical findings	Necrotizing fasciitis SSSS TEN
Bleeding Into the Skin		
Petechiae	Pinpoint (< 2-mm), nonblanching, round macules Not palpable	*Hematologic/oncologic:* ITP, leukemia *Infectious:* sepsis (meningococcal, staphylococcal, streptococcal), RMSF, other viral, bacterial, and fungal causes *Vasculitis:* HSP, SLE *Trauma:* accidental, inflicted
Purpura	2-mm to 1-cm nonblanching spots May be palpable	
Ecchymoses	> 1-cm nonblanching spots May be palpable	
Target Lesions: Round or Oval Macules With Red Edges and Clearing or Dusky Centers		
	Circular/ovoid macules with erythematous periphery and clearing centers, which can become vesicular or dusky Symmetrical eruption Can involve the palms of the hands and soles of the feet Minimal epidermal detachment (< 10% BSA)	EM SJS: atypical targetoid lesions
Vesicobullous Lesions: Blisters Filled With Clear, Nonpurulent Fluid **Vesicle, < 1-cm Diameter; Bullae, > 1-cm Diameter**		
	Characteristically on the face and/or trunk Mucosal involvement of the lips, mouth, nose, conjunctiva, genitals, and rectum (+) Nikolsky sign Initially may be erythematous macules or atypical targetoid lesions which progress to vesicles and bullae May become pustular Painful	SJS TEN
	Initial erythema progressing to fragile bullae Prominent on flexural surfaces No mucosal involvement (+) Nikolsky sign May become pustular Painful	SSSS

Continued

Table 16–1. Serious Rash Morphologic Appearances, continued		
Rash Type	**Description**	**Possible Diagnoses**
	Erythroderma or morbilliform rash, progressing to vesicles, bullae, and/or purpura Head-to-toe progression May involve the mucous membranes Prominent facial and periorbital edema	DRESS
	Similarly sized, clustered vesicles on an erythematous base, usually in areas of eczema Vesicles become hemorrhagic erosions and/or pustules History of skin diseases that can alter the skin barrier	Eczema herpeticum

Abbreviations: BSA, body surface area; DRESS, drug reaction with eosinophilia and systemic symptoms; EM, erythema multiforme; HSP, Henoch-Schönlein purpura; ITP, idiopathic thrombocytopenic purpura; MIS-C, multisystem inflammatory syndrome in children; RMSF, Rocky Mountain spotted fever; SJS, Stevens-Johnson syndrome; SLE, systemic lupus erythematosus; SSSS, staphylococcal scalded skin syndrome; TEN, toxic epidermal necrolysis; TSS, toxic shock syndrome.
+ indicates a positive finding.

Table 16–2. Differential Diagnosis of Serious Rashes	
Clinical Features	**Differential Diagnosis**
Drug Reaction With Eosinophilia Syndrome and Systemic Symptoms	
Eruption begins 2–6 wk after starting the inciting drug (eg, antiepileptics, sulfonamides) Symmetrical erythroderma or morbilliform rash becomes vesicular and/or purpuric Triad of fever, rash, and internal organ involvement May have lymphadenopathy (cervical or generalized), pharyngitis, and/or facial swelling Eosinophilia, atypical lymphocytosis May have abnormal LFT and TFT results and abnormal renal function	Acute generalized exanthematous pustulosis Infectious mononucleosis Leukemia Lymphoma Reactivation of HHV-6 SJS/TEN Viral syndrome
Eczema Herpeticum	
History of eczema or other skin disease Fever Uniform-sized papulovesicles on an erythematous base, which progress to erosions and crusting Laboratory workup: PCR, viral culture, Tzanck smear May have keratoconjunctivitis or secondary bacterial infection	Acute generalized exanthematous pustulosis Other viral infections: coxsackie, disseminated zoster, varicella Superinfected eczema

Table 16–2. Differential Diagnosis of Serious Rashes, continued

Clinical Features	Differential Diagnosis
Erythema Multiforme	
Symmetrical distribution of target lesions Usually involves palms of the hands and soles of the feet in a symmetrical distribution Palpable Mucosal involvement may be seen; usually only the lips and oral cavity	Drug reaction Kawasaki syndrome Mycoplasma Other hypersensitivities (drug reaction, SJS) TEN Urticaria Vasculitis Viral syndrome, especially herpes simplex
Henoch-Schönlein Purpura	
Patient usually < 7 y old Initial maculopapular or urticarial rash Usually progresses to palpable purpura of lower extremities and buttocks Afebrile May have arthralgia/arthritis, hematuria, and/or abdominal pain May develop ileoileal intussusception	Acute abdomen Drug reaction EM ITP JIA Meningococcemia Other vasculitis RMSF SLE
Idiopathic Thrombocytopenic Purpura	
Patient 2–5 y of age, well appearing History of viral infection or viral immunization 1–6 wk prior Petechiae and ecchymoses (nonpalpable) Bleeding and bruising with minimal or no trauma No generalized lymphadenopathy or hepatosplenomegaly ↓ Platelet count of normal or increased size Normal WBC, Hgb level, reticulocyte count, and MCV	Aplastic anemia Collagen vascular disease Drug reaction EBV HIV Inflicted trauma Leukemia
Kawasaki Disease	
Patient usually < 5 y of age Fever > 5 d with marked irritability Polymorphic eruption with late desquamation Cracked lips, strawberry tongue, edema of the dorsum of the hands/feet, nonpurulent conjunctivitis with limbic sparing, cervical lymphadenopathy	Adenovirus Drug reaction JIA MIS-C Scarlet fever Serum sickness SSSS TSS Viral infection: enterovirus, EBV, parvovirus

Continued

Table 16–2. Differential Diagnosis of Serious Rashes, continued

Clinical Features	Differential Diagnosis
Meningococcemia	
Fever with rapid progression to toxicity and possible vascular collapse Petechiae and palpable purpura, particularly of distal extremities	Bacterial sepsis HSP Kawasaki disease Leptospirosis RMSF Vasculitis Viral infection
Multisystem Inflammatory Syndrome in Children	
Hypotension Abdominal pain, nausea, vomiting Diffuse nonspecific rash Edema and/or erythema of hands and feet Dry, red lips and/or other mucosal changes Arrhythmia, myocarditis, pericarditis Fever with elevated inflammatory markers Abnormalities in 2 or more organ systems Positive COVID-19 PCR or serology, or exposure to SARS-CoV-2 within the past 4 weeks	Kawasaki disease Sepsis TSS Viral syndrome
Necrotizing Fasciitis	
Rapidly progressing cellulitis with severe pain level out of proportion to the visible lesion Becomes edematous, with bullae, areas of hemorrhage, necrosis, and/or erythroderma Fever, marked toxicity, hypotension, altered mental status Worsens despite antibiotics	Severe cellulitis Other soft-tissue infection
Rocky Mountain Spotted Fever	
Erythematous macules beginning on the wrists and ankles Rash spreads centrally, becoming petechial and purpuric Illness may begin with headache, myalgia, malaise, GI complaints Patient may have a history of tick bite (60% of cases) Hyponatremia, thrombocytopenia, transaminitis	Enterovirus Encephalitis Kawasaki disease Meningococcemia Mycoplasma Secondary syphilis *Streptococcus* Viral syndrome
Staphylococcal Scalded Skin Syndrome	
Initial erythema progressing to fragile bullae, especially prominent on the flexion creases Fever Fissures around the eyes, nose, and mouth *without mucous membrane involvement* (+) Nikolsky sign	Epidermolysis bullosa Nutritional deficiency Pemphigus Scalding burn TEN TSS

Table 16–2. Differential Diagnosis of Serious Rashes, continued

Clinical Features	Differential Diagnosis
Systemic Lupus Erythematosus	
Erythema over the nose and cheeks, spreading in a butterfly distribution Fever, myalgia, fatigue, headache, arthralgia, behavioral changes Arthritis, pleuritis, pericarditis (+) ANA, anti–double-stranded DNA, antiphospholipid antibodies, anti-Smith antibodies	Fibromyalgia Lymphoma Malignancies Rheumatologic diseases Viral syndrome
Toxic Epidermal Necrolysis/Stevens-Johnson Syndrome	
Triggers include new medications started in the past month (antiepileptics, sulfonamides, β-lactams, macrolides) and infections (herpes simplex, mycoplasma) Symmetrical purpuric/erythematous/targetoid macules and bullae that coalesce Rapid progression to detachment of the epidermis, exposing the underlying raw, red skin Epidermal detachment < 10% in SJS, 10%–30% in SJS/TEN overlap, > 30% in TEN Hemorrhage, crusts, and erosions on multiple mucosal surfaces (lips, tongue, buccal mucosa, rectum, genital mucosa) Conjunctivitis, keratitis, uveitis (+) Nikolsky sign ↑ Liver transaminase levels, CRP level/ESR, hypoalbuminemia Hematuria/proteinuria	Acute generalized exanthematous pustulosis Bullous disorder Burns Chikungunya Drug eruption Epidermolysis bullosa EM Graft vs host disease Kawasaki syndrome SSSS
Toxic Shock Syndrome	
May be staphylococcal or streptococcal Prodrome of malaise and myalgia, followed by vomiting, diarrhea, altered mental status Diffuse macular erythroderma Fever, hypotension, tachycardia, multiorgan failure Mucous membrane involvement Desquamation 1–2 wk later, especially of the palms and soles ↑ Platelet count and fibrinogen and albumin levels ↓ Liver transaminase levels, D-dimer levels, CRP levels/ESR, CPK levels, BUN/Cr levels	Drug reaction Kawasaki disease Leptospirosis Meningococcal infection MIS-C RMSF, or other tick-borne disease Septic shock SJS/TEN Typhoid fever Viral syndrome

Abbreviations: ANA, antinuclear antibodies; BUN, blood urea nitrogen; CPK, creatine phosphokinase; Cr, creatinine; CRP, C-reactive protein; EBV, Epstein-Barr virus; EM, erythema multiforme; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; Hgb, hemoglobin; HHV-6, human herpesvirus 6; HSP, Henoch-Schönlein purpura; ITP, idiopathic thrombocytopenic purpura; JIA, juvenile idiopathic arthritis; LFT, liver function test; MCV, mean corpuscular volume; MIS-C, multisystem inflammatory syndrome in children; PCR, polymerase chain reaction; RMSF, Rocky Mountain spotted fever; SJS, Stevens-Johnson syndrome; SLE, systemic lupus erythematosus; SSSS, staphylococcal scalded skin syndrome; TEN, toxic epidermal necrolysis; TFT, thyroid function test; TSS, toxic shock syndrome; WBC, white blood cell count.

+ indicates a positive finding; ↑, increased; ↓, decreased.

Drug Reaction With Eosinophilia and Systemic Symptoms Syndrome

For drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, immediately discontinue any medication that could be a possible etiology and treat the patient with prednisone (1–2 mg/kg/d) for at least a few weeks, followed by a slow taper. Transfer the patient to an intensive care unit (ICU) if there is significant hepatic, renal, or other systemic involvement.

Eczema Herpeticum

Treat eczema herpeticum with acyclovir, 5 to 10 mg/kg every 8 hours intravenously (IV), if the renal function is normal. Change to oral medication once no new lesions are erupting.

Idiopathic Thrombocytopenic Purpura

In idiopathic thrombocytopenic purpura (ITP), avoid medications that affect platelet function, such as nonsteroidal anti-inflammatories and salicylates. Consult a hematologist if the patient has bleeding other than petechiae and bruising or a platelet count less than 20,000/mm^3 (20×10^9/L).

Meningococcemia

Immediately obtain a blood culture and treat the patient with intravenous (IV) antibiotics, either ceftriaxone (100 mg/kg/d divided into doses administered every 12 hours, with a maximum of 2 g per dose and 4 g/d) or cefotaxime (200 mg/kg/d divided into doses administered every 6 hours, with a maximum of 12 g/d). Administer antibiotic prophylaxis to the patient's household and nursery or child care contacts, as well as persons who have contact with the patient's secretions. Options include a single dose of oral ciprofloxacin (> 1 month of age, 20 mg/kg; maximum, 500 mg), rifampin (< 1 month of age, 5 mg/kg taken orally twice a day for 2 days; > 1 month of age, 10 mg/kg taken orally twice a day for 2 days; maximum, 600 mg per dose), or a single dose of intramuscular ceftriaxone (125 mg if < 15 years of age; 250 mg if > 15 years of age).

Multisystem Inflammatory Syndrome in Children

See Chapter 65, Multisystem Inflammatory Syndrome in Children.

Necrotizing Fasciitis

In the event of necrotizing fasciitis, immediately consult a surgeon to perform debridement. Administer broad-spectrum antibiotics to prevent infection with aerobic and anaerobic organisms. Begin treatment with piperacillin/tazobactam, basing the dose on the piperacillin (< 2 months of age,

300–400 mg/kg/d divided into doses administered every 6 hours; 2–9 months of age, 240 mg/kg/d divided into doses administered every 8 hours; > 9 months of age, 300 mg/kg/d divided into doses administered every 8 hours; maximum dose, 16 g/d) *plus* vancomycin (if normal renal function, 15 mg/kg/d, with a maximum dose of 1,250 mg; < 13 years of age, administer a dose every 6 hours; > 13 years of age, administer a dose every 8 hours).

Rocky Mountain Spotted Fever

Treat a patient of any age with doxycycline (4.4 mg/kg/d divided into doses administered twice a day; maximum of 100 mg per dose). Transfer the patient to an ICU if unstable or if close monitoring is required.

Staphylococcal Scalded Skin Syndrome

Obtain a CBC and electrolyte levels. Culture any potential source of infection, such as the nasopharynx, conjunctiva, umbilicus, and diaper area. The bullae will be sterile, given that this is a toxin-mediated illness. Admit the patient to an ICU or burn unit and depending on the local antibiogram, treat with a penicillinase-resistant penicillin such as oxacillin or nafcillin (100–150 mg/kg/d administered every 6 hours, 12-g/d maximum), cefazolin (50–100 mg/kg/d administered every 6 hours, 60-g/d maximum), or linezolid (< 12 years of age, 10 mg/kg every 8 hours; ≥ 12 years of age, 600 mg every 12 hours; maximum, 600 mg per dose). In areas with high incidence of methicillin-resistant *Staphylococcus aureus*, administer vancomycin, as for necrotizing fasciitis.

Systemic Lupus Erythematosus

Defer treatment decisions to a rheumatologist (see Chapter 60, Systemic Lupus Erythematosus).

Toxic Epidermal Necrolysis

Admit the patient to a burn unit and treat like a severe burn, with meticulous skin care and aggressive fluid resuscitation. Place the patient in reverse isolation if the rash is extensive. Discontinue any medication that could be a possible cause.

Toxic Shock Syndrome

Obtain a CBC, blood cultures, electrolyte levels (including blood urea nitrogen and creatinine), liver function tests, D-dimer, fibrinogen, and prothrombin time/partial thromboplastin time. Admit the patient to an ICU and provide fluid resuscitation as needed. Treat with ceftriaxone (100 mg/kg/d divided into doses administered every 12 hours, with a maximum of 2 g per dose and

4 g/d), *and* clindamycin (40 mg/kg/d divided into doses administered every 6 hours; 4.8-g/d maximum) *and* vancomycin, as for necrotizing fasciitis. Remove any possible foreign bodies (tampons) and drain any infected wounds.

Indications for Consultation

- **Burn service:** TEN/SJS
- **Cardiology:** Kawasaki disease, MIS-C
- **Dermatology:** DRESS syndrome, eczema herpeticum, systemic lupus erythematosus (SLE), SSSS, TEN/SJS
- **Hematology:** ITP
- **Infectious diseases:** Meningococcemia, MIS-C, necrotizing fasciitis, TSS
- **Nephrology:** HSP
- **Ophthalmology (if the eyes are involved):** Eczema herpeticum, SLE, TEN/SJS
- **Rheumatology:** HSP (severe), MIS-C, SLE
- **Surgery:** Necrotizing fasciitis

Disposition

- **Burn unit:** TEN/SJS
- **Pediatric ICU:** Meningococcemia, MIS-C shock, TSS, necrotizing fasciitis, SSSS
- **Discharge criteria:** Nontoxic appearance, adequate oral hydration, no need for IV medication

Pearls and Pitfalls

- The distribution of the rash and the presence of mucosal involvement are often key features for determining the correct diagnosis.
- Rapid diagnosis and treatment are important. If the patient appears seriously ill, consult a specialist and treat the patient early.
- Some causes of rashes require notification of the local departments of health.
- Painful rashes can be a sign of severe underlying disease.

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CHAPTER 17

Skin and Soft-Tissue Infections

Introduction

Skin and soft-tissue infections (SSTIs) encompass a variety of disease processes that affect the dermis and subcutaneous layer of the skin. Most cases are caused by either *Staphylococcus aureus* or *Streptococcus pyogenes* (group A *Streptococcus*), and most patients admitted to the hospital present with cellulitis or abscess. Recently, there has been an increase in admissions attributable to SSTIs, particularly those caused by methicillin-resistant *S aureus* (MRSA). As a result, knowledge of local antibiotic susceptibilities is critical for proper evaluation and management of SSTIs.

Usually, an SSTI can be managed on an outpatient basis. Admitted patients generally have an atypical history, rapidly progressing infection, or extensive area or serious site of involvement; are unable to tolerate oral antibiotics; have not received the appropriate empirical antimicrobial coverage; or have signs of sepsis/systemic infection.

Clinical Presentation

History

Important considerations in SSTIs are immune status, exposure to animals, bite wounds, exposure to marine environments, possible foreign body, penetrating injuries, trauma, surgery, travel history, and current/recent country of residence. Assess the patient for MRSA risk factors, such as prior MRSA infection, MRSA nasal colonization, recent hospitalization, recent antibiotic use, a family member with previous MRSA infection, and local MRSA epidemiology.

Physical Examination

At presentation, SSTIs appear with a combination of erythema, warmth, induration, and pain/tenderness, and may be accompanied by fever, lymphangitis, or lymphadenitis. Cellulitis is specifically characterized by erythema, warmth, and tenderness, with poorly defined borders. It involves the deeper dermis and subcutaneous fat and lacks the fluctuance of an underlying suppurative focus. However, it may be a sentinel for a deeper or more complicated pyogenic infection, such as an abscess, fasciitis, or bone involvement. Erysipelas is a form of streptococcal cellulitis with sharply demarcated borders that typically affects the lower limbs and face.

A skin or subcutaneous abscess involves the dermis and deeper tissues. The superficial skin will usually have a warm, erythematous, tender nodule

or mass, often with underlying fluctuance. In some cases, a central superficial pustule may be seen. Purulent lesions and rapidly evolving infections are more commonly associated with MRSA.

Laboratory Workup

No laboratory tests are necessary if the patient is well appearing and immunocompetent. Blood cultures are rarely positive in uncomplicated SSTI and are not routinely indicated. However, obtain blood cultures if the patient is immunocompromised or if there is a high concern for sepsis or septic shock. Obtain a C-reactive protein level and/or an erythrocyte sedimentation rate if an underlying fasciitis or associated osteoarticular infection is possible. Obtain a Gram stain and bacterial culture of any abscess drainage, but do not perform a superficial swab for culture from intact skin or perform a needle aspirate for culture when there is no detectable abscess.

Radiology Examinations

In general, imaging is not needed. However, if the patient has a rapidly spreading cellulitis or if there is concern for deeper infection, order ultrasonography (US) to determine whether there is a drainable abscess. If there is concern for foreign body, perform screening US or plain-film radiography, but if the object is deep, the patient will likely need to undergo magnetic resonance (MR) imaging. Also perform MR imaging when there is a concern about fasciitis, pyomyositis, osteomyelitis, or a more extensive infection, or if the site of involvement is near a vital structure.

Differential Diagnosis

Generally, confirming the diagnosis of an SSTI is straightforward. However, there are a number of conditions with similar appearances that either are more serious or require different therapy (Table 17–1).

Treatment

General principles of management include closely monitoring the extent and progression of the infection by marking the margins of the affected area.

The first-line treatment for a fluctuant abscess is incision and drainage. Depending on the size of the wound and local practice, keep the abscess cavity open with either a drain or packing. Abscesses are more likely to be attributable to *S aureus*. Treat with a systemic antibiotic (see below) while awaiting culture identification and susceptibility results. Use warm compresses if an underlying abscess has not been drained.

Table 17–1. Differential Diagnosis of Skin and Soft-Tissue Infections

Diagnosis	Differentiating Features
Abscess	Well-demarcated, overlying erythema May be fluctuant or spontaneously draining
Bite wound (human or animal)	May be a puncture wound or an open wound Requires different empiric therapy to target animal or human oral flora and different management depending on location (eg, hand, face)
Cellulitis	Poorly demarcated macular or raised edges Erythematous and warm
Erysipelas	Well-demarcated or raised edges Extremely painful (St Anthony's fire)
Fungal infection (deep)	Superficial crusted lesion (papule, pustule, plaque) May have a dark discoloration (ecthyma) May have a history of foreign body at the same site
Hidradenitis suppurativa	Affects apocrine sweat glands or sebaceous glands Superficial pustules and deep follicular rupture May cause scarring and tract formation
Local allergic reaction (insect bite)	Pruritus Central punctum within the swelling Usually seen in skin not covered by clothing
Necrotizing fasciitis	Has a "wooden-hard" feel Painful edges with an anesthetic center Pain may be out of proportion Crepitus may be present
Necrotizing SSTI	Deeper and more devastating than cellulitis Constant pain, bullae, ecchymosis, systemic signs
Panniculitis	Inflammation of subcutaneous fat tissue Tender skin nodules or papules
Pyoderma gangrenosum	Pustule or lesion with surrounding edema Progresses to ulcerated lesion Associated with systemic disorders (leukemia)
Pyomyositis	Purulent foci within individual muscle groups Severe localized pain
Staphylococcal scalded skin syndrome	Diffuse erythematous rash with wrinkled appearance (+) Nikolsky sign

Abbreviation: SSTI, skin and soft-tissue infection.
+ indicates a positive finding.

The microbiology of SSTI is of particular importance in guiding specific antimicrobial management (Table 17–2). Because of the increasing prevalence of MRSA, use intravenous (IV) or oral clindamycin. However, if there is a significant rate of clindamycin resistance in the community (> 15%–20%) or if the patient has a history of frequent hospitalizations or clindamycin-resistant *S aureus*, administer oral or IV trimethoprim/sulfamethoxazole *and* a

first-generation cephalosporin (cefazolin) *or* a semisynthetic penicillin (nafcillin) for adequate *S pyogenes* coverage. Another option for MRSA coverage is oral or IV linezolid. Oral or IV doxycycline is an alternative in a patient who does not have severe or disseminated staphylococcal disease. If the organism identity and sensitivities are known, change to directed monotherapy.

If an apparent focal cellulitis or abscess fails to respond to the above choices for empirical antimicrobial coverage or if the patient is initially seriously ill or toxic, use IV vancomycin. Routine monitoring of vancomycin trough levels varies by institution but generally is not necessary in SSTIs. In cases of critical illness, failure to respond to therapy, or especially complicated infection (eg, extending to the central nervous system, endocarditis), consult with a hospital pharmacist or infectious diseases specialist to guide monitoring of drug levels. In serious staphylococcal infections, add empirical bactericidal coverage for methicillin-susceptible *S aureus*, either nafcillin or a first-generation cephalosporin, particularly if the involved site is near a vital structure.

For a septic-appearing patient, add ceftriaxone or cefepime to the staphylococcal coverage if there are concerns for gram-negative rod involvement (eg, environmental contamination or an immunocompromised host).

When a patient does not respond appropriately to antibiotics, perform imaging to look for a deeper source of infection, foreign body, or adjacent deep venous thrombosis. Start with US.

Indications for Consultation

- **Infectious disease:** Unusual exposures, immunocompromised patient, failure to respond to therapy, severe illness, institutional approval of certain antimicrobial agents
- **Pediatric surgery or interventional radiology:** Abscess drainage

Disposition

- **Intensive care unit transfer:** Sepsis or a severe disease, such as necrotizing SSTI, necrotizing fasciitis, or very large area of skin desquamation (such as in staphylococcal scalded skin syndrome)
- **Discharge criteria:** Afebrile or improving fever curve, stable or receding margins of involvement, tolerance of oral antibiotics or home IV therapy arranged

Follow-up

Primary care: 2 to 3 days to evaluate the continued response to treatment and removal of packing and/or drain (if placed)

Table 17–2. Common Antibiotics for Skin and Soft-tissue Infections[a]

Antibiotic	Usual Dose	Considerations
Cefazolin	100 mg/kg/d divided every 6–8 h Maximum: 1 g per dose or 3 g/d	Avoid in penicillin allergy
Cefepime	100 mg/kg/d divided every 12 h Maximum: 4 g/d	For possible gram-negative rod involvement
Ceftriaxone	100 mg/kg/day divided every 12 h Maximum: 4 g/d	For possible gram-negative rod involvement
Clindamycin	40 mg/kg/d divided every 6–8 h Maximum: 600 mg per dose or, if necrotizing, 900 mg per dose	Avoid if local resistance rate is > 15%–20%
Doxycycline	2–4 mg/kg/d divided every 12 h Maximum 100 mg per dose and 200 mg/d	Low risk of dental side effects when course is < 21 days
Linezolid	< 12 y: 30 mg/kg/d divided every 8 h > 12 y: 1,200 mg/d divided every 12 h Maximum: 600 mg per dose	Generally expensive, may require prior authorization May cause bone marrow suppression
Nafcillin	150 mg/kg/d divided every 6 h Maximum: 12 g/d, or 2 g per dose	Avoid in penicillin allergy
Trimethoprim/sulfamethoxazole	8–12 mg/kg/d divided every 12 h (dose based on trimethoprim component) Maximum: 320 mg/d of trimethoprim	Contraindicated in sulfa allergy Caution in glucose-6-phosphate dehydrogenase deficiency May cause rash or hypersensitivity reactions (eg, Stevens-Johnson syndrome)
Vancomycin	45–60 mg/kg/d divided every 6–8 h; use 60 mg/kg/d only if serious illness/shock Maximum: 3.6 g/d	May cause renal toxicity, monitor serum creatinine If necessary, target trough or area under the curve with pharmacy consult

[a] Consult local formulary for comprehensive dosing guidelines, as well as local hospital antibiogram for organism susceptibility in the hospital and/or community.

Pearls and Pitfalls

- Streptococcal cellulitis may be caused by a nephritogenic strain, placing the patient at risk for subsequent acute glomerulonephritis.
- Purulent cellulitis, where pustules or any purulent areas are present, is more often caused by *S aureus*.
- Clindamycin solution has good enteral bioavailability but may have an unpleasant taste. Ask the pharmacy to flavor it to improve patient adherence. Or, prescribe the capsules and have the parent sprinkle the contents onto a spoon of applesauce or pudding.
- Inducible clindamycin resistance may present as a recrudescence of symptoms after several days of improvement.

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Ear, Nose, Throat

CHAPTER 18

Mastoiditis

Introduction

Mastoiditis is a bacterial infection of the mastoid bone and air cells. It is the most common suppurative complication of acute otitis media (AOM), resulting in bone inflammation and destruction.

Acute mastoiditis can be categorized into acute mastoiditis with periostitis (purulent material in mastoid cavities) or coalescent mastoiditis (destruction of bony septa between mastoid air cells; may be followed by abscess formation). As infection progresses, the mastoid walls may be destroyed, causing spread to contiguous structures. This leads to complications such as subperiosteal abscess, Bezold abscess, intracranial abscess, facial nerve palsy, and/or venous sinus thrombosis.

The primary pathogen is *Streptococcus pneumoniae*, with *Hemophilus influenzae, Streptococcus pyogenes*, and *Staphylococcus aureus* (including methicillin-resistant *S aureus*) causing a minority of cases. Anaerobes, such as *Fusobacterium necrophorum*, are being identified more often, and *Pseudomonas aeruginosa*, though generally a contaminant, may be implicated in a patient with recurrent AOM or recent antibiotic use.

Clinical Presentation

History

Usually there is a history of AOM during the preceding 2 weeks. Typical complaints include fever (> 38.3 °C [> 101 °F]) along with headache, otalgia and/or otorrhea, pain over the mastoid process, and displacement of the pinna. A younger patient may have nonspecific complaints, such as irritability, anorexia, and fatigue. A patient with complications may also report hearing loss, vertigo, tinnitus, or symptoms associated with central nervous system disease.

Chronic mastoiditis may occur and can be subclinical or present with prolonged otorrhea and otalgia.

Physical Examination

In mastoiditis, the mastoid process and postauricular area are swollen, erythematous, tender (can be severe), and occasionally fluctuant. The auricle is displaced both anteriorly and inferiorly (or down and outward in a patient < 2 years of age), while the ipsilateral tympanic membrane frequently, but not always, shows signs of AOM (erythema, bulging, loss of landmarks).

With advanced disease, the neurologic examination is nonfocal, although in advanced disease, cranial nerve involvement may occur (most frequently cranial nerves VI and VII or the ophthalmic branch of cranial nerve V). As a result, the patient may have facial palsy, double vision, and/or transient hearing loss. Complications may also be associated with a palpable mass, meningeal signs, altered mental status, or a toxic appearance.

Laboratory Workup and Radiology Examinations

Mastoiditis can be diagnosed clinically. However, if the presentation is atypical, there is no response to antibiotics after 48 hours, or the patient has evidence of complications, perform computed tomography (CT) of the temporal bones. Plain mastoid radiographs are unreliable. Typical findings include clouding of the mastoid air cells and loss of the intermastoid cell septa secondary to the osteomyelitic process. Fluid in the middle ear and mastoid, without the loss of bony septa, can be seen with AOM and is nondiagnostic. Other findings may include abscess formation and intracranial extension. Persistent infection in the mastoid cavity can lead to coalescent mastoiditis or empyema of the temporal bone.

Obtain a complete blood cell count, erythrocyte sedimentation rate (ESR), and/or C-reactive protein (CRP) level. Typically, the patient has a leukocytosis with a left shift, as well as increased CRP level and ESR. Also obtain a blood culture, although a positive culture is unusual. If the patient undergoes surgical intervention (myringotomy, tympanostomy tubes, or mastoidectomy), obtain cultures of mastoid or middle ear fluid.

Differential Diagnosis

Usually the diagnosis is clear, based on fever, ipsilateral AOM, and displacement of the pinna with swelling, erythema, and tenderness of the posterior auricular area. Distortion or swelling of the pinna may also be seen with an insect bite reaction or a chondritis. The differential diagnosis of mastoiditis is summarized in Table 18–1.

Treatment

Consult with an otolaryngologist. Uncomplicated acute mastoiditis can usually be managed conservatively, with parenteral antibiotics and myringotomy with or without tympanostomy tube placement, particularly if there is no spontaneous ear drainage. More invasive surgical measures (most commonly a mastoidectomy) are indicated for lack of improvement within 48 hours or evidence of complications.

Table 18–1. Differential Diagnosis of Mastoiditis	
Diagnosis	**Clinical Features**
AOM	No erythema, tenderness, or swelling over the mastoid Pinna not displaced
Basilar skull fracture	No fever or ipsilateral AOM Pinna not displaced Ecchymoses over the mastoid, which may be bilateral
Chondritis	Erythema and swelling contiguous with break in the skin No ipsilateral AOM
Insect bite reaction	No fever Punctum may be evident No ipsilateral AOM
Langerhans cell histiocytosis	Recurrent AOM Seborrheic rash
Posterior auricular lymphadenopathy	Mobile, circumscribed Pinna not displaced
Otitis externa	Otorrhea and otalgia No tenderness or swelling over the mastoid No erythema unless associated periauricular cellulitis Pinna not displaced

Abbreviation: AOM, acute otitis media.

After a CT is performed, a lumbar puncture is indicated if the patient presents with altered mental status or signs of intracranial extension. Consult a neurosurgeon if intracranial extension is confirmed. However, do not delay starting antibiotics if there is any concern for intracranial involvement.

Begin treatment with intravenous (IV) ceftriaxone (100 mg/kg/d, divided into doses administered every 12 hours; 4-g/d maximum) or IV cefotaxime (200 mg/kg/d, divided into doses administered every 6–8 hours; 12-g/d maximum). For patients with a history of recurrent otitis media or recent antibiotic therapy, use IV ceftazidime (150 mg/kg/d, divided into doses administered every 8 hours; 6-g/d maximum) or IV cefepime (150 mg/kg/d, divided into doses administered every 8 hours; 6-g/d maximum) plus IV vancomycin (60 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum). Also add vancomycin if intracranial spread is suspected, if there is no response to therapy within 24 hours, or if there is a high local rate of clindamycin resistance. Linezolid (30 mg/kg/d divided into doses administered every 8 hours; 1,200-mg/d maximum) is an alternative to clindamycin or vancomycin in areas with high clindamycin resistance. Continue parenteral antibiotics for 7 to 10 days or until the infection has resolved (afebrile, improved inflammatory markers, improved physical examination findings). Follow with oral antibiotics based on culture results for an additional 10 to

14 days, although a longer course of parenteral therapy is necessary if there is intracranial extension. Add a topical antimicrobial agent for chronic mastoiditis (ciprofloxacin drops, 0.25 mL, administered twice a day for 7 days).

Indications for Consultation

- **Neurology and neurosurgery:** Signs of intracranial extension
- **Otolaryngology:** All patients

Disposition

- **Intensive care unit transfer:** Intracranial spread or associated meningitis
- **Discharge criteria:** Patient afebrile for 48 hours, with significant clinical improvement and downward trending of inflammatory markers

Follow-up

- **Primary care:** 1 week
- **Otolaryngology:** 2 weeks

Pearls and Pitfalls

- An infant may not have the classic displacement of the pinna.
- Not every case of mastoiditis is associated with an ipsilateral AOM.
- A patient with mastoiditis is at risk for hearing loss, so audiology follow-up is necessary.

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CHAPTER 19

Neck Masses

Introduction

The etiology of a pediatric neck mass can be congenital or acquired (inflammatory and neoplastic processes). Most involve lymph nodes and are benign and inflammatory (reactive cervical lymphadenopathy or lymphadenitis). The most common congenital neck masses are branchial cleft anomalies (BCAs) and thyroglossal duct cysts (TDCs). Malignant processes are rare but must always be considered in the differential diagnosis.

Cervical lymphadenopathy is a common and generally benign finding among many preschool- and school-aged children. Most often, it is a reactive adenopathy secondary to a viral or bacterial illness. Adenitis is an infection of the node itself, most commonly *Staphylococcus aureus* or group A *Streptococcus*, although viral, anaerobic, nontuberculous mycobacteria and *Mycobacterium tuberculosis* can also result in cervical adenitis. Cervical adenopathy can also be secondary to a systemic disease (especially Epstein-Barr virus [EBV], cytomegalovirus [CMV], autoimmune diseases, and malignancies).

Congenital anomalies may be present at birth or may not become apparent until a rapid phase of growth or infection occurs. Thyroglossal duct cysts and branchial cleft sinuses and fistulas typically become apparent during infancy and early childhood, whereas branchial cleft cysts appear later in adolescence or early adulthood. Lymphoma and thyroid carcinomas most often occur in older children and adolescents.

Clinical Presentation

History

Ask about the rate of growth of the mass and any associated symptoms. Rapid growth suggests a benign process, except for non-Hodgkin lymphoma. Slow growth associated with systemic symptoms (fever, fatigue, weight loss, night sweats) is more typical of malignancy. Cysts often fluctuate in size, increasing with upper respiratory tract infections. Chronic, intermittent drainage is consistent with a sinus tract and/or fistula. Ask about prior antibiotic treatment, because a failure of empirical treatment is concerning for either atypical organisms (such as nontuberculous mycobacteria) or malignancy. Also, ask about tuberculosis risk factors and exposure to cats (*Bartonella*).

With cervical lymphadenopathy, the history is often diagnostic. Determine the duration of the adenopathy. Ask about exposure to sick persons and animals (kittens or puppies, *Bartonella henselae;* rabbits or ticks, tularemia;

goats, cattle, or swine, brucellosis), travel (area endemic for tuberculosis), dental history (caries, abscess), ingestion of unpasteurized animal products (brucellosis, *Mycobacterium bovis*), or raw or undercooked meat (toxoplasmosis). Assess the patient's immunization status, especially focusing on the mumps vaccination.

With reactive adenopathy, there is usually a history of preceding or concurrent viral or bacterial infection in the head or neck. The onset of adenitis may be insidious, or there may be a history of exposure to such an illness. A patient with a systemic disease may have symptoms such as fever, weight loss, and fatigue.

Physical Examination

Perform a thorough examination of the head, neck, oral cavity, skin, and respiratory tract to look for infections that may be draining into the affected node(s). Assess the characteristics of the mass, including the location, consistency, mobility, and signs of inflammation (redness, warmth, tenderness). A fluctuant mass is usually an abscess or cyst. An orifice suggests a sinus tract or fistula.

The location of the mass usually suggests the most likely diagnoses. Masses located anterior to the sternocleidomastoid muscle are usually benign, except for thyroid malignancies. Thyroglossal duct cysts are asymptomatic midline masses that move with tongue protrusion and swallowing. They are found anywhere from the base of the tongue to the thyroid gland. Second branchial cleft cysts, which account for more than 90% of BCAs, are located along the anterior border of the sternocleidomastoid muscle. First branchial cleft cysts can be located anywhere from the external auditory canal to the angle of the mandible.

Also look for generalized lymphadenopathy and hepatosplenomegaly, which can suggest a systemic process, such as certain viral syndromes (EBV, HIV) or malignancy. Cranial nerve deficits, stridor, and tracheal deviation suggest impingement on surrounding structures.

Adenitis appears as a tender, enlarged node, initially firm but becoming more fluctuant with time. The node may be erythematous, with warm, adherent overlying skin. The physical examination is different for a nontuberculous mycobacterial infection, in which the node is often nontender, without warmth, but with a violet or purplish color, while the patient is well appearing, without fever. A tuberculous node typically has overlying erythema and often suppurates, and the patient usually presents with systemic signs and symptoms (fever, weight loss, fatigue, night sweats). Reactive lymph nodes are typically multiple, shotty, discrete, nontender, mobile, nonfluctuant, and smaller than 2 cm in diameter. The overlying skin is intact, with normal texture and color.

A hemangioma presents as a compressible, soft, red to blue mass that is present at birth or shortly thereafter. There will be a period of rapid growth followed by slow involution.

Findings that are suggestive of malignancy include a firm, painless mass that is matted or fixed to underlying structures, a persistent solitary lymph node larger than 2 cm in diameter, a mass that has not responded to antibiotic treatment, and a supraclavicular mass.

Laboratory Workup

If a malignancy is suspected, order a complete blood cell count (CBC) with differential and peripheral blood smear, a complete metabolic panel (including phosphorus and lactate dehydrogenase levels), and a uric acid level (to assess for tumor lysis syndrome). Also obtain a blood culture if there is fever and signs of sepsis and an urgent chest radiograph. If tuberculosis is suspected, perform a purified protein derivative skin test or obtain an interferon-γ release assay (patient > 2 years old). If *Bartonella* bacteria is suspected, order *B henselae* titers.

No laboratory testing is necessary for adenitis, but obtain a culture and Gram stain if the node is drained. If systemic disease is a concern (generalized lymphadenopathy, hepatosplenomegaly, weight loss, night sweats, hard or irregular-shaped node), perform a CBC, evaluation of erythrocyte sedimentation rate or C-reactive protein level, transaminase levels, EBV and CMV serology, and blood culture (if febrile and toxic appearing). Test for *Bartonella* bacteria, brucellosis, and HIV if the history and physical examination suggest the possibility. Perform a tuberculin skin test (TST) if the patient has persistent cervical lymphadenopathy, especially if the node is firm, rubbery, or matted. If the patient is at least 2 years old, a blood-based interferon-γ release assay may be used in place of a TST.

If the presentation is atypical or concerning for malignancy, discuss with the surgeon whether a fine-needle aspiration (FNA) or biopsy is indicated. Certain conditions, such as mycobacterial infection and lymphovascular malformations, can be complicated by FNA. If aspiration is performed, order a Gram stain, routine anaerobic and aerobic cultures, histopathology, and cytology.

When a diagnosis of TDC is assigned, check the thyroid studies to assess the patient for hypothyroidism because ectopic thyroid glands are commonly associated with TDCs.

Radiology Examinations

If there is diagnostic uncertainty, order ultrasonography (US) to evaluate the mass. The US will also help to determine if fluid is present for drainage or diagnostic sampling. Depending on the results, computed tomography (CT) or magnetic resonance (MR) imaging may be needed to fully visualize the mass, especially if there is a tract or fistula. If malignancy is suspected, discuss

the case with the radiologist and consulting surgeon and/or oncologist to determine the best radiologic modality (US with or without CT or MR imaging). Chest radiography may be urgently indicated if respiratory compromise or significant mediastinal involvement is suspected. For a TDC, perform a thyroid scan to look for thyroid tissue before surgical excision.

Differential Diagnosis

The priorities are to rule out a neoplasm and address a life-threatening complication, such as airway compression. The differential diagnosis of neck masses is summarized in Table 19–1, and the differential diagnosis of cervical lymphadenitis is summarized in Table 19–2.

Table 19–1. Differential Diagnosis of Neck Masses

Diagnosis	Clinical Features
Congenital Neck Masses	
Branchial cleft cyst	Recurrent abscesses in the same location, such as the lower border of the sternocleidomastoid Cyst may be draining
Dermoid cyst	Midline painless, doughy, or rubbery mass that moves with the doughy overlying skin Does not move with tongue protrusion or swallowing
Ectopic cervical thymus	Cervical or submandibular mass (could be mediastinal) Usually painless and solid
Hemangioma	Red to blue soft mass that is present at birth or shortly thereafter Compressible Rapid growth phase, followed by slow involution
Lymphovascular malformation	Soft, painless, compressible, transilluminates Located in the posterior triangle
Teratoma	Common cause of neonatal airway obstruction Firm mass with irregular borders Imaging: bulky, heterogeneous mass with solid and cystic components
Thyroglossal duct	Soft, mobile, and nontender mass in the midline mass Moves with swallowing and protrusion of the tongue
Benign Neoplastic Masses	
Lipoma	Soft, painless, subcutaneous mass
Thyroid nodule	Midline nodule that moves with the thyroid gland Consider the nodule to be malignant until proven otherwise
Malignant Neoplastic Masses	
Hodgkin lymphoma	Slow growing Painless lymph node that feels either rubbery or firm Location: anterior or posterior cervical, preauricular, supraclavicular Fever, night sweats, weight loss, hepatosplenomegaly

Table 19–1. Differential Diagnosis of Neck Masses, continued	
Diagnosis	**Clinical Features**
Neuroblastoma	Metastatic disease (primary abdominal or thoracic tumor) Lateral or retropharyngeal neck mass Proptosis, periorbital swelling, ecchymoses Primary cervical disease Symptoms of mass impingement on surrounding organs (cranial nerve palsies, Horner syndrome, cough, stridor, dysphagia)
Non-Hodgkin lymphoma	Rapidly enlarging Painless, firm to hard lymph node (spinal accessory, supraclavicular) Fever, weight loss, bone and joint pain
Rhabdomyosarcoma	Painless, hard Anterior and posterior cervical location Symptoms of mass impingement on surrounding organs (hoarseness)
Thyroid carcinoma	Firm mass that feels different from other thyroid tissue Patient has a history of irradiation

Table 19–2. Differential Diagnosis of Cervical Lymphadenitis	
Diagnosis	**Clinical Features**
Adenitis (*Staphylococcus*, *Streptococcus*, anaerobic bacteria)	Node is erythematous, warm, and tender Unilateral
Bartonella bacteria	Scratch or bite from a kitten or puppy 2–8 weeks prior Patient well appearing May have conjunctivitis
Branchial cleft cyst	Recurrent abscesses in the same location, such as the lower border of the sternocleidomastoid Cyst may be draining
EBV (mononucleosis-like illness)	Fatigue Generalized lymphadenopathy Hepatomegaly and/or splenomegaly
Kawasaki disease	$\geq$ 5 d of fever Mucous membrane changes Nonpurulent conjunctivitis Edema of the hands and feet Polymorphous rash Unilateral nonsuppurative node $>$ 1.5 cm
Nontuberculous mycobacteria	Afebrile Node is nonerythematous and nontender Evolves over weeks to months
Parotitis	Obscures the angle of the jaw Drainage from the Stensen duct
Tuberculosis	Fever, fatigue, weight loss, night sweats Overlying erythema Node may drain spontaneously

Abbreviation: EBV, Epstein-Barr virus.

Treatment

If methicillin-resistant *S aureus* is a concern, treat bacterial adenitis parenterally, initially with clindamycin (40 mg/kg/d, divided into doses administered every 6–8 hours; 2.7-g/d maximum) or linezolid (30 mg/kg/d divided into doses administered every 8 hours; 1,200-mg/d maximum). Otherwise, use nafcillin or oxacillin (150 mg/kg/d, divided into doses administered every 6 hours; 12-g/d maximum), cefazolin (75 mg/kg/d, divided into doses administered every 8 hours; 6-g/d maximum), or ampicillin/sulbactam (150 mg/kg/d, divided into doses administered every 6 hours; 8-g/d maximum). If the patient's condition deteriorates, or if the patient does not respond to therapy after 48 hours, add vancomycin (45 mg/kg/d, divided into doses administered every 8 hours; 4-g/d maximum). Also, order warm compresses every 4 hours. If the node becomes fluctuant, arrange for incision and drainage by a general surgeon or otolaryngologist, and request a Gram stain and routine aerobic and anaerobic cultures. Perform US if it is unclear whether the node is ready for drainage. Switch to an equivalent oral antibiotic once the patient responds to treatment.

If bartonellosis is suspected, treat the patient as for a bacterial adenitis, with adequate staphylococcal and streptococcal antimicrobial coverage. Although azithromycin, rifampin, trimethoprim/sulfamethoxazole, or gentamicin may offer some advantage, it is not necessary to specifically treat an immunocompetent patient who is not acutely or severely ill.

Surgical excision and culture constitute the treatment of choice if a nontuberculous mycobacterial infection is suspected. Avoid incision and drainage, which can result in a chronic draining fistula. If complete excision is not possible, arrange for curettage, and administer antimycobacterial therapy with azithromycin (5 mg/kg/d; 500-mg/d maximum) or clarithromycin (15 mg/kg/d, divided into doses administered every 12 hours; 1-g/d maximum) plus rifampin (20 mg/kg/d, divided into doses administered every 12 hours; 600-mg/d maximum) and/or ethambutol (15 mg/kg/d; 2.5-g/d maximum).

The treatment for EBV, CMV, and other mononucleosis-like syndromes is supportive. However, if the patient has significant upper airway obstruction, insert a nasopharyngeal tube (nasal trumpet) and administer methylprednisolone (1 mg/kg/d). (If so, order a Gram stain and routine aerobic and anaerobic cultures.) When the patient is clinically improved, change to an equivalent oral antibiotic regimen or a narrow-spectrum antibiotic if culture results are known to complete a 10- to 14-day course of treatment.

If a malignant mass is suspected, consult an oncologist for recommendations about additional imaging, blood work, and excisional biopsy. Do not give the patient corticosteroids, especially if there are no cardiopulmonary

concerns. Also discuss which surgical service is most appropriate for managing the patient's condition, as well as whether to transfer the patient to an oncology or surgical service.

For a BCA, TDC, or other congenital neck mass, consult a surgeon (in otolaryngology or general surgery) to discuss the timing of surgery, which can usually be scheduled as an outpatient procedure.

Indications for Consultation

- **General surgery or otolaryngology:** Incision and drainage or surgical excision needed
- **Infectious disease:** Suspected *Mycobacterium* infection
- **Oncology:** Malignant neck masses
- **Otolaryngology or general surgery:** TDC, BCA, or any other neck mass that requires biopsy or surgical excision

Disposition

- **Intensive care unit transfer:** Airway compromise or a rapidly progressing infection that is not responsive to parenteral therapy
- **Tertiary care center transfer:** If malignancy is considered, to expedite obtaining and processing biopsy specimens
- **Discharge criteria:** Patient clinically improving, without respiratory distress, and tolerating oral intake (including antibiotics, if prescribed); appropriate diagnostic and treatment plan in place (surgical intervention or oncologic consultation if indicated)

Follow-up

- **Primary care:** 3 to 4 days
- **If surgery was performed:** 1 to 3 days with the surgical service
- **Hematology/oncology (malignancy suspected):** Immediate
- **Infectious diseases:** 1 week (suspected *Mycobacterium* infection)

Pearls and Pitfalls

- Posterior cervical adenopathy is almost always reactive or viral.
- A well-appearing patient with adenitis can be discharged on oral antibiotics and warm compresses, with follow-up for incision and drainage if the node becomes fluctuant.
- Do not administer steroids if a neoplastic process is a possibility.
- Adenopathy that persists for more than 3 weeks requires further workup, including tuberculosis testing and possible biopsy for malignancy.

- Consult a surgeon before any drainage attempts because some conditions, such as *Mycobacterium* infection, can be complicated by aspiration.
- About 1% of patients with a preoperative diagnosis of TDC will have a median ectopic thyroid gland that contains all of the functional thyroid tissue.

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CHAPTER 20

Orbital and Periorbital Cellulitis

Introduction

Orbital (postseptal) cellulitis and periorbital (preseptal) cellulitis are major infections of the orbital tissues. Periorbital cellulitis is a superficial infection, whereas orbital cellulitis involves deeper structures behind the orbital septum. Orbital cellulitis is an ocular emergency as it is associated with significant morbidity and mortality, including intracranial extension of infection in up to 5% of patients.

The orbital septum is a tough, fibrous membrane that runs from the periosteum of the orbital bones to the tarsal plates. It functions as a barrier between the superficial skin/subcutaneous tissues of the periorbital space and the deep intraorbital structures, preventing superficial (ie, periorbital/preseptal) infections from extending inward. It also prevents orbital cellulitis from extending beyond the supraorbital and infraorbital ridges. However, the valveless venous system of the orbital space can facilitate extension of an infection to intracranial structures.

Periorbital cellulitis often results from disruption of the skin or mucosal barrier from trauma, dental abscess, insect or animal bites, or abrasions to the periorbital region. Common organisms are the same for superficial skin infections, including *Staphylococcus aureus* and group A *Streptococcus*. Less often, sinusitis can extend to the periorbital spaces, so that nasopharyngeal organisms such as *Streptococcus pneumoniae* and anaerobes may be involved. Rare causes associated with specific exposures include fungi and mycobacteria.

Orbital cellulitis is a complication of sinusitis (most often chronic ethmoid sinusitis) through the thin and porous medial orbital wall (lamina papyracea), although it can also occur from direct trauma or surgery. It is most common during the winter months, secondary to group A *Streptococcus*, *S pneumoniae,* or *S aureus. Pseudomonas, Klebsiella, Eikenella,* and *Enterococcus* are less common organisms, while fungal pathogens (rare) are a concern in an immunocompromised patient. A polymicrobial infection with both aerobic and anaerobic bacteria can occur in an older adolescent.

Clinical Presentation

History

Ask about recent upper respiratory infections, sinus infections, facial trauma, insect or animal bites, and chronic sinusitis. In addition, confirm that the patient has normal immune status and is up to date on immunizations.

Physical Examination

Periorbital Cellulitis

The patient typically presents with swelling, warmth, and redness of the periorbital region, at times in association with an obvious break in the skin integrity (insect bite or a scratch). Importantly, there is no proptosis, chemosis, pain with eye movement, or ophthalmoplegia. Fever may or may not be present. The orbital septum effectively limits the spread of preseptal cellulitis, so the infection does not spread backward to the orbital space.

Orbital Cellulitis

The patient typically presents with fever, malaise, and warm, tender, erythematous eyelid swelling. There may also be a purulent nasal discharge. The cardinal signs are proptosis, chemosis, pain with eye movement, and ophthalmoplegia, which may be noted by the patient despite severe lid swelling, preventing direct observation of the extraocular movements. However, not all of these signs are always present. Decreased visual acuity or presence of visual field defects, which may manifest initially or later in the course of the disease, is an ophthalmologic emergency secondary to involvement of the optic nerve. Suspect increased intraocular pressure if the patient has headache and vomiting. An unremitting headache and altered mental status suggest intracranial extension.

Laboratory Workup and Radiology Examinations

If orbital cellulitis is suspected, perform contrast-enhanced computed tomography (CT) of the orbits and sinuses to look for an orbital abscess, subperiosteal abscess, or intracranial extension. Head CT is inadequate because head CT protocols specifically avoid imaging of the orbital space to reduce radiation exposure to the lens of the eye. However, order CT of the head, orbits, and sinuses if intracranial extension is suspected based on history and physical examination. Depending on institutional expertise, ultrasonography (US) can differentiate between orbital and periorbital cellulitis. Also, obtain a complete blood cell count, C-reactive protein level, and blood culture. Perform a lumbar puncture if there is concern for meningeal involvement, provided there is no evidence of increased intracranial pressure. No laboratory testing is necessary for periorbital cellulitis. Specifically, the blood culture result is rarely positive.

An x-ray sinus series will not allow differentiation of orbital from periorbital cellulitis, because sinus involvement complicates a significant percentage of cases of periorbital cellulitis. Orbital US can identify orbital abscesses, but a more thorough evaluation of intracranial extension requires magnetic resonance imaging.

Differential Diagnosis

It is essential to distinguish between orbital cellulitis and periorbital cellulitis, because more aggressive medical and surgical intervention is necessary with orbital disease. Passively open the patient's eyelids and examine the eyes for conjunctival injection, discharge, proptosis, chemosis, pain with eye movement, and ophthalmoplegia, and check the patient's visual acuity. Lack of ocular swelling beyond the infraorbital and supraorbital ridges suggests periorbital cellulitis. The differential diagnosis is summarized in Table 20–1.

Table 20–1. Differential Diagnosis of Orbital and Periorbital Cellulitis

Diagnosis	Clinical Features
Eyelid Edema	
Conjunctivitis	May be bilateral No fever or toxicity
EBV	Dacryocystitis Lacrimal gland/duct inflammation Other signs of EBV infection
Insect/animal bite	Punctum may be evident Patient may have a history of a bite No fever or toxicity
Allergic reaction	No fever or toxicity Patient may have urticaria or swelling elsewhere Pruritus
Nephrotic syndrome	No fever or toxicity Usually bilateral eye swelling with edema in other dependent areas Proteinuria
Trauma	Patient may have a history or evidence (ecchymoses) of trauma No fever or toxicity
Hordeolum	No fever or toxicity Obstructed gland is often evident
Exophthalmos	
Orbital neoplasm	Slowly progressive swelling May have visual changes No fever or toxicity
Hyperthyroidism	Tachycardia, palpitations, lid lag, heat intolerance Goiter may be palpated
Forehead Swelling	
Preseptal cellulitis	Patient may have a history of trauma or a break in the skin No limitation of extraocular movement, proptosis, or chemosis
Pott puffy tumor	Occurs typically after 7 years of age (when the frontal sinus develops) History is compatible with frontal sinusitis No or limited orbital swelling

Abbreviation: EBV, Epstein-Barr virus.

Treatment

Periorbital Cellulitis

Treat as for any other soft-tissue infection (see Chapter 17, Skin and Soft-Tissue Infections), using the local antibiograms to determine whether methicillin-resistant *S aureus* coverage is necessary. Also, treat any associated sinusitis (see Chapter 22, Sinusitis). Topical treatment is not effective or indicated.

Orbital Cellulitis

If orbital cellulitis is suspected or confirmed, promptly start antibiotics and consult both an otolaryngologist and an ophthalmologist for possible surgical intervention. Treat with one of the following intravenous (IV) antibiotic regimens, depending on local antibiograms:

IV vancomycin (40–60 mg/kg/d, divided into doses administered 4 times per day; 4-g/d maximum)
plus
IV or IM (if IV access is not available) ampicillin/sulbactam (300 mg/kg/d, divided into doses administered every 6 hours; 12-g/d ampicillin/sulbactam maximum; 8-g/d ampicillin component maximum)
or
If the patient has a severe penicillin allergy, use ciprofloxacin (20 to 30 mg/kg/d, divided into doses administered every 12 hours; 1.2-g/d maximum).

Medical management is successful in most cases, including those with a small subperiosteal abscess (< 4 mL). Indications for surgical intervention are progression of clinical symptoms despite 24 to 48 hours of appropriate IV antibiotics, impairment of visual acuity, or intracranial abscess. However, a cavernous sinus thrombosis requires immediate surgical intervention.

Sinus-clearing medications, including nasal decongestants (1% phenylephrine for no more than 2 days) and nasal steroids may be useful. Nasal sinus rinses, if tolerated, are also beneficial if there is no intracranial extension.

Preliminary evidence suggests that IV dexamethasone for 24 to 48 hours is a useful adjunct that can decrease length of hospitalization with minimal adverse outcomes, particularly if orbital cellulitis is secondary to sinusitis or there is a subperiosteal abscess. Give 0.3 mg/kg/d (6 mg/d maximum) every 6 hours for 3 days. Do not use dexamethasone as monotherapy without antibiotics.

Indications for Consultation (Suspected or Confirmed Orbital Cellulitis)

- **Ophthalmology:** All patients
- **Otolaryngology:** All patients

Disposition

Periorbital Cellulitis

- **Discharge criteria:** Patient afebrile for 24 to 48 hours, with significant clinical improvement; continue oral antibiotics for 7 to 14 days of total treatment.

Orbital Cellulitis

- **Intensive care unit transfer:** Intracranial extension and/or raised intracranial pressure.
- **Interinstitutional transfer:** Ophthalmology or otolaryngology service not immediately available.
- **Discharge criteria:** Patient afebrile for 48 hours with significant clinical improvement, including normal visual acuity and extraocular movements and a downward trend of the inflammatory markers; continue oral antibiotics for a minimum of 2 weeks' total treatment. A longer course is required for complicated orbital cellulitis.

Follow-up (Orbital Cellulitis)

- **Otolaryngology and/or ophthalmology:** Weekly during the antibiotic course of treatment

Pearls and Pitfalls

- A small subperiosteal abscess may respond to IV antibiotics and not require drainage.
- Orbital cellulitis carries a 10% risk of residual loss of visual acuity.
- Ninety percent of cases of orbital cellulitis result from the direct spread of sinusitis (most commonly ethmoid). Twenty percent of cases of periorbital cellulitis result from dental abscess and 15 percent from extraocular trauma.

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CHAPTER 21

Peritonsillar and Retropharyngeal Abscesses

Introduction

Deep neck infections involve the potential spaces and facial planes in the neck. The most common are peritonsillar and retropharyngeal abscesses.

A peritonsillar abscess (PTA) is a suppurative bacterial infection located in the space between the tonsil and the superior pharyngeal constrictor muscle. It is the most frequent deep neck infection in older children and adolescents but is relatively uncommon in young children.

A retropharyngeal abscess (RPA) involves the retropharyngeal space, which is the area between the pharynx and precervical vertebrae fascia that extends from the skull into the superior mediastinum. Retropharyngeal lymph nodes drain the nasopharynx, adenoids, posterior paranasal sinuses, and middle ear structures. These nodes are prominent in young children but begin to atrophy by 6 years of age, accounting for the higher incidence of RPA in younger children and relatively rare occurrence in adolescents, except after posterior pharyngeal wall trauma. A preceding oropharyngeal infection leads to retropharyngeal cellulitis that organizes into a phlegmon and then into an abscess. Although the incidence of RPA has increased with the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA), the percentage of patients undergoing surgical intervention has decreased, with a trend toward initial nonsurgical medical management.

These infections are polymicrobial. The most common pathogens are *Streptococcus pyogenes* (group A *Streptococcus*), *S aureus* (including MRSA and methicillin-sensitive *S aureus* [MSSA]), and mixed oropharyngeal anaerobes (including *Fusobacterium*, *Prevotella*, *Bacteroides*, *Porphyromonas,* and *Peptostreptococcus* species).

The morbidity and mortality of pediatric deep neck infections result from extension into adjacent structures. Complications may include airway obstruction, abscess rupture and subsequent aspiration, mediastinitis, internal jugular vein thrombosis (Lemierre syndrome), carotid artery pseudoaneurysm, and sepsis. These complications are very rare because of early diagnosis and treatment.

Clinical Presentation

History

A patient with a PTA usually has a history of a recent infection, such as tonsillitis, streptococcal pharyngitis, or viral respiratory illness (especially mononucleosis). Typical complaints include fever, severe sore throat, drooling, dysphagia, a muffled or "hot potato" voice, and trismus (inability to fully open the mouth secondary to irritation and reflex spasm of the internal pterygoid muscle). Other symptoms include odynophagia (painful swallowing), neck pain, and ipsilateral ear pain.

A young child with an RPA usually presents with an antecedent history of ear, nose, throat, or nonspecific upper respiratory tract infection, whereas an older patient will often have a history of preceding pharyngeal trauma (penetrating foreign body, endoscopy, intubation, dental procedure). The most common symptoms at presentation are fever, neck pain, neck swelling, sore throat, dysphagia, and odynophagia. Other complaints may include decreased oral intake, muffled voice, trismus, and drooling. Stridor and upper airway obstruction are uncommon symptoms at presentation in children.

Physical Examination

A patient with a PTA may present with trismus, a bulging tonsil covered with exudate, and deviation of the uvula away from the affected side. Other findings include halitosis, pooling of saliva in the floor of the mouth, and tender ipsilateral cervical lymphadenopathy.

Typical findings in a child with an RPA include neck tenderness, limitation of neck movements (especially neck extension), and torticollis. Cervical lymphadenopathy is common. Inspection of the oropharynx may reveal midline or unilateral posterior pharyngeal swelling, but this is absent in more than 50% of younger children.

Laboratory Workup

No laboratory testing is needed. If the patient is toxic appearing or does not respond to empirical antibiotic therapy, attempt to assign a definitive microbial diagnosis by arranging surgical incision and drainage and sending specimens for Gram stain and aerobic and anaerobic cultures.

Radiology Examinations

Imaging is not necessary to diagnosis a PTA and is contraindicated in a patient with airway compromise. However, perform computed tomography (CT) of the neck with intravenous (IV) contrast if it is difficult to differentiate PTA

from other deep neck space infections or if there is a concern for a serious complication.

If the diagnosis of retropharyngeal infection is equivocal and the patient has no signs of airway obstruction, obtain a screening lateral neck radiograph. This will confirm retropharyngeal swelling but will not allow differentiation between cellulitis, phlegmon, and abscess. Proper radiographic technique is important to avoid an artificially thickened appearance of the retropharyngeal soft tissues. Ensure that the radiograph is taken during inspiration, with the neck extended and the patient in a true lateral position. Widened prevertebral soft tissues, exceeding the anteroposterior diameter of the adjacent vertebral body, are consistent with retropharyngeal inflammation.

If an RPA is suspected on the basis of clinical assessment or soft tissue swelling noted on radiographs, order a neck CT with IV contrast. This will allow identification of the location of the infection and any extension into other adjacent neck or chest spaces. Findings suggestive of an abscess include ring enhancement and irregular abscess border (referred to as "scalloping").

Differential Diagnosis

The differential diagnosis of deep neck infections is summarized in Table 21–1.

Table 21–1. Differential Diagnosis of Neck Infections

Diagnosis	Clinical Features
Angioedema	Patient has a history of allergies or exposure to a trigger Swelling of the lips/tongue, urticarial rash Stridor and respiratory distress
Bacterial tracheitis	Abrupt onset of upper airway obstruction in a patient recovering from a viral illness (croup, influenza) Copious, purulent secretions
Croup	Harsh, barky cough; stridor; and drooling No limitations to neck movement No posterior pharyngeal swelling
PTA	Older children and adolescents Severe sore throat, muffled voice, and trismus Exudative tonsillitis with uvula deviation
RPA	Preschool-aged children No peritonsillar swelling or uvula deviation Limited neck extension
Meningitis	Toxic appearing and irritable, with photophobia Limited neck flexion and other meningeal signs
Uvulitis	Swelling and erythema of the uvula No peritonsillar swelling

Abbreviations: PTA, peritonsillar abscess; RPA, retropharyngeal abscess.

Treatment

Immediate surgical drainage is indicated for any patient with airway compromise in the setting of a deep neck space infection. For a patient with a PTA, arrange either needle aspiration or incision and drainage. The type of initial drainage procedure varies based on the age and cooperation of the child, the availability of a provider trained in needle aspiration, and the otolaryngologist's preference. A quinsy tonsillectomy (tonsillectomy with simultaneous abscess drainage) is indicated if the initial abscess drainage is inadequate, as evidenced by abscess recurrence or persistence of symptoms. It is also preferred if the patient has a history of severe or recurrent pharyngitis or obstructive sleep apnea.

It is now common practice to treat an RPA medically for 24 to 48 hours and obtain an otolaryngology consult if there is no improvement. Risk factors for an increased likelihood of failing medical therapy include patient age younger than 4 years and abscess size greater than 2.2 cm on CT imaging. If there has been no clinical improvement after 24 to 48 hours of antibiotic therapy, obtain an initial (or repeat) neck CT with IV contrast to evaluate the patient for the presence of a drainable fluid collection.

Medical management for both RPA and PTA includes analgesia (until discussed with the otolaryngologist), hydration, and antibiotics. Treat with IV clindamycin (45 mg/kg/d, divided into doses administered every 8 hours; maximum, 900 mg per dose), although IV ampicillin/sulbactam (200 mg/kg/d of ampicillin, divided into doses administered every 6 hours; maximum, 3 g per dose) will suffice if the local prevalence of MRSA is low. However, in communities with high rates of clindamycin-resistant *Staphylococcus* bacteria (MRSA or MSSA), treat with clindamycin *and either* IV vancomycin (15 mg/kg/d, divided into doses administered every 8 hours; 4-g/d maximum) *or* IV linezolid (< 12 years of age, 30 mg/kg/d, divided into doses administered every 8 hours; 12 years or older, 20 mg/kg/d, divided into doses administered every 12 hours; 1.2-g/d maximum).

Continue IV therapy until the patient is afebrile and has clinically improved, at which time transition to an oral regimen, such as empirical clindamycin (45 mg/kg/d, divided into doses administered every 8 hours; maximum, 600 mg per dose) or a narrow-spectrum antibiotic, based on known sensitivities, to complete a 14-day course of treatment.

For a patient with a PTA, the surgeon may schedule a tonsillectomy for 1 to 3 months in the future, particularly if the disease course was complicated or the patient experiences recurrences.

Indications for Consultation

- **Anesthesia:** Signs of airway compromise, including stridor, increased work of breathing, hypoxemia
- **Otolaryngology:** No response to antibiotics, drainage procedure needed, recurrent abscess formation

Disposition

- **Intensive care unit transfer:** Signs of airway compromise or complications, such as severe aspiration pneumonia, mediastinitis, internal jugular vein thrombosis, or carotid artery pseudoaneurysm
- **Discharge criteria:** Patient afebrile with significant clinical improvement, including decreased pain and good oral intake

Follow-up

- **Primary care:** 3 to 5 days
- **Otolaryngology (if surgery was performed):** During the outpatient antibiotic course

Pearls and Pitfalls

- If there are signs of airway compromise, promptly consult both an otolaryngologist and an anesthesiologist and move the patient to a setting where an emergent artificial airway can be secured.
- PTA recurs in 5% to 15% of patients.

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CHAPTER 22

Sinusitis

Introduction

Obstruction of the sinus ostia can be caused by inflammation of the mucosal lining secondary to an upper respiratory tract infection (URTI) or allergic symptoms. This impedes mucous drainage and facilitates the overgrowth of bacteria, leading to acute bacterial sinusitis. Outpatient watchful waiting or oral antibiotic treatment suffices for most cases of acute bacterial sinusitis, but inpatient therapy is required if there is evidence of toxicity, failure of outpatient treatment, an underlying immunodeficiency, or serious complications.

Serious complications of bacterial sinusitis can occur secondary to the spread of infection. The most common are periorbital and orbital cellulitis or abscess. Less often, intracranial extension can cause a brain abscess, meningitis, or cavernous venous sinus thrombosis. Uncommonly, osteomyelitis of the frontal bone with subperiosteal abscess (Pott puffy tumor) may result from frontal sinusitis, most commonly in a teenaged male.

A history of recurrent bacterial sinusitis raises the possibility of an underlying chronic allergic condition, immunodeficiency, or defect (anatomic or mechanical) causing poor sinus drainage (cystic fibrosis, immotile cilia syndrome, sinonasal polyps).

The most common causes of acute bacterial sinusitis are *Streptococcus pneumoniae*, nontypeable *Hemophilus influenzae*, and *Moraxella catarrhalis*. However, with severe, complicated, and chronic infections, *Staphylococcus aureus* (including methicillin-resistant strains), *Pseudomonas* species, anaerobic bacteria, and fungi may be involved.

Clinical Presentation

History

Uncomplicated acute bacterial sinusitis presents with persistent, severe, or worsening symptoms. The *persistent* presentation involves nasal symptoms and/or cough that continue, without improvement, for more than 10 days. In a *severe* presentation, there is a purulent nasal discharge with fevers greater than 39 °C (102.2 °F) for 3 to 4 days. *Worsening* symptoms are biphasic ("double sickening"). The patient seems to be recovering from an initial viral URTI but then develops worsening respiratory and/or nasal symptoms. There may be low-grade fever, nasal discharge of any quality, cough (which may be worse at night), headache (which can be positional), or facial pain or pressure.

Complications occur in approximately 5% of hospitalized children with bacterial sinusitis, especially if there is a nasogastric and/or endotracheal tube in place. A patient with a severe complication, such as intracranial extension or orbital cellulitis, will have rapidly progressive or fulminant disease, presenting with vomiting, oral intolerance, severe headache, eye pain and visual disturbances, forehead swelling, cranial nerve palsies, nuchal rigidity, lethargy, and somnolence.

Physical Examination

Perform thorough ear, nose, throat, and neurologic examinations. Congestion and/or rhinorrhea will most likely be present. The patient may experience pain with palpation over the sinuses or the maxillary molars. Nasal speculum examination of the nasopharynx might reveal a purulent discharge material from under the middle turbinate. With intracranial spread, the patient may appear toxic, with unstable vital signs, painful ophthalmoplegia, nuchal rigidity, and cranial nerve VI palsy secondary to increased intracranial pressure. Focal forehead swelling is suspicious for Pott puffy tumor.

The presentation of the complications of acute bacterial sinusitis is summarized in Table 22–1.

Laboratory Workup

No specific laboratory testing is needed, other than aerobic and anaerobic cultures when sinus drainage is performed. Obtain a blood culture if the patient appears toxic. If intracranial extension is suspected, perform a lumbar

Table 22–1. Complications of Sinusitis

Diagnosis	Clinical Features
Brain abscess	Headache Altered mental status
Cavernous sinus thrombosis	Toxicity, headache Altered mental status Ophthalmoplegia (cranial nerves III, IV, V1, V2, VI) Signs of increased intracranial pressure
Meningitis	Headache Photophobia Meningismus
Orbital cellulitis or abscess	Proptosis, chemosis Limited extraocular movements
Pott puffy tumor	Marked forehead swelling May have signs of increased intracranial pressure
Preseptal cellulitis	May have a break in the skin integrity No ophthalmoplegia No chemosis No visual changes or extraocular movement limitation

puncture to obtain a cerebrospinal fluid cell count and culture, provided there is no imminent concern for brain herniation.

Radiology Examinations

Routine imaging of the sinuses is unnecessary to diagnose simple acute sinusitis. However, a patient admitted with sinusitis complications, treatment failure, or severe disease often requires imaging. If orbital cellulitis is suspected, obtain maxillofacial/orbits CT (computed tomography) with intravenous (IV) contrast. Obtain head CT or magnetic resonance imaging with IV contrast to evaluate for possible intracranial extension, meningitis, or Pott puffy tumor. Obtain a contrast-enhanced magnetic resonance venography if there is concern for cavernous sinus thrombosis.

Differential Diagnosis

The differential diagnosis includes allergic or viral rhinosinusitis (afebrile), cluster headache (no nasal discharge), preseptal cellulitis (break in the local skin integrity with localized swelling), nasal polyp (no sinus tenderness), and odontogenic infections (tenderness of teeth and/or gums). Always rule out a nasal foreign body in a child with purulent nasal discharge, especially if it is unilateral and/or foul smelling.

Treatment

Treat acute bacterial sinusitis with either ceftriaxone (100 mg/kg/d, divided into doses administered every 12 hours; 4-g/d maximum), ampicillin/sulbactam (200–400 mg/kg/d, divided into doses administered every 6 hours; 8-g/d maximum ampicillin component), or levofloxacin (10–20 mg/kg/d divided into doses administered every 12 hours; 500-mg/d maximum). Add vancomycin (60 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum) and metronidazole (30 mg/kg/d divided every 6 hours; 4-g/d maximum) if there is a serious complication (orbital cellulitis, intracranial extension, cavernous sinus thrombosis, Pott puffy tumor) or a failure of appropriate inpatient therapy.

Tailor the antibiotic choices based on the clinical response, culture results (if any), and community patterns of antimicrobial resistance. Continue the intravenous antibiotics until the symptoms improve, then change to oral antibiotics to complete at least a 14-day course of treatment. In a more severe or complicated case, the patient may require antibiotic therapy for up to 4 weeks.

Consult an otolaryngologist and infectious diseases specialist for consideration of sinus drainage if the patient does not improve or deteriorates after 48 hours of adequate empirical therapy, or presents or develops signs of

a complication. Consult a neurosurgeon if there is concern for intracranial extension. If the patient has a venous sinus thrombosis, consult a hematologist and start anticoagulation therapy.

Do not use adjunctive therapies, such as antihistamines, mucolytics, or decongestants.

Indications for Consultation

- **Allergy and immunology:** Suspicion of an immunodeficiency or recurrent episodes of sinusitis that may be allergic in nature
- **Hematology:** Central venous sinus thrombosis requiring anticoagulation
- **Infectious disease:** Recurrent sinusitis, isolation of a rare or treatment-resistant pathogen, complication of sinusitis, sinusitis unresponsive to standard antimicrobial therapy
- **Neurosurgery:** Possible intracranial extension
- **Ophthalmology:** Possible orbital or intracranial extension
- **Otolaryngology:** Recurrent or chronic sinusitis, complication of sinusitis, need for sinus aspiration

Disposition

- **Intensive care unit transfer:** Intracranial extension, sepsis
- **Discharge criteria:** Patient afebrile for 24 to 48 hours, clinical improvement, and good oral intake, including the ability to take the appropriate antibiotic

Follow-up

- **Primary care:** 1 week, to assess the need for an extended antibiotic course
- **Otolaryngology (if involved):** 1 week

Pearls and Pitfalls

- If the patient is asymptomatic, do not treat an incidental finding of sinus inflammation seen on CT images.
- If the patient has recurrent bacterial or chronic sinusitis, obtain an evaluation for allergic rhinitis, cystic fibrosis, immunodeficiency, Kartagener syndrome and other immotile cilia syndromes, and polypoid disease.
- Plain radiographs, transillumination, and ultrasonographic images of the sinuses are unreliable.

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CHAPTER 23

Stridor

Introduction

Stridor is a sign of upper airway obstruction caused by turbulent airflow. Stridor may also be an expiratory or biphasic respiratory sound. Inspiratory stridor usually indicates obstruction above the glottis, whereas expiratory stridor suggests obstruction below the glottis in the distal trachea. Biphasic stridor suggests a fixed glottic or subglottic obstruction. Although infectious croup is the most common cause of acute stridor, there are many other etiologies for acute and chronic stridor (Table 23–1). Consider these other etiologies when there is a lack of upper respiratory tract symptoms, sudden onset of stridor, and/or chronic or recurrent stridor.

Clinical Presentation

Croup (laryngotracheobronchitis) is a disease of the upper airway in which the pharynx, larynx, trachea, and bronchi become inflamed and edematous. Specifically, involvement within the cricoid cartilage in the subglottic area causes airway obstruction. The narrowest part of the pediatric airway is located here, and even 1 mm of edema decreases airflow exponentially. Parainfluenza viruses, particularly type 2b, are the most common cause of infectious croup, but other viral etiologies include rhinovirus, respiratory syncytial virus, influenza, enterovirus, adenovirus, and SARS-CoV-2. Viral infectious croup occurs between 6 months and 3 years of age with most cases occurring by 1 year of age, but it may present as young as 3 months. There is a slight male predominance, and the disease occurs more frequently in the fall and winter months. Bacterial causes are rare and include *Mycoplasma pneumoniae* and *Corynebacterium diphtheriae*.

History

Viral infectious croup usually presents with a gradual onset of nonspecific upper respiratory symptoms, including coryza, cough, sore throat, and low-grade fever. On day 2 or 3 of illness, the patient develops a hoarse voice, barky or seal-like cough, stridor, and tachypnea, which are often worse at night. Symptoms typically resolve within 1 to 2 days but may last up to 1 week.

Physical Examination

In viral infectious croup, stridor is primarily inspiratory and monophasic. However, if the narrowing extends beyond the thoracic inlet, it can be biphasic. Mild disease is characterized by absent to minimal stridor and retractions

Table 23–1. Differential Diagnosis of Stridor

Diagnosis	Clinical Features
Acquired/Congenital Causes of Stridor in Young Infants	
Laryngomalacia	Onset at birth or within the first several weeks after birth Typically worsens around 4–8 months with resolution by 12–24 months Stridor worsens with supine position, agitation (crying and excitement), feeding, and viral URTIs Infant is otherwise well
Subglottic hemangioma	Presents between 2 weeks and 6 months of age, with peak symptoms around 2 months Biphasic stridor, hoarseness, barky cough (similar to croup), respiratory distress, and difficulty feeding Stridor increases in frequency and severity as the hemangioma grows Cutaneous hemangiomas of head and neck are often present
Subglottic stenosis	May be congenital or acquired May present with prolonged, unusually severe, or recurrent croup Prolonged intubation is a major risk factor for acquired stenosis Severe cases tend to present with biphasic stridor and respiratory distress with dyspnea and increased work of breathing
Tracheomalacia and external airway compression	May be present at birth and usually improves by 6–12 months of age Infant is otherwise well Symptoms may include persistent barky/brassy cough, biphasic stridor, wheezing, dyspnea, cyanosis, and respiratory distress Crying, feeding, and viral respiratory infections tend to worsen symptoms Stridor may be positional May be associated with congenital syndromes
Vocal cord paralysis	Risk factors include difficult delivery where the neck is stretched (breech or vertex delivery) or compressed (looped umbilical cord, use of forceps), intrathoracic or central nervous system abnormalities that cause compression of the nerve supply, and injury from intubation or surgical procedure (especially cardiac surgery) Unilateral: mild inspiratory/biphasic stridor, hoarseness, intermittent aspiration and feeding difficulties Bilateral: more severe, with cyanosis, severe stridor, apnea, and significant respiratory distress requiring emergent airway management
Other Causes	
Anaphylaxis	History of allergies or exposure to an offending substance Acute onset of stridor/cough/wheezing Swelling of the face/lips/tongue Urticarial rash Nausea/vomiting/diarrhea/abdominal pain
Bacterial tracheitis	Age 6 years or younger Sudden onset of upper airway obstruction and respiratory distress following a viral respiratory illness (croup, influenza) Rapid deterioration with toxic appearance with high fever Copious, purulent secretions at suctioning

Table 23–1. Differential Diagnosis of Stridor, continued	
Diagnosis	**Clinical Features**
Foreign body aspiration	Peak age 2–3 years Developmental delay/autism History of choking/gagging Sudden onset of cough/stridor/drooling/dyspnea/wheezing No prodrome of URTI or fever
Severe hypocalcemia (extremely rare)	Laryngospasm causes stridor May also have irritability, tetany, seizures, bronchospasm, carpopedal spasm, prolonged QTc, arrhythmias, and/or left ventricular failure
Retropharyngeal abscess	Age 2–4 years Fever, sore throat, dysphagia with drooling Muffled stridor without barking cough Limited neck movement, especially neck extension
Spasmodic croup	Recurrent episodes of nighttime barky cough and stridor No history of URTI or fever

Abbreviation: URTI, upper respiratory tract infection.

with normal respiratory effort. In moderate disease, stridor is present at rest and worsens with agitation. Other findings include mild to moderate retractions and decreased lung aeration. Severe disease and impending respiratory failure are characterized by agitation, decreased mental status, continuous stridor, severe retractions, markedly decreased lung aeration, cyanosis, and/or hypoxemia.

Laboratory Workup

Croup is a clinical diagnosis, and routine imaging is not warranted. If an anteroposterior neck radiograph is obtained, look for subglottic narrowing (steeple sign). However, this finding may be absent. Similarly, viral testing is only indicated if the results would change management (eg, influenza, SARS-CoV-2). Often, obtaining a radiograph or viral nasopharyngeal swab only agitates the patient, worsening airway obstruction and respiratory distress.

Differential Diagnosis

Suspect a congenital or acquired anatomic airway abnormality in a young infant with unusually persistent or severe disease, chronic or recurrent episodes of stridor, or age less than 3 months. In such cases, order 2-view chest radiography and consult an otolaryngologist or pediatric pulmonologist to discuss additional diagnostic workup, such as laryngoscopy and further imaging. Similarly, consider other diagnoses in older infants and children when viral upper respiratory symptoms are absent and clinical clues such as sudden

onset of symptoms or specific physical examination findings (eg, hemangioma, urticaria) are present. The differential diagnosis of stridor beyond viral infectious croup is summarized in Table 23–1.

Treatment

Systemic steroids are the mainstay of treatment for viral infectious croup and will decrease the severity and duration of symptoms, length of hospitalization, use of racemic epinephrine, need for intubation, and need for transfer to the intensive care unit (ICU). Dexamethasone is preferred because of its long half-life, low cost, and ease of administration. Give a single dose (0.3 mg/kg; 12-mg maximum) if the patient has stridor at rest or respiratory distress, but not if there is only a barking cough. Oral, intravenous (IV), and intramuscular (IM) routes are equally effective, so reserve IM or IV administration for a patient who cannot tolerate oral medication or who has severe respiratory distress. The benefit of repeat steroid dosing is unclear, but if the patient continues to need repeated nebulized epinephrine treatments, give a second dose of dexamethasone 24 to 48 hours after the first one.

Nebulized epinephrine has a rapid onset and will alleviate airway obstruction until the dexamethasone becomes effective. Administer 0.05 mL/kg (0.5-mL maximum), diluted in 3 mL of normal saline, to a patient with moderate to severe disease. The dose can be repeated, if necessary, in 4 hours.

If there is severe airway obstruction with signs of impending respiratory failure, the patient will require intubation and ICU admission. Because of the significant subglottic edema, use an endotracheal tube that is at least 0.5 mm smaller than the size calculated for the patient's age.

Avoid agitating the patient, because crying increases negative intrathoracic pressure and worsens airway obstruction. Do not administer humidified oxygen unless the patient is hypoxic, because it does not improve symptoms, and forcing a mask on an agitated patient only exacerbates respiratory distress. Similarly, attempting to perform a blood gas analysis prior to intubation will only serve to agitate the patient.

Indications for Consultation

- **Anesthesia:** Emergent airway management required
- **Otolaryngology:** Significant airway compromise; age less than 3 months; long duration of symptoms (> 1 week); recurrent croup episodes (> 2 episodes per season); concern for epiglottitis, bacterial tracheitis, foreign body aspiration, or airway burn; or evaluation for congenital or acquired airway narrowing/abnormality

Disposition

- **ICU transfer:** Severe respiratory distress and hypoxemia
- **Discharge criteria:** Mild respiratory distress, no nebulized epinephrine treatment in 6 hours, adequate oral intake

Follow-up

- **Primary care:** 1 to 2 days
- **Otolaryngology:** 1 to 2 weeks, if the patient has an underlying airway anomaly

Pearls and Pitfalls

- Reserve nebulized epinephrine for a patient with moderate to severe disease.
- The cricoid cartilage is located in the subglottic area and is the narrowest part of the pediatric upper airway. Only 1 mm of edema in this area can decrease airflow by as much as 80%.
- When intubating a patient with croup, use an endotracheal tube size that is 0.5 mm smaller than the size calculated for the patient's age.

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Endocrinology

CHAPTER 24

Acute Adrenal Insufficiency

Introduction

Adrenal crisis is a rare but life-threatening emergency, with a high mortality rate, unless recognized and treated promptly. At presentation, adrenal crisis may be a sign of adrenal insufficiency, or it may occur when a patient with known adrenal insufficiency does not receive adequate hormonal replacement. A patient being tapered off chronic glucocorticoid therapy is also vulnerable. Because the signs and symptoms of adrenal insufficiency are nonspecific, the diagnosis may not be suspected until late in the disease course, when the patient presents with a life-threatening cardiovascular collapse or severe hypoglycemia.

Primary adrenal insufficiency is consequent to diseases that affect the adrenal gland itself. The most common cause of primary adrenal insufficiency is congenital adrenal hyperplasia (CAH). Other etiologies include damage to the adrenals from infection (commonly tuberculosis, HIV, and fungal infections), hemorrhage, autoimmune diseases, metabolic diseases (adrenoleukodystrophy), medications (ketoconazole, etomidate), and postpartum. Secondary adrenal insufficiency might be caused by deficient adrenocorticotropic hormone (ACTH) production or suppression from prolonged pharmacologic doses of glucocorticoids. A patient with primary or secondary adrenal insufficiency requires additional doses of glucocorticoids when subjected to physiological stress. Inadequate or no replacement may precipitate an adrenal crisis.

Clinical Presentation

History

The patient may initially present with nausea, abdominal pain, and vomiting, a clinical picture that is frequently misdiagnosed as a gastrointestinal (GI) illness. A neonate may have atypical genitalia (virilized female), electrolyte abnormalities, poor weight gain, and/or shock. Acute decompensation can occur rapidly and is often precipitated by stress from surgery, trauma, or infection. A patient with undiagnosed adrenal insufficiency may have chronic complaints, such as weakness, fatigue, anorexia, and weight loss. A history of a psychiatric illness (anorexia, depression) or other endocrine problems (diabetes, hypothyroidism) may also be present. Salt craving can occur in a patient with chronic primary adrenal insufficiency.

Physical Examination

The patient will typically appear unwell and have clinical evidence of hypovolemia. Tachycardia, hypotension, shock, and altered mental status are common. Skin hyperpigmentation in areas not exposed to sunlight, such as the axillae and palmar creases, can occur in a patient with chronic primary adrenal insufficiency. A female neonate may have ambiguous genitalia.

Laboratory Workup

If adrenal insufficiency is suspected, order a chemistry panel to look for metabolic acidosis, hyperkalemia, hypoglycemia, and hyponatremia. If the crisis is triggered by infection, inflammatory markers and white blood cell count may be increased. If possible, obtain blood to evaluate cortisol, ACTH, aldosterone, and plasma renin before administering exogenous steroids. However, *do not delay definitive treatment* if these tests cannot be obtained immediately. If CAH is suspected in a neonate, obtain blood for a 17-hydroxyprogesterone level.

Differential Diagnosis

Consider adrenal crisis in a critically ill patient who is unresponsive to fluid resuscitation (60 mL/kg), particularly if the patient has a history of previous adrenal insufficiency or is receiving replacement or pharmacologic doses of exogenous corticosteroids (Table 24–1).

Table 24–1. Differential Diagnosis of Acute Adrenal Insufficiency

Diagnosis	Clinical Features
Acute surgical abdomen	Guarding, rebound tenderness
Diabetic ketoacidosis	Polyuria, polydipsia, weight loss, severe dehydration ↑ blood glucose, osmolarity ↓ bicarbonate, glucosuria, acidosis
Gastroenteritis	Diarrhea is common ↓ bicarbonate, ↑ blood urea nitrogen
Intestinal obstruction	May have bilious vomiting, abdominal distention
Pyloric stenosis	Typically presents at 10 days–6 weeks of age Forceful, projectile vomiting ↓ chloride, ↓ potassium, metabolic alkalosis
Sepsis	Fever, cough, respiratory distress, petechia, or purpura ↑ white blood cell count and inflammatory markers, ↑ lactate, acidosis

↓ indicates decreased; ↑, increased.

Treatment

Fluids

Immediately treat suspected adrenal crisis with 20-mL/kg boluses of 0.9% normal saline solution, up to a total of 60 mL/kg within the first hour. Once the patient's blood pressure has stabilized, continue administration of 0.9% normal saline with 5% dextrose at 1.5 to 2 times the maintenance rate.

Steroids

Administer stress doses of steroids simultaneously with the fluid resuscitation. Intravenous (IV) hydrocortisone is the treatment of choice because of its mineralocorticoid activity. The dosing is as follows:

- 0 to 3 years of age, 25 mg
- 3 to 12 years of age, 50 mg
- 12 years of age or older, 100 mg

Follow this with the same IV dose per day, either continuously or divided into 4 daily doses. Administer the hydrocortisone intramuscularly if IV access is not readily available.

Glucose

If blood glucose is low (< 50 mg/dL [2.8 mmol/L]), give a bolus of 0.5 to 1 g/kg of 25% dextrose (4 mL/kg) to restore euglycemia (see Chapter 28, Hypoglycemia). Alternatively, for infants and children, use 5 to 10 mL/kg of 10% dextrose.

Potassium

If the patient is hyperkalemic (> 6 mEq/L [6 mmol/L]), immediately obtain an electrocardiogram. If the findings are consistent with hyperkalemia (peaked T waves [T wave > one-half the R- or S-wave], shortening of the QT interval, prolonged PR interval, widened QRS complex), or if the potassium level is greater than 7 mEq/L (7 mmol/L), initiate treatment in an intensive care setting. The immediate goal is to transiently redistribute total body potassium: 25% dextrose (2 mL/kg administered over 30 minutes; repeat every 30 minutes) and/or nebulized albuterol, along with regular insulin (0.1 U/kg). Also administer 10% calcium gluconate (1 mL/kg = 100 mg/kg per dose, delivered every 5–10 minutes) to provide myocardial stability. To enhance potassium excretion, use a loop diuretic (IV furosemide 1–2 mg/kg, administered every 6 hours) and rectal polystyrene sulfonate (1 g/kg).

Additional Treatment

If an underlying illness precipitated the adrenal crisis, further treatment may be needed (eg, antibiotics for bacterial infections).

Stress Dosing

In a patient with known adrenal insufficiency who is hospitalized for fever, vomiting, diarrhea, inadequate oral intake, burns, or surgery, start stress doses of steroids. Administer hydrocortisone, as noted above (0–3 years of age, 25 mg; 3–12 years of age, 50 mg; 12 years or older, 100 mg), 3 or 4 doses per day, for 24 to 48 hours. Consult a pediatric endocrinologist if prolonged stress dosing is required or if major surgery or sepsis is the cause.

Indications for Consultation

- **Endocrinology:** Acute adrenal crisis; a history of adrenal insufficiency in a patient admitted to the hospital for major surgery or sepsis; a history of prolonged exposure to glucocorticoids; stress dosing anticipated for more than 48 hours
- **Intensivist:** Adrenal crisis

Disposition

- **Intensive care unit transfer:** Adrenal crisis.
- **Discharge criteria:** The cause of fever, infection, or trauma that precipitated the crisis has been identified and treated, the patient is able to tolerate oral medications and maintain hydration, and the family has been educated about stress dosing.

Follow-up

- **Pediatric endocrinologist:** 1 to 2 weeks
- **Primary care:** 2 to 4 weeks

Pearls and Pitfalls

- Adrenal crisis can initially mimic a GI illness.
- Do not delay treatment of an adrenal crisis while awaiting confirmatory testing.
- Suspect adrenal crisis if there is hypotension and shock disproportionate to the underlying illness.
- Hydrocortisone is the drug of choice for adrenal crisis because of its glucocorticoid and mineralocorticoid effects. Methylprednisolone is an alternative.
- At discharge, recommend that the patient has a medical emergency bracelet and carries an emergency medical information card.

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CHAPTER 25

Diabetes, Diabetic Ketoacidosis, and Type 2 Diabetes

Introduction

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus (T1DM). DKA occurs when there is a disruption in the balance between insulin and the counterregulatory hormones from either a lack of circulating insulin or increased counterregulatory hormones in response to stress (trauma, acute gastroenteritis, sepsis). This imbalance leads to a catabolic state, which precipitates the hallmarks of DKA: hyperglycemia, hyperosmolality, increased lipolysis, ketonemia, and metabolic acidosis. An osmotic diuresis ensues, causing dehydration and the production of more counterregulatory hormones, further disrupting the balance.

Diabetic ketoacidosis can be the initial presentation of T1DM. In a patient with known T1DM, DKA tends to occur when there is missed insulin dosing or mismanagement of insulin during an illness or in the setting of a severe febrile or gastrointestinal (GI) illness. Although DKA is a more common presentation in T1DM, as many as 25% of children with type 2 diabetes mellitus (T2DM) initially present with DKA. Cerebral edema (CE) is a potentially fatal complication of DKA, most commonly presenting 4 to 12 hours after treatment is initiated.

Type 2 Diabetes Mellitus

The incidence and prevalence of T2DM in children and adolescents has increased dramatically over the last decade, accounting for one-third of newly diagnosed cases of diabetes. It is caused by insulin resistance and impaired insulin secretion from pancreatic islet β-cells. Youth-onset T2DM differs both from T1DM in children and adult-onset T2DM in that it is not mediated by an autoimmune process but is often caused by a precipitous decline in β-cell function, followed by the rapid development of diabetes complications. However, the presentation of T2DM may mimic that of T1DM, so inpatient management may be required.

Hyperglycemic Hyperosmolar Nonketotic Syndrome

Rarely, an older patient with T2DM may present with hyperglycemic hyperosmolar nonketotic syndrome (HHNK). This is characterized by severe

hyperglycemia (blood glucose > 600 mg/dL [> 33.3 mmol/L]) and elevated osmolarity (serum osmolarity > 330 mOsm/kg), in the absence of significant acidosis or ketosis.

Clinical Presentation

History

A patient with DKA often presents with a history of polyuria, polyphagia, polydipsia, and weight loss, sometimes accompanied by nausea, vomiting, or severe abdominal pain. However, nocturia, enuresis, or nonspecific systemic complaints (lethargy or fatigue) can be the initial symptoms.

Ask whether the patient was small for gestational age birth weight or if they have a history of polycystic ovary syndrome (PCOS), a maternal history of diabetes or gestational diabetes, or a family history of T2DM in a first- or second-degree relative.

On occasion, the patient may present with specific reports of hyperglycemia, glucosuria, or ketonuria, especially if another family member's glucometer or urine dipsticks were used at home.

Physical Examination

A patient in DKA presents with signs of dehydration (delayed capillary refill time, dry mucous membranes, tachycardia, skin tenting), Kussmaul breathing (rapid, deep sighing), and possibly a fruity breath odor. In severe cases, there may be evidence of hypovolemic shock (hypotension, oliguria, weak pulse, cool extremities). In addition, the patient may have an altered mental status or be obtunded, which is worrisome for CE. Other signs of CE associated with intracranial hypertension are inappropriate slowing of the heart rate and increasing blood pressure.

Type 2 diabetes mellitus is associated with obesity, so measure the height and weight and calculate the body mass index. Also look for signs of insulin resistance (acanthosis nigricans) or of PCOS (hirsutism, severe acne).

A patient with HHNK may have profound volume and electrolyte depletion, even more severe than a patient with DKA. However, signs of dehydration may be masked because of obesity and preservation of intravascular volume secondary to the hypertonicity.

Laboratory Workup

Use the following laboratory criteria to confirm the diagnosis of DKA:

- **Diabetes:** Hyperglycemia (blood glucose level > 200 mg/dL [> 11.1 mmol/L])

- **Ketosis:** Ketonemia (serum β-hydroxybutyrate level > 3 mmol/L) and/or ketonuria
- **Acidosis:** Venous pH level less than 7.3 or bicarbonate level less than 15 mEq/L (< 15 mmol/L)

For any patient suspected of having DKA, obtain a complete blood cell count and a comprehensive metabolic panel, as well as osmolality, hemoglobin A_{1c} (HbA_{1c}), and β-hydroxybutyrate levels. Perform a venous blood gas analysis for serum pH and a urinalysis to check for ketones. If DKA is the presentation of new-onset diabetes, also obtain levels of C-peptide, insulin (if C-peptide is not obtained), insulin autoantibody, islet cell autoantigen 512, glutamic acid decarboxylase 65 antibody, thyroid stimulating hormone, thyroxine, thyroid peroxidase antibody, and thyroglobulin antibody (to evaluate for autoimmune thyroid disease). If infection is suspected, obtain appropriate cultures (urine, blood, throat, wound, etc) and treat as indicated.

The serum sodium level may be low because of dilutional hyponatremia or pseudohyponatremia, when the excess glucose in the extracellular space causes osmotic movement of water into the space, resulting in a relatively lowered sodium concentration. As the hyperglycemia is corrected with treatment and the osmotic movement of water is reversed, the serum sodium level will increase.

$$\text{Corrected sodium level} = \text{serum sodium level} + 1.6 \times [(\text{serum glucose level in milligrams per deciliter} - 100)/100]$$

Although the initial potassium level may be high, there is a total body depletion of potassium as intracellular stores are lost from transcellular shifts (exchange of K^+ for extracellular H^+; glycogenolysis and proteolysis from insulin deficiency causes potassium efflux from cells); osmotic diuresis, which leads to increased urinary losses; and additional GI losses, if the patient is vomiting. However, the measured serum potassium level may be normal, high, or low. If timely measurement of serum potassium level is not available, obtain an electrocardiogram to look for evidence of hypokalemia (flat T waves, appearance of U waves, widened QT interval) or hyperkalemia (peaked T waves, short QT interval). Once correction of electrolyte abnormalities is started, the serum potassium level will decline. Close monitoring and replacement, as needed, are essential.

Differential Diagnosis

Although there are a number of different causes of metabolic acidosis, polyuria, and hyperglycemia, only DKA causes all 3. The differential diagnosis is summarized in Table 25–1.

Table 25–1. Differential Diagnosis of Diabetic Ketoacidosis

Diagnosis	Clinical Features
Glycosuria	
Fanconi syndrome	Normal serum glucose level Hypophosphatemia, uricosuria, aminoaciduria Growth failure
Benign familial glycosuria	Normal serum glucose level
Hyperglycemia	
Corticosteroid administration	↑ Serum glucose level No metabolic acidosis
Nonketotic hyperosmolar state	↑ Serum glucose level and osmolality No or minimal ketosis; no metabolic acidosis Stupor or coma
Stress	↑ Serum glucose level No ketonuria No metabolic acidosis
Metabolic Acidosis, Ketosis	
Salicylate poisoning	Metabolic acidosis (with or without respiratory alkalosis) No ketosis Serum glucose level ↓ or ↑ (usually < 300 mg/dL [< 16.65 mmol/L])
Sepsis	Fever, toxic appearance Source of infection may be apparent Serum glucose level normal or increased No Kussmaul breathing or fruity breath odor
Severe gastroenteritis/ dehydration	May have diarrhea Lactic acidosis can cause metabolic acidosis Serum glucose level mildly increased, decreased, or normal
Starvation	No hyperglycemia or glycosuria Bicarbonate level usually > 18 mEq/L (> 18 mmol/L)
Polyuria	
Postsurgical/relief of obstructive uropathy	No glucosuria/ketonuria Serum glucose level normal No metabolic acidosis
Urinary tract infection	Urinary symptoms: dysuria, urgency No metabolic acidosis Serum glucose level normal

↑ indicates elevated; ↓, decreased.

Treatment

Diabetic Ketoacidosis

Consult with a pediatric endocrinologist and/or pediatric intensivist early in the course of treatment. Obtain the patient's height and weight (compare to the premorbid weight) after assessing the severity of dehydration and level

of consciousness. The goals of therapy are restoring the circulating volume, correcting metabolic derangements, avoiding treatment complications (hypokalemia, CE), and identifying and treating the underlying cause (infection, insulin pump malfunction, etc) of the DKA.

Initial Management

The total fluid goal is 1.5 to 2 times maintenance. Start at 2,500 mL/m^2/d, which is approximately maintenance fluids plus about 6% deficit, using an isotonic fluid (normal saline or lactated Ringer solution). Administer an initial normal saline bolus of 10 mL/kg, delivered over 1 hour, and subtract this amount from the total fluid goal. Repeat once if clinically indicated. Exercise caution when administering initial fluids so as not to potentiate CE. However, if there is evidence of shock, fluid resuscitation is the priority.

If CE is suspected, elevate the head of the bed to 30 degrees, reduce the intravenous (IV) fluid rate by one-third, and administer IV mannitol (0.5–1.0 g/kg) or hypertonic (3%) saline (5–10 mL/kg). Consider intubation if there is impending respiratory failure. After the patient is stabilized, order computed tomography of the head to confirm the diagnosis and to look for other intracranial pathologic findings (ie, thrombosis or hemorrhage).

If there is no evidence of shock or severe dehydration, begin a regular insulin drip (0.1 U/kg/h) after initiating fluid resuscitation to counteract the ongoing catabolic state. Use the two-bag system to efficiently correct metabolic derangements (Box 25–1).

Monitoring

Successful management of DKA requires meticulous monitoring and frequent adjustments in treatment, based on the patient's response. Monitor the patient's vital signs, neurologic status, and fluid intake and output. Obtain finger-stick glucose measurements every hour to adjust the fluid infusion to prevent hypoglycemia. Add dextrose to the infusion early if the rate of glucose decrease is greater than 90 mg/dL/h ($>$ 5.0 mmol/L/h) or if the patient develops hypoglycemia (target glucose is 100–180 mg/dL [5.6–10 mmol/L]). Check electrolyte levels and perform a blood gas assessment every 2 to 4 hours until the bicarbonate level is greater than or equal to 15 mEq/L ($\geq$ 15 mmol/L), then every 6 hours until metabolic derangements have normalized. Test the patient's urine for ketones at every void until the ketones are cleared.

Transition

Clinical improvement occurs as the metabolic derangements are corrected and the signs of DKA resolve. Transition the patient to oral fluids and appropriately reduce IV fluids when the bicarbonate level is greater than or equal to

Box 25–1. Two-Bag System

Potassium
- $K^+ \leq 5.5$ mEq/L (≤ 5.5 mmol/L)
  - Bag A: LR/NS + 1.5 mEq (1.5 mmol/L) KCl/100 mL + 2 mmol KPO_4/100 mL
  - Bag B: D10 LR/NS + 1.5 mEq (1.5 mmol/L) KCl/100 mL + 2 mmol KPO_4/100 mL
- $K^+ \geq 5.5$ mEq/L (≥ 5.5 mmol/L)
  - Bag A: LR/NS
  - Bag B: D10 LR/NS

IV rate
Use the blood glucose level to determine the ratio between the Bag A and Bag B IV rates.
Total IV rate (mL/h) = Bag A rate (mL/h) + Bag B rate (mL/h)

Glucose level
- ≥ 300 mg/dL (≥ 16.67 mmol/L): Use only Bag A
- 251–300 mg/dL (13.94–16.67 mmol/L): 75% Bag A and 25% Bag B
- 201–250 mg/dL (11.17–13.89 mmol/L): 50% Bag A and 50% Bag B
- 151–200 mg/dL (8.39–11.11 mmol/L): 25% Bag A and 75% Bag B
- ≤ 150 mg/dL (≤ 8.33 mmol/L): Use only Bag B

Abbreviations: D10, 10% dextrose; IV, intravenous; KCl, potassium chloride; KPO_4, potassium phosphate; LR, lactated Ringer solution; NS, normal saline.

15 mEq/L (≥ 15 mmol/L) or the pH is greater than or equal to 7.3. The most convenient time to transition the patient to a subcutaneous (SC) insulin regimen is prior to a meal. Administer rapid-acting SC insulin approximately 15 to 30 minutes or regular SC insulin 1 to 2 hours before stopping the insulin infusion. If an intermediate or long-acting SC insulin preparation is used, allow a longer overlap time with the insulin infusion to prevent worsening acidosis. Continue to monitor finger-stick glucose levels hourly while the patient is receiving the insulin infusion. Once the infusion is stopped, monitor the blood glucose level before meals, at bedtime, and at 2:00 am.

Normalization of electrolytes and serum glucose may take a few days, during which time some of the autoantibody panel results can help confirm the diagnosis, as a lack of autoantibodies usually correlates with T2DM. If T2DM is diagnosed, start the patient on an oral glycemic agent, metformin 500 mg daily (not weight based). This can be titrated in the outpatient setting to achieve glycemic control and the HbA_{1c} target.

Consult with a nutritionist familiar with diabetes to review dietary needs and skills such as carbohydrate counting for T1DM or starting a weight loss program for an obese patient with T2DM.

Hyperglycemic Hyperosmolar Nonketotic Syndrome

The management of HHNK differs in that the priorities are fluid administration and frequent laboratory monitoring, with less use of insulin. Fluid administration alone will significantly correct electrolyte derangements. However, the infrequent indications for an insulin drip are ketosis or when

the serum glucose is declining slowly (< 50 mg/dL/h [< 2.8 mmol/L/h]) with fluid administration. Stop the insulin once the ketosis resolves and the serum glucose concentration drops by more than 100 mg/dL/h (5.5 mmol/L/h).

Carefully monitor the patient's vital signs, neurologic status, and fluid intake and output. Adjust the fluid rate and composition to achieve a decline in serum sodium of 0.5 mEq/L/h (0.05 mmol/L/h) and a decrease of the serum glucose of 75 to 100 mg/dL/h (4.2–5.5 mmol/L/h). An osmotic diuresis may occur with fluid replacement, which increases the risk of vascular collapse and shock, so replace urinary losses 1:1 with 0.45% normal saline. Monitor serum electrolytes every 2 to 4 hours because deficits of potassium, phosphate, and other electrolytes are common and require adjustments of the fluid composition.

Technology in Diabetes Mellitus Management

Over the past 30 years, diabetes management has increasingly benefited from technological innovations, including glucose sensing, insulin delivery, glucose-responsive insulin delivery (GRID) systems, and data management tools. Automated GRID systems and hybrid closed-loop systems offer options for improvement in glycemic control and reduction in hypoglycemia risk. Data downloading and remote monitoring from insulin pumps and continuous glucose monitoring (CGM) are possible, with uploading of data to health care professionals. This can facilitate dosing adjustments and more precise diabetes management than periodic face-to-face visits alone.

Glucose Monitoring

Continuous glucose monitoring has become the standard of care, offering the benefits of improved quality of life, reduced risk of hypoglycemia, and less glycemic variability. Most continuous glucose monitors last 6 to 14 days and are minimally invasive, with sensors placed on the arms or abdomen.

A continuous glucose monitor consists of a sensor, transmitter, and display device. Interstitial glucose is measured at 1- to 5-minute intervals and is displayed on demand or in real time. Real-time CGM has the added benefit of built-in alarms when sensing both hypoglycemia and hyperglycemia, based on predefined threshold values.

An inpatient can continue to use a properly functioning continuous glucose monitor, with hospital bedside capillary blood glucose (CBG) checks to calibrate and monitor accuracy of the readings. However, CGM is less accurate in the hypoglycemic range and with rapidly changing glucose values. If clinical symptoms do not correlate with readings, use hospital bedside CBG checks or venous glucose samples and forgo CGM.

Insulin Delivery

Insulin delivery systems consist of insulin pens and pumps, with optional Bluetooth technology for cloud upload and data sharing. This facilitates accurate insulin delivery that is convenient and customizable. Although insulin delivery systems have been shown to be safe, the risk of DKA remains the same.

During inpatient care, the continued use of an insulin delivery system might be appropriate, depending on the acute medical issues being addressed. If the patient is significantly ill or admitted for DKA or ketosis, remove the insulin pump and use traditional CBG monitoring and multiple insulin injection therapy. Consider a pump malfunction if a patient without a history of acute illness or strenuous exercise presents with acute hypoglycemia or hyperglycemia. Remove the device and institute traditional diabetes in-hospital management with frequent glucose monitoring.

Glucose-responsive Insulin Delivery

Glucose-responsive insulin delivery systems include CGM and insulin delivery with automated suspension of insulin delivery when low glucose levels are predicted. Hybrid single-hormone closed-loop systems are more complex and address hypoglycemia and hyperglycemia. Glucose-responsive insulin delivery systems provide a reduced risk of hypoglycemia, particularly overnight.

Indications for Consultation

- **Endocrinologist:** DKA, NNHK, initial diagnosis of T1 or T2DM
- **Nutritionist:** For discharge planning, once the DKA or HHNK has resolved

Disposition

- **Intensive care unit transfer:** Severe DKA (pH level $<$ 7.1), insulin drip (varies by institution), new-onset DKA in a patient younger than 5 years, altered mental status, signs of sepsis, CE, HHNK
- **Discharge criteria:** Euglycemia maintained on a carbohydrate-consistent diet and an appropriate insulin regimen, family/patient instructed on monitoring glucose levels and managing hypo-/hyperglycemia, and necessary follow-up arranged

Follow-up

- **Primary care physician:** 1 to 2 weeks
- **Endocrinologist:** Within 1 week

Pearls and Pitfalls

- The measured sodium level increases with decreasing hyperglycemia during DKA treatment and does not indicate worsening hypertonicity.
- In DKA, the anion gap is usually 20 to 30 mmol/L. A gap greater than 35 mmol/L suggests concurrent lactic acidosis.
- When hydrating a patient in DKA, the serum pH level may initially decrease as lactic acid is mobilized from the periphery.
- During DKA treatment, if the biochemical derangements are not correcting, consider other potential causes of impaired insulin response (infection, errors in insulin preparation) and adjust the insulin therapy if warranted.
- The routine use of bicarbonate to correct metabolic acidosis is associated with CE and is therefore contraindicated unless there is profound acidosis and cardiac dysfunction. In addition, avoid giving fluids at a rate over 4 $L/m^2/d$.
- The current obesity epidemic has made it more difficult to distinguish between T1DM and T2DM. Consult with an endocrinologist early in the hospital course.
- The diabetes care team must explore social determinants of health with the family as they implement culturally inclusive interventions.
- Most insulin pumps are not automatic and require as much self-care as metered-dose inhaler therapy.
- Ask the patient and family about the manufacturer, model, and special instructions related to their particular device. They may be better informed than the inpatient staff.

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CHAPTER 26

Diabetes Insipidus

Introduction

Diabetes insipidus (DI) is classified as either central, which results from a deficiency of antidiuretic hormone (ADH), or nephrogenic, which is secondary to insensitivity to ADH in the kidneys. Both etiologies prevent water reabsorption in the kidneys, leading to hypotonic polyuria. Central DI is caused by genetic defects, congenital abnormalities (septo-optic dysplasia, holoprosencephaly), disruptions in hypothalamic-pituitary ADH production (trauma, neoplasms, infections, autoimmune disorders), or idiopathic causes. Nephrogenic DI may be genetic, idiopathic, or acquired, including kidney disease (chronic renal failure, pyelonephritis, obstructive uropathy, polycystic kidney disease), medications (amphotericin B, gentamicin, lithium), and electrolyte disorders (hypokalemia, hypercalcemia).

Clinical Presentation

History

The patient may present with nonspecific findings, such as irritability, intermittent fever, vomiting, seizures, hypotonia, or failure to thrive. Obtain a detailed history to assess fluid intake, urine output, and voiding pattern. The patient's parents may report polydipsia, polyuria, and clear-colored urine. Extreme thirst and nighttime fluid intake can also lead to sleep disturbances and daytime tiredness. However, polydipsia may be absent if the patient does not have an intact thirst mechanism. Enuresis in a previously toilet-trained child is also common. A patient with known DI may present with some other cause for disruption of homeostasis, such as an intercurrent illness.

Physical Examination

The initial priority is to assess the patient for evidence of severe dehydration or shock (dry mucous membranes, delayed capillary refill time, skin tenting, weak peripheral pulse). Also, look for other sequelae of pituitary gland dysfunction (adrenocorticotropic hormone or growth hormone deficiency), visual and central nervous system dysfunction (headache, visual field changes), and craniofacial midline defects (septo-optic dysplasia). In addition, in a patient with known DI, look for signs of intercurrent viral or bacterial illnesses.

Laboratory Workup

Once polyuria is confirmed, simultaneously check the serum osmolality and electrolyte levels, as well as urine osmolality, urine specific gravity, and glucose levels. If intracranial pathology is suspected, perform brain and pituitary magnetic resonance (MR) imaging with gadolinium-based contrast material, because computed tomography lacks the detail necessary to properly evaluate the hypothalamus and pituitary gland.

The key laboratory findings in DI are

- Urine output greater than the upper limit of normal (150 mL/kg/d for infants; 110 mL/kg/d for young children; 40 mL/kg/d for older children)
- Inappropriately low urine specific gravity (< 1.005) or urine osmolality (< 300 mOsm/kg; often remains < 150 mOsm/kg), with simultaneous serum hyperosmolality (> 300 mOsm/kg)
- Urine osmolality less than serum osmolality

Consult a pediatric endocrinologist to perform a water deprivation test, followed by a vasopressin test, to differentiate between central and nephrogenic DI. The differential diagnosis of polyuria is summarized in Table 26–1.

Table 26–1. Differential Diagnosis of Polyuria

Diagnosis	Clinical Features
Cushing syndrome	Hyperglycemia Characteristic physical findings: round face, upper body fat, striae
Fanconi syndrome	Acidosis, hypokalemia, hyperchloremia Rickets, osteomalacia Growth failure
Hypercalcemia	↑ Calcium level (> 12.0 mg/dL [> 3.0 mmol/L]) Weakness, altered mental status
Medication side effect	Amphotericin, cisplatin, clozapine, cyclophosphamide, demeclocycline, foscarnet, furosemide, ifosfamide, lithium, methicillin, rifampin, vinblastine
Osmotic diuresis (diabetes)	Hyperglycemia ↑ Serum osmolality Serum sodium level normal or ↓
Postobstructive diuresis	Serum sodium level/osmolality normal Urine osmolality normal or ↓
Primary polydipsia Psychogenic (compulsive) Dipsogenic (abnormal thirst)	Serum and urine osmolality normal to low normal
Renal concentrating defect	Polycystic kidney Renal failure Sickle cell tubulopathy
Urinary tract infection	Urinary symptoms: dysuria, urgency

↑ indicates increased; ↓ decreased.

Treatment

Consult with an endocrinologist and/or nephrologist.

Fluid Replacement

- **Resuscitation:** The initial priority in DI is fluid resuscitation with 0.9% normal saline if the patient presents with hypovolemic shock (see Chapter 13, Shock). Then, correct the hypernatremia and dehydration after calculation of the fluid deficit by using 0.45% normal saline over 48 hours to prevent a rapid decrease in serum sodium levels and cerebral edema.
- **Free water deficit (in milliliters):** Calculate the free water deficit as follows: 4 mL/kg × body weight (in kilograms) × (Na^+ concentration measured − Na^+ concentration desired [145 mEq/L or 145 mmol/L]). Then, administer this volume as dextrose 5% in 0.45% normal saline at a rate of 3 to 6 mL/kg/h.
- **Maintenance and ongoing urine losses:** Calculate maintenance fluids (1,600 mL/m^2/d) and ongoing fluid loss from urine output, and replace these amounts with 0.45% normal saline.
- **Monitor:** Monitor the serum sodium level every 1 to 2 hours, to ensure that it falls slowly, until it is 145 mEq/L (145 mmol/L), then every 3 to 6 hours until the sodium level is normal. The goal is a rate of correction of < 0.5 mEq/L/h (< 0.5 mmol/L/h) or < 10 mEq/L/d (< 10 mmol/L/d) to prevent cerebral edema.

In an infant or young child with high fluid volume needs, thiazide diuretics can paradoxically reduce urine output. Give hydrochlorothiazide 1 to 3 mg/kg/d divided into doses administered once or twice daily. Switch to desmopressin (see dosing below) once the patient is tolerating a solid diet. If hypokalemia develops, add amiloride 0.30 to 0.625 mg/kg/d divided into doses administered twice daily. Consult with an endocrinologist and/or nephrologist before ordering these medications.

Central DI

Treat central DI with desmopressin, which is available in oral, intranasal, and subcutaneous preparations. Desmopressin decreases urine output by causing increased water reabsorption in the renal collecting ducts. Oral is the preferred route over intranasal because there is less risk of hyponatremia and fewer side effects (eye irritation, headache, flushing, vomiting, tachycardia). The doses are

- **Oral:** Start with 2 to 3 mcg/kg/d divided into doses administered twice daily, then titrate to the desired response (< 12 years of age, 100–800 mcg/d; ≥ 12 years of age, 100–1,200 mcg/d; divided into 2 daily doses).

- **Intranasal:** 3 months to 12 years of age, 5 to 30 mcg/d, divided into doses administered twice a day; 12 years or older, 5 to 40 mcg/d, divided into doses administered 3 times a day.
- **Subcutaneous:** 2 to 4 mcg/d, divided into doses administered twice a day; an infant may require very small doses.

Nephrogenic DI

Manage nephrogenic DI with a low-sodium diet (300–500 mg/d) and diuretics. Use amiloride (0.30–0.625 mg/kg/d divided into doses administered twice daily) with hydrochlorothiazide (1–3 mg/kg/d, divided into doses administered once to twice a daily) for hypokalemia, and indomethacin (1–2 mg/kg/d divided into doses administered twice daily) with hydrochlorothiazide for persistent polyuria.

Indications for Consultation

- **Endocrinology:** All patients
- **Nephrology:** Nephrogenic DI
- **Neurology, neurosurgery, and/or oncology:** Abnormal MR imaging findings

Disposition

- **Intensive care unit transfer:** Patient has severe dehydration and hypovolemic shock that requires fluid resuscitation and tightly controlled sodium reduction; patient will be undergoing water deprivation and vasopressin tests.
- **Discharge criteria:** Clinical improvement, electrolyte abnormalities corrected, pharmacologic regimen in place, comorbid conditions adequately managed, and family educated about measuring urine output and administering doses of desmopressin.

Follow-up

- **Primary care:** 1 to 2 weeks
- **Endocrinologist:** 2 to 3 days

Pearls and Pitfalls

- Surgical or accidental trauma may cause central DI in a previously healthy child if the pituitary gland is damaged.
- At presentation, central DI may be the initial sign of a brain tumor (germinoma, craniopharyngioma).
- Langerhans cell histiocytosis with involvement of the brain, bones, or other organs may develop years after diagnosis of central DI.

- The current standard of reference for diagnosing DI is the measurement of vasopressin production during graded hyperosmolar stimulation. Simpler tests to better aid in diagnosis (measurement of copeptin) are being developed.

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Hyperthyroidism

Introduction

Hyperthyroidism is rare in children, but if unrecognized, it can have potentially fatal consequences. The most common cause (95%) of hyperthyroidism in pediatrics is Graves disease (autoimmune hyperthyroidism), which primarily affects female adolescents. There is a strong genetic predilection and association with other autoimmune diseases within the family or in the same patient. Other causes of hyperthyroidism include pituitary and thyroid adenomas, Hashitoxicosis, suppurative or subacute viral thyroiditis, and drug-induced (amiodarone, iodine) thyrotoxicosis.

Thyroid storm, or thyrotoxic crisis, is a rare, multisystem medical emergency that may be precipitated by acute illness, surgery, or abrupt withdrawal of antithyroid medications in a patient with hyperthyroidism. It can be fatal if untreated.

Clinical Presentation

History and Physical Examination

Hyperthyroidism has widespread systemic effects, so the patient may present with fatigue or hyperactivity, weight loss despite increased appetite, diarrhea, muscular weakness, and psychological and growth disturbances. Physical examination findings include tachycardia; hypertension; widened pulse pressure; proptosis; warm, moist skin; fine hand tremor noted with arm extension; and thyromegaly.

A patient with thyroid storm will have an acute onset of high fever, tachycardia, hypotension, arrhythmias, vomiting and diarrhea, agitation, acute psychosis, hepatic failure, and coma.

Laboratory Workup

Perform thyroid function tests: a low thyroid-stimulating hormone (TSH) level with increased triiodothyronine (T_3) and thyroxine (T_4) levels establishes a diagnosis of hyperthyroidism. Thyroid-stimulating antibodies are present in autoimmune thyroiditis. If the free T_4 level is normal but the TSH level is suppressed, then measure the free T_3 level (T_3 toxicity). Also check the white blood cell count, glucose, lactate dehydrogenase, and liver transaminase, as well as cortisol, which may be consistent with a relative adrenal insufficiency.

If the patient is negative for thyroid-stimulating antibodies, obtain ultrasonography or scintigraphy of the thyroid. This will help determine increased thyroid hormone production and guide initial antithyroid treatment.

No specific laboratory workup is necessary to establish a diagnosis of thyroid storm. The diagnosis depends on the presence and severity of the signs and symptoms listed in the Clinical Presentation section.

Differential Diagnosis

Hyperthyroidism and thyroid storm may or may not be a continuum, with symptom overlap. Consider acute drug intoxication, acute mania, severe viral gastroenteritis, pheochromocytoma, and diabetic ketoacidosis in the differential diagnosis. A patient with acute mania might demonstrate impaired judgment, euphoria, irritability, hallucinations, and unpredictable, violent behavior. A patient with severe viral gastroenteritis will not demonstrate mental status changes unless there are concurrent metabolic abnormalities. Pheochromocytoma may be mistaken for a thyroid storm because of anxiety, weight loss, sweating, and tachycardia. However, a patient with thyroid storm is typically hypotensive and febrile, with muscular weakness and possibly stigmata of preceding hyperthyroidism, such as proptosis. A patient with diabetic ketoacidosis will have hyperglycemia with ketosis.

Consumption of biotin, a water-soluble vitamin often found in dietary supplements marketed for hair, skin, and nail growth, can also lead to falsely abnormal thyroid studies resembling hyperthyroidism in otherwise euthyroid individuals.

Treatment

Thyroid storm can be life-threatening. Therefore, initiate treatment immediately if the diagnosis is suspected. Obtain an urgent endocrinology consultation and provide hydration with normal saline as a 20-mL/kg bolus, repeated as needed, followed by maintenance fluids. Other supportive care includes use of antipyretics and cooling blankets, restoring electrolyte imbalances, and providing cardiorespiratory support. Under the direction of an endocrinologist, the treatment for hyperthyroidism is antithyroid drug therapy with methimazole. Do not use propylthiouracil, given the increased risk of drug-induced hepatic necrosis in children and adolescents. β-Blockers (eg, propranolol, atenolol), corticosteroids, inorganic iodide, and plasmapheresis may be needed, with expert consultation. Once thyroid storm has resolved, definitive therapy involves either radioiodine ablation or thyroidectomy to achieve permanent hypothyroidism.

Consultation

- **Endocrinology:** All patients

Disposition

- **Intensive care unit transfer:** Thyroid storm, until the patient's hemodynamic status is normal and body temperature is stabilized
- **Discharge criteria:** Patient clinically euthyroid and tolerating medications

Follow-up

- **Primary care:** 1 week
- **Endocrinology:** 1 to 2 weeks

Pearls and Pitfalls

- Obtain baseline absolute neutrophil count and liver function tests before starting methimazole, because agranulocytosis is a potential side effect.

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CHAPTER 28

Hypoglycemia

Introduction

Hypoglycemia is defined as a low glucose value that produces a neuroendocrine response and associated symptoms, with a rapid resolution after the return to euglycemia. For infants and children, hypoglycemia is a blood glucose value less than 60 mg/dL (< 3.3 mmol/L). Always obtain a critical sample (see Laboratory Workup section) if the blood glucose is less than 50 mg/dL (< 2.8 mmol/L). See Chapter 85, Hypoglycemia of the Newborn, for the care of infants less than 72 hours of chronological age.

Most often, hypoglycemia is found in a patient who is known to have diabetes, or the hypoglycemia is physiological and associated with acute illness, fasting, sepsis, or inadequate oral intake (in cases of nausea and/or vomiting). In such situations, no specific workup is necessary.

Ketotic hypoglycemia is a relatively common disorder of unknown etiology that manifests as hypoglycemia after prolonged (often overnight) fasting in a young child who is acutely ill.

Potentially serious but uncommon etiologies include disorders of insulin (gene/enzyme–related hyperinsulinism, insulinoma, infant of a diabetic mother, Beckwith-Wiedemann syndrome), glycogen storage diseases (glucose 6-phosphatase deficiency), defective counterregulatory/neuroendocrine responses (hypopituitarism), defective glycogenolysis/gluconeogenesis (pyruvate carboxylase deficiency, galactosemia), abnormal fatty acid oxidation (inborn errors of metabolism, medium-chain acyl-CoA dehydrogenase), defective glucose transporters ("GLUT" deficiency), ingestions, and acute and chronic illness including sepsis.

Clinical Presentation

History

Common autonomic symptoms include anxiety, dizziness, nausea and vomiting, diaphoresis, irritability, and weakness, although some patients do not report any symptoms. There may also be central nervous system symptoms, such as confusion, seizures, psychiatric outburst, and altered mental status.

Ask about recent meals and duration of fasting, illnesses, and similar previous episodes, as well as a family history of a disease that predisposes the patient to hypoglycemia. Determine if the patient has access to hypoglycemic medications.

Physical Examination

The patient may be tachycardic, hypothermic, and diaphoretic, with altered mental status ranging from somnolence to encephalopathy to coma. However, the patient may have a normal examination.

Laboratory Workup

For a term infant without risk factors for hypoglycemia, glucose reference ranges are similar among age groups beyond about 48 to 72 hours of chronological age.

Indications for performing reference laboratory tests include physical examination findings suggestive of an inborn error of metabolism (hepatosplenomegaly, hypotonia) and family history of unexplained infant death, inborn errors of metabolism, or an episode that cannot be clearly explained despite a detailed history. It is imperative that laboratory testing (the "critical sample") be performed at the time of the hypoglycemic event, because it will have the highest yield. Ideally, this testing would occur under an endocrinologist's guidance, but do not delay conducting tests while awaiting consultation.

The critical sample includes assessing

- Blood, including electrolytes, lactate, β-hydroxybutyrate, growth hormone, cortisol, insulin/C-peptide, serum free fatty acids, total and free carnitine, acyl-carnitine profile, and ammonia. Send specific toxicology studies if ingestion is suspected and an alanine level if ketotic hypoglycemia is suspected.
- Urine ketones, glucose levels, reducing substances, and urine organic acids.

Differential Diagnosis

Because various disorders may cause hypoglycemia, a detailed history and physical examination, paired with evaluation of supporting laboratory values, is crucial (see Table 28–1).

Treatment

The treatment for hypoglycemia is glucose, with a goal of maintaining a blood glucose level greater than 70 mg/dL (> 3.88 mmol/L). If the patient is able to safely swallow, offer oral sugar (eg, fruit juice, glucose tablets, table sugar, glucose gel). Otherwise, administer an intravenous (IV) dextrose bolus of 0.25 to 0.5 g/kg (maximum dose of 25 g). For a patient younger than 5 years, give 2.5 to 5 mL/kg of 10% dextrose solution (D10W); between 5 and 12 years of age, 1 to 2 mL/kg of 25% dextrose (D25W); 12 years or older, 1 to 2 mL/kg of D25W. Infuse the dextrose bolus over several minutes (2–3 mL/min) to avoid causing rapid glucose swings.

Table 28–1. Differential Diagnosis of Nonphysiological Hypoglycemia

Possible Disorders	Suggestive Features
Adrenal insufficiency Growth hormone deficiency	Severe hypoglycemia with missed meals ↑ Ketones, ↓ insulin level Acidosis
Enzyme deficiencies	Severe constant hypoglycemia ↑ Ketones, ↑ lipid/free fatty acid levels, ↓ insulin level
Fatty acid oxidation defect	Severe hypoglycemia with missed meals (−) Ketones, ↑ FFA level, ↓ insulin level, abnormal transaminase levels, abnormal acylcarnitine profile and urine organic acid levels
Galactosemia	Hypoglycemia after ingesting milk or milk products ↑ Ketones, elevated transaminase levels, ↓ insulin level
Glycogen storage disease	Hypoglycemia with growth restriction Hepatomegaly ↑ Ketones and blood lactate, cholesterol, triglyceride, and uric acid levels Acidosis
Hyperinsulinism	Recurrent, severe hypoglycemia shortly after meals History of other family members affected (−) Ketones ↑ Insulin level, ↓ FFA level
Ketotic hypoglycemia	Severe hypoglycemia with missed meals ↓ Alanine level, ↑ ketones
Ingestions (ethanol, oral hypoglycemic agents, β-blockers, salicylates)	Suggestive history ↓ Ketones, ↓ FFA

Abbreviation: FFA, free fatty acids.
↑ indicates increased; ↓, decreased; (−), negative finding.

Check the glucose level after 15 minutes, and if persistently low, repeat the bolus. After the bolus(es), for an infant, start an IV continuous infusion of 10% dextrose at a rate of 6 to 9 mg/kg/min. For an older patient, start an IV infusion of 5% dextrose at a rate of 2 to 3 mg/kg/min.

$$\text{Glucose infusion rate (mg/kg/min)} = \frac{\text{Glucose concentration (g/dL)} \times \text{Infusion rate (mL/kg/h)}}{6}$$

Reserve higher-dextrose concentrations for a patient with central access because of extravasation risk. If IV access cannot be obtained, administer subcutaneous or intramuscular glucagon (0.03 mg/kg; maximum 1 mg per dose).

Indications for Consultation

- **Endocrinologist, metabolic disorder specialist, or geneticist:** Suspected hyperinsulinism or inborn error of metabolism

Disposition

- **Intensive care unit transfer:** Hemodynamic instability, high glucose infusion rate that requires central line access
- **Discharge criteria:** Euglycemia restored and maintained, and patient/family educated about signs/symptoms of hypoglycemia and appropriate interventions

Follow-up

- **Primary care:** Within 1 week
- **Endocrinology:** 1 month; sooner if workup is still required
- **Genetics:** 1 to 2 weeks, if an underlying abnormality or inborn error of metabolism is suspected or diagnosed

Pearls and Pitfalls

- Hypoglycemia is a medical emergency. Do not withhold treatment of a symptomatic patient to perform blood tests.
- Obtain critical laboratory samples during periods of hypoglycemia or diagnostic fasting, ideally with endocrinologist consultation.
- Glucose meters provide rapid assessment of plasma glucose levels and allow for frequent testing, but none of the commercially available devices is as accurate as laboratory testing.

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Equipment

CHAPTER 29

Feeding Tubes

Introduction

Feeding tubes are commonly used in children as an alternative means of providing nutrition, hydration, and medications, especially for the patient with a chronic feeding problem. Feeding tube management in such a child is best served by a multidisciplinary team of specialists, including nurses, dietitians, therapists, care coordinators, and equipment suppliers.

Types of Feeding Tubes

There are 2 types of feeding tubes.

Depending on institutional preference, enterostomy tubes are inserted endoscopically, surgically, or percutaneously under fluoroscopic guidance. Examples include gastrostomy tubes (G-tubes), gastrojejunal tubes (GJ-tubes), and jejunal tubes (J-tubes). All of these are indicated for longer-term use (> 8–12 weeks).

Oronasal tubes include nasogastric (NG), orogastric, nasoduodenal, and nasojejunal tubes. These are generally reserved for short-term use or as a bridge to a more permanent enterostomy tube. They are associated with an increased risk of dislodgment and migration.

Enterostomy Tubes

Enterostomy tubes have 3 main components (Box 29–1): an internal portion (balloon, mushroom, bulb, pigtail) within the stomach that prevents inadvertent tube withdrawal; an external stabilizing portion, which is often a disk or bar near the skin; and a feeding port that is either close to the stabilizer in low-profile devices or attached to a longer tube in traditional tubes.

Typically, traditional tubes are initially placed and then replaced with a low-profile device (G button) after 6 to 12 weeks. However, the timing is dependent on local practice.

Indications for G-Tubes

Gastrostomy tubes are useful in a number of clinical situations, such as a patient with a chronic oral-motor feeding problem (ie, neuromuscular disease, brain injury, autism, feeding aversion) associated with an inability to maintain hydration orally, prolonged feeding times, and risk of pulmonary aspiration. Other indications include failure to thrive as a result of inadequate caloric intake due to a specific disease process (eg, cystic fibrosis, congenital heart

Box 29–1. Types of Enterostomy Tubes
Low profile (button tubes): Device is flush to the skin
G-tube with a mushroom-shaped dome tip
G-tube with a silicone balloon tip that can be inflated with saline
GJ-tube with a silicone balloon tip that can be inflated with saline
Combination G-tube and GJ-tube with a silicone balloon tip that can be inflated with saline
Non–low profile: Device has a long external portion
G-tube with an internal pigtail loop and an external locking device
G-tube with an internal balloon tip and an external port for inflating/deflating the balloon
G-tube with a mushroom or wing tip to secure the tube to the stomach
G-tube with a round bolster to secure the tube to the stomach
GJ-tube with a gastric loop and a distal loop that sits in the jejunum

Abbreviations: GJ-tube, gastrojejunal tube; G-tube, gastrostomy tube.

disease, chronic renal failure, malignancy) and the need to deliver an elemental diet or essential medications for the treatment of disease processes (eg, ketogenic diet, inflammatory bowel disease, eosinophilic esophagitis, inborn error of metabolism).

Indications for Jejunal Feedings (GJ- and J-Tubes)

Be selective when ordering GJ-tubes, which bypass the stomach and pyloric sphincter, as they are associated with more mechanical problems, such as clogging and migrating. They also present a greater inconvenience for families. A GJ-tube is especially useful in a patient with severe gastroesophageal reflux (GER), who is already receiving maximal GER medical treatment but remains at risk for aspiration. Also, patients with gastrointestinal anatomic anomalies, such as superior mesenteric artery syndrome, can benefit from a jejunal feeding.

Complications Associated With G-, GJ-, and J-Tubes

Complications related to enteral tubes can occur both early (within < 30 days of the procedure) and late. Complication rates depend on the technique of placement. Late, minor complications are common with all techniques.

Early (Procedure Related)

Early complications include bleeding, infection (peristomal or systemic), puncture of other intra-abdominal organs (colon, liver), misplacement of the tube (into the small or large bowel), peritonitis, esophageal tear (percutaneous endoscopic gastrostomy), aspiration, anesthetic-related complications, and death (rare).

Late

Late complications include issues with the tube (blockage, dislodgment, breakage), peristomal wound infections, stomal enlargement with leakage

around the tube, erosion of the internal bumper into the gastric wall (buried bumper syndrome), peritonitis caused by displacement of the tube into the peritoneum (rare), and intussusception around the distal portion of the tube (GJ-tube).

Management of Enterostomy Tube Placement Complications

Peritonitis (All Tubes)

Peritonitis is a rare complication that occurs within 48 hours after insertion, or during the first weeks after, when the tract between the stomach wall and skin is not yet formed. Causes include leakage of gastric contents into the peritoneal space, dislodgment of the tube into the peritoneum, and perforation of other organs or vessels during the procedure. The patient presentation is similar to other causes of peritonitis, with fever, irritability, vomiting, and peritoneal signs.

Management involves general measures, including discontinuing feedings, placing an NG-tube for gastric drainage, administering broad-spectrum antibiotics (see Chapter 106, Acute Abdomen), and aggressive fluid management. In addition, obtain a radiograph or fluoroscopic study with contrast material (tube check) to confirm tube placement and assess for the presence of pneumoperitoneum. If there is a concern about intra-abdominal collections or bleeding, perform ultrasonography (US) or computed tomography. In some cases, an emergent laparotomy will be necessary to investigate and manage a possible perforation.

Vomiting (All Tubes)

Always consider non–tube-related causes, including GER, which may worsen after the placement of an enterostomy tube. Gastrostomy tubes, particularly those with a long internal portion or without a securing mechanism (Mac-Loc [Cook Medical], Foley catheter), can then migrate into the duodenum or esophagus. Perform a contrast-enhanced study (G-tube check). Gastrojejunal tubes can also migrate, becoming malpositioned, or promote reflux (from duodenum to stomach). In addition, intussusception can be a complication with certain tubes in young infants (discussed later in this section).

Clogging (All Tubes)

Obstruction or clogging of an enteral tube is usually caused by a medication (Box 29–2), thickened feeding materials, or failure to flush the tube after feedings. A tube with a thinner outside diameter is also more prone to blockage.

Box 29–2. Some Medications and Substances That Commonly Block Enterostomy Tubes	
Cholestyramine resin	Magnesium oxide
Ciprofloxacin	Nelfinavir mesylate
Clarithromycin	Pancrelipase
Cornstarch	Pyridoxine (vitamin B_6)
Iron (liquid)	Sodium polystyrene sulfonate
Lactulose	

To relieve the obstruction, gently flush with warm water by using a 1- to 3-mL syringe. If this is ineffective, repeat with a carbonated beverage or cranberry juice. However, in some cases, the tube may have to be removed.

Intussusception (Primarily GJ-Tubes)

Intussusception is a rare complication and has been reported with pigtail catheters, as the distal portion of the tube acts as a lead point for a small bowel intussusception. The highest risk is in a patient younger than 1 year, who can present with bilious vomiting and irritability. Diagnosis is confirmed with abdominal US, and management includes tube removal and placing a temporary Foley catheter into the stomach. Recurrences may be prevented by shortening the tube. However, recurrences are an indication for discontinuing the GJ feedings and trying other options, such as fundoplication and continuous gastric feedings.

Dislodged Tube (All Tubes)

If tube dislodgment occurs more than 6 to 8 weeks after the initial insertion, when the tract has been formed, insert a temporary Foley catheter as soon as possible, because the stoma can close within 1 to 2 hours. Use a Foley catheter that is the same size or one size smaller than the G-/GJ-tube. Apply some lubricating jelly to the Foley catheter and insert it 4 to 6 cm into the stoma, fill the balloon of the Foley catheter with 3 mL of sterile or distilled water, and tape the catheter to the patient's abdomen. Confirm the position in the stomach by withdrawing the stomach contents through a syringe. For a child who is fed by G-tube, the Foley catheter can be used for feeding or medications until a replacement tube is inserted. For a patient with GJ-tube dislodgment, initiate temporary gastric feedings only if it is medically safe (ie, the patient is not at a high risk of aspiration).

However, if the dislodgment occurs within 8 weeks of initial insertion, when the tract is not completely formed, do *not* immediately insert a temporary Foley catheter. The patient is at risk of peritoneal placement of the tube and subsequent peritonitis. Obtain a contrast-enhanced study of the tract prior to using the Foley catheter or any other replacement tube.

Skin Infection (All Tubes)

Good care of a G-tube site can help prevent site infections. Clean the stoma daily with soap and water, keep the stoma dry, and avoid covering the stoma site with dressings. An infection presents with redness around the site and/or pus, but evaluate for other causes of redness, which may be confused for infection (Table 29–1). If there is an inadequate response to treatment, obtain a peristomal culture and/or US imaging.

Feeding Via an Enterostomy Tube

Decisions regarding the type and route of feeding depend on medical condition, indication for the tube, and gut physiology. A nutritionist can aid in formula selection based on caloric needs. Basic considerations follow.

Bolus Feedings

Calculate the daily caloric requirement and deliver one-eighth of the total every 3 hours (or one-sixth every 4 hours, or one-fourth every 6 hours, etc), with each bolus delivered over 1 hour. Adjustments can be made accordingly. However, if the patient is receiving transpyloric feedings, do not use boluses because the small intestine (unlike the stomach) is not capable of receiving fluids in this manner.

Caloric and Fluid Needs

Calories and fluids will vary widely, depending on the patient and the indication(s) for the tube. For example, a patient with severe neurologic delay and a decreased metabolic rate will have a lower caloric need than an

Table 29–1. Differential Diagnosis of Peristomal Erythema

Diagnosis	Presentation	Management
Bacterial infection	Rarely complicated by abscess formation	Topical bacitracin/polymyxin Oral antibiotics (cephalexin)
Fungal infection	Erythema with satellite lesions May have coexisting oral thrush or diaper candidiasis	Topical antifungal cream Oral nystatin for coexistent oral candidiasis
Granulation tissue	Pinkish-red, moist tissue May bleed May be painful	Warm saline compresses No dressings or creams Silver nitrate cautery
Irritation secondary to leakage of gastric contents	Erythema, breakdown, or ulceration	Keep area dry Barrier cream (zinc oxide) Consider application of a topical antacid
Skin sensitivity/contact dermatitis	Red, scaly, dry skin	Remove all dressings Change the adhesive tape

otherwise active patient with cystic fibrosis. As a general rule, calculate a fluid/calorie estimate, then track the patient over a period of 3 to 5 days to ensure adequate tube function, adequate weight gain, and appropriate hydration.

Types of Formula

There is nothing particularly unique about a tube-fed patient in terms of the choice of nutrition, although this may depend somewhat on the reason(s) why the tube was placed. Allow the gut physiology to drive the choice of breast milk or formula. As an example, initially order that the patient be fed with one of the standard formulas or breast milk (for an infant) or one of the higher-calorie products (for a young child), if there are no contraindications.

Discharge Planning

Discharge planning may be complex. Try to determine the family's preferences. A case manager or a social worker can be helpful in the transition of the patient and family from the inpatient to the outpatient setting in terms of medical equipment and formula delivery. Intensive family teaching about use of enterostomy tubes can improve family comfort. One useful common strategy for facilitating the transition to the home environment is to implement daytime bolus feedings (allowing the patient time off the feeding pump) and overnight continuous feedings, then monitor the patient for a day or two.

Pearls and Pitfalls

- The delivered tube feeding volume is often less than what was ordered because the feedings are frequently stopped, delayed, or withheld for multiple reasons. Base calorie counts on volume delivered, not ordered.

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CHAPTER 30

Lines and Pumps

Introduction

Access is necessary to deliver fluids and medications when a patient is unable to take them adequately by mouth. A variety of different types of access are available, including peripheral venous, central venous, intraosseous (IO), and pump placement.

Types and Placement of Lines

The Michigan Appropriateness Guide for Intravenous Catheters in Pediatrics (MiniMAGIC) 2020 provides recommendations for the selection and placement of vascular access (Table 30–1).

Peripheral Venous Access

Use a peripheral intravenous catheter (PIVC) when intravenous (IV) access is needed for less than 7 days. Take care with the administration of irritant fluids or medications, avoiding solutions with a dextrose concentration greater than

Table 30–1. Recommendations for Appropriate Access Selection

Intravenous Catheter Type	Appropriate Uses
PIVC	Peripherally compatible fluids Duration: term neonate ≤ 7 days; infant/child/adolescent ≤ 14 days ≥ 2 blood draws per day for no more than 7 days
Umbilical	Peripherally compatible fluids for term neonate for ≤ 7 days Nonperipherally compatible fluids for term neonate for ≤ 30 days
PICC	Peripherally compatible fluids for neonate for ≥ 8 days; for infant/child/adolescent ≥ 15 days Nonperipherally compatible fluids for any length of time Frequent blood draws (≥ 2 per day) for child/adolescent for ≥ 15 days
Nontunneled CVAD	Nonperipherally compatible fluids for infant for ≤ 14 days Unstable, critically ill patient for fluids or hemodynamic monitoring
Tunneled, cuffed CVAD	Peripherally or nonperipherally compatible fluids for term neonate/infant/child/adolescent for ≥ 31 days Frequent blood draws (≥ 2 per day) for term neonate/infant for ≥ 31 days
TIVD	Peripherally compatible fluids for child/adolescent for ≥ 31 days Nonperipherally compatible fluids for term infant/child/adolescent for ≥ 31 days
IO	Unstable, critically ill patient

Abbreviations: CVAD, central venous access device; IO, intraosseous; PICC, peripherally inserted central catheter; PIVC, peripheral intravenous catheter; TIVD, totally implanted venous device.

Derived from Ullman AJ, Bernstein SJ, Brown E, et al. The Michigan Appropriateness Guide for Intravenous Catheters in pediatrics: MiniMAGIC. *Pediatrics*. 2020;145(suppl 3):S269–S284.

12.5%, pH less than 5 or pH greater than 9, or an osmolarity greater than 600 mOsm, as well as dilute irritant medications (epinephrine, potassium, dopamine, calcium). Place the PIVC in the forearm or hand, although the foot and scalp are alternatives in a neonate, using the smallest bore catheter that can handle the anticipated flow rate. Possible complications include cellulitis, phlebitis, or thrombosis (Table 30–2). Transition to oral medications as soon as it is safe, to avoid the need for central vascular access.

Central Venous Access

Indications for central venous access include IV access that is needed for 8 days or more, frequent blood draws ($\geq$ 2 per day) are anticipated, or the patient will be receiving irritant fluids or medications that are not compatible with peripheral access. Complications include dermatitis, cellulitis, central line–associated blood stream infection, thrombosis, and cardiac rhythm dysfunction (Table 30–2). A peripherally inserted central catheter (PICC) can be used up to 18 months, while tunneled CVADs and implantable catheters can be used for months to years.

Peripherally Inserted Central Catheter

Insert a PICC into a large peripheral vein in the forearm, then advance into the basilic, brachial, or cephalic vein (children and adolescents). Alternatively, advance the catheter only as far as the axilla (midline PICC). A PICC can be placed at the bedside or with the assistance of interventional radiology. Verify central placement with radiography.

Central Venous Access Device

Also known as a central catheter, these can be nontunneled or tunneled and cuffed. Insert a nontunneled central catheter at the bedside into the

Table 30–2. Common Complications of Central Lines, Ports, Catheters, and Baclofen Pump

Diagnosis	Clinical Features
Arterial puncture	Bleeding, hematoma
Blood stream infection	Fever, positive blood culture
Cardiac rhythm dysfunction	Ventricular dysrhythmias, bundle branch block
Dermatitis/cellulitis	Erythema, hardness, tenderness to palpation
Device or line occlusion, failure, breakage	Unable to deliver medication or fluids Symptoms from lack of medication
Hemorrhage or hematoma	Visible bleeding or blood collection
Phlebitis	Pain, inflammation
Pneumothorax Venous air embolism	Rare event with central line insertion, tachypnea, chest pain
Venous thrombosis	Extremity pain, edema

femoral, internal jugular, or subclavian vein. A tunneled cuffed central catheter can be placed into the cephalic or jugular vein by either surgery or interventional radiology.

Implanted Port/Totally Implanted Venous Device

A totally implanted venous device (TIVD) requires surgical placement. The TIVD is subcutaneous and accessed by a needle that remains in place for the duration of the treatment.

Intraosseous Access

An IO is used for rapid fluid or medication administration in a critically ill patient. Typically, it is placed in the proximal tibia and then replaced as soon as possible with vascular access.

Baclofen Pump

A baclofen pump is used to treat spasticity and muscular hypertonia. It is surgically placed in the lower abdominal wall, with a catheter that delivers baclofen directly to the intrathecal space. Baclofen pumps need to be refilled every 1 to 6 months. Infectious complications include superficial infections, organ space infections, deep infections, bacteremia, and meningitis. The most common organisms are *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Enterococcus faecalis*, *Escherichia coli*, and *Proteus mirabilis*. Other complications include granuloma, cerebrospinal fluid (CSF) fistula, CSF leak, pump malfunction/failure, pump migration, or catheter-related complications (Table 30–2). Pump or catheter malfunction can cause baclofen withdrawal within 3 days. Side effects from baclofen withdrawal and baclofen toxicity are summarized in Table 30–3.

Laboratory Workup and Radiology Examinations

Check for pump or catheter malfunction with anteroposterior and lateral abdominal radiographs, but a contrast study may be needed. Use duplex ultrasonography to diagnose catheter-related venous thrombosis. If patient with a central line is febrile, obtain blood cultures from both ports.

Table 30–3. Side Effects From Baclofen Withdrawal or Overdose

Diagnosis	Side Effects
Baclofen toxicity	Altered mental status, respiratory depression, constipation, urinary retention, drooling, seizure, headaches, hypotonia, emesis, dizziness
Baclofen withdrawal	Increased spasticity, elevated body temperature, pruritus, seizures, emesis, insomnia, rhabdomyolysis, disseminated intravascular coagulation

Differential Diagnosis

Common complications for lines and pumps are summarized in Table 30–2.

Flushes and Tissue Plasminogen Activator

Line care with appropriate flush is necessary to keep IV catheters open and reduce the risk of infection and occlusion. Use a flush before and after medication administration, after blood draws, and 2 to 3 times a day for lines without continuous infusions. For peripheral venous lines, administer saline flushes. Heparin flushes for central venous devices can prevent clot formation, but check with your institution's pharmacy regarding concentration and dose of heparin flushes, as they vary. To unblock a central venous catheter, use recombinant tissue plasminogen activator.

Indications for Consultation

- **Infectious disease:** To determine if access or device removal is necessary when there is a blood stream infection
- **Interventional radiology or vascular access team:** PICC placement
- **Neurosurgery:** Baclofen pump placement, concern for complications from baclofen pump such as CSF fistula, CSF leak, pump malfunction/failure, or pump migration
- **Surgery:** Placement of a CVAD or baclofen pump
- **Wound team:** Cellulitis or dermatitis at insertion site

Disposition

- **Intensive care unit transfer:** Baclofen withdrawal or overdose
- **Discharge criteria:** Follow-up arranged, including home health nurse services if indicated

Follow-up

- **Primary care:** 1 to 2 weeks
- **Surgical subspecialist (if involved):** As needed, for device replacement or malfunction
- **Return to ED:** Fever with a central line in place

Pearls and Pitfalls

- If a patient with a central line has fever, obtain blood culture from each port of the central line.
- For peripheral access, avoid fluids or medications with pH less than 5, pH greater than 9, or osmolarity greater than 600 mOsm.

- Consider PICC when vascular access is needed for 8 days or more.
- A 3F or larger PICC is needed to obtain blood specimens.
- The only sure way to avoid PICC complications is not to have the PICC. Carefully review the necessity of the PICC before placement or discharge, including whether there are any oral medication options.

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Ethics and Palliative Care

CHAPTER 31

Do Not Resuscitate/Do Not Intubate

Introduction

The purpose of do not resuscitate (DNR)/do not intubate (DNI) orders is to reflect the limitation of care discussions that health care professionals have with seriously ill patients (or their surrogates). These conversations occur when it appears that attempted resuscitation would be medically ineffective or not in the patient's best interest. Also known as *do not attempt resuscitation* ("DNAR") or *allow natural death* ("AND") orders, these are not to be used in isolation. Rather, they should be part of a larger discussion with the patient (if appropriate) and the parents/guardians as to the overall goals of treatment. DNR/DNI orders are not synonymous with forgoing all medical interventions, and if so specified, DNR/DNI orders can remain in effect should a cardiorespiratory arrest occur while the patient is undergoing other intensive therapies, such as chemotherapy. They can be specific for inpatients or outpatients, or apply to both settings, as a part of a comprehensive advanced care plan. Laws and regulations that govern their application vary from state to state, but in many municipalities the POLST (Physician Orders for Life-Sustaining Treatment) forms are designed to be used across care settings.

DNR orders are specific to the event of a cardiopulmonary arrest. Other forms, such as advance directives or POLST, may describe additional components of advance care planning, such as pain control, symptom management, medically provided fluids and nutrition, and the psychosocial needs of the family.

Most hospitals have DNR/DNI policies or guidelines, as well as forms or order sets. As a child matures into adolescence, there may be guidelines related to obtaining the patient's assent, in addition to the consent of the parents or guardians. In general, always consider the wishes of the adolescent when making decisions about limiting life-sustaining medical treatments.

Process

When a child or adolescent has a life-limiting illness or condition, or is nearing the end of life, arrange for the attending physician, pertinent consultants, patient (if appropriate), and family to discuss the nature and direction of the patient's care. This dialogue is best accomplished when the child or family is *not in a crisis* and can be facilitated by the early inclusion of a palliative care team or provider. For a patient cared for by hospitalists or intensivists, it is especially important to include physicians from the child's medical home in

the process. If the patient is a ward of the state, involve the designated medical decision maker(s).

Once the overall goals are identified, develop and institute an individual plan to help accomplish them, as resuscitation options are varied. Some patients and families may prefer only comfort measures in the event of an arrest, in which case no cardiopulmonary resuscitation should be initiated. In other cases, a "limited DNR" order can be created, defining which therapies would be acceptable. For example, positive-pressure ventilation with bag, mask, and suctioning might be permitted, while chest compressions, intubation, mechanical ventilation, and cardiac medications are not. The more specific the delineation of the plan, the more effectively it can be performed according to the patient's and family's wishes.

Limitation of care conversations, and the goals of care that were identified, must be documented in the medical record and verified by an attending physician, with corresponding orders to match. Although it is desirable to have specific orders in place, formal DNR/DNI orders are not an absolute requirement to withholding these interventions. However, discourage parental "signing" of DNR/DNI orders, as it is not required in most states, and it may place an undue burden on the parents by suggesting that they approved allowing their child to die.

As soon as the DNR/DNI plan is ordered, discuss and review it with all members of the health care team so that it is clearly understood by everyone responsible for its implementation. If there is a lengthy hospitalization, periodically review the DNR/DNI orders to ensure that the patient and family continue to feel that the DNR/DNI orders support the goals of care. But be judicious, as overdoing this can cause them to question their decisions and lead to significant family distress.

Some hospitals may have policies that define how frequently the orders must be reviewed or rewritten, and some facilities may allow an out-of-hospital DNR/DNI order to remain in effect after the patient is hospitalized, although the order may need prompt renewal (ie, within 24 hours of hospitalization). Others may require new orders to be instituted at admission, so it is useful to become familiar with a given hospital's policies. If a well-defined care plan is in place, a brief discussion at the start of each hospitalization can be beneficial to ensure that no changes have occurred. At the same time, the current team can be informed of the patient's and family's wishes.

DNR/DNI orders are typically rescinded, and then must be reinstituted, when a patient goes into surgery, since surgery and anesthesia increase the chance that a patient may require some type of "resuscitation." Some institutions are now recommending an approach called "required reconsideration"

prior to surgery to help clarify the situation. According to this policy, the anesthesiologist and surgeon meet with the patient/family and attending physician to discuss the goal(s) of the DNR order, including whether or not, and how, to incorporate it into the overall surgical plan.

DNR/DNI orders may be used at home and may therefore stay in effect for longer periods. However, this regulation varies among states, so providers should become familiar with their state regulations and forms. In some municipalities, an outpatient form, such as the POLST or MOLST (Medical Orders for Life-Sustaining Treatment), may be helpful to communicate out-of-hospital goals of care. In such a case, provide copies of the orders to the home care agency involved and to local emergency departments, law enforcement, and emergency responders, as appropriate.

Follow-up

- DNR/DNI may be time limited and may require renewal *per hospital policy*. Be aware of the relevant hospital policies and state and local laws and regulations.
- Revisit and possibly revise DNR/DNI orders if the patient's situation changes.
- DNR/DNI orders can be rescinded at any time.

Pearls and Pitfalls

- A delay in initiating discussions about the overall goals and possible resuscitation for a patient with a life-limiting condition is the major obstacle to having a clear plan in place. Ideally, this conversation occurs at admission and not during a crisis.
- Clearly and concisely document the plan.
- The existence of an outpatient DNR/DNI does not automatically transfer to the inpatient setting. Admission creates the need for a new inpatient DNR/DNI order.

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CHAPTER 32

Informed Consent, Assent, and Confidentiality

Introduction

Informed consent is defined as the voluntary agreement of an individual or their authorized representative who has the legal authority to give such agreement. This consent must be exercised within the context of free choice, without any application of inducement or coercion. To give informed consent, an individual must have sufficient knowledge and understanding to be able to make a knowledgeable decision.

Health care providers may have a different level of education and understanding than patients and their guardians. This knowledge gap can add complexity and potential misunderstandings to conversations surrounding informed consent. To bridge this gap, communicate with the patient and/or representative using terms and language that are understood by the individual giving consent.

The duty to inform is limited to those disclosures a reasonable medical practitioner would be expected to make under similar circumstances. These disclosures may be verbal or written and must include the risks and benefits of the proposed course of treatment, along with alternative therapies.

Pediatrics, by definition, deals with many patients who are unable to directly give legal informed consent. In the United States, the age of adulthood, and therefore consent, is a matter of state and local law. In most cases, a minimum age of 18 years is one requirement, although some court decisions have held that a minor's consent is sufficient if they are mature enough to understand the significance and consequences of the proposed treatment. Therefore, age is not always the sole criterion to determine the capacity to legally provide informed consent (see Minors Providing Consent, later in this chapter).

Because most pediatric patients cannot provide consent, pediatricians usually employ the concept of assent. Obtaining assent is a method for the medical provider to demonstrate respect for the child by acknowledging their right to fully understand their own illness. Assent requires an affirmative agreement, not merely a failure to object to the proposed course of care. Assent occurs when a child actively demonstrates their willingness to agree to participate with the care plan.

The position of the American Academy of Pediatrics (AAP), articulated in its technical report "Informed Consent in Decision-Making in Pediatric

Practice," is that "only patients who have appropriate decisional capacity and legal empowerment can give their informed consent to medical care. In all other situations, parents or other surrogates provide informed permission for diagnosis and treatment of children with the assent of the child whenever appropriate." The AAP further recognizes that developmentally appropriate children 7 years and older can provide assent, which will help to "foster the moral growth and development of autonomy in young patients." Assent is not legally binding and is not absolutely required to proceed with a proposed therapy. In these cases, the AAP has stated that "in situations in which the patient will have to receive medical care despite his or her objection, the patient should be told that fact and should not be deceived."

Physicians are often trained on how to obtain consent, but they are rarely taught how to properly obtain the assent of a minor. It is vitally important to inform the patient, in developmentally appropriate terms, of what to expect with the evaluation and treatment plan that is proposed. In addition, assess for any factors, such as coercion, that may affect the patient's responses. If assent is obtained, interpret it as a positive expression of willingness by the patient to accept the plan of care. The AAP has stated that "assent should only be solicited if some element of refusal will be respected."

Conflicts

The provision of medical care to children is often based on proxy consent given by their personal representative, which is usually a parent or guardian. This can cause conflict if the interests of the proxy conflict with the patient's interests and beliefs.

When there is such a conflict, there are two key ethical principles that can be used to mediate. One is the best-interest standard, and the other is the harm principle, both of which are somewhat subjective. The best-interest standard is used when a proxy attempts to consider a patient's interests and make decisions that maximize benefits and minimize harm for the patient. The best-interest standard often requires a judgment about the degree to which the child's interests are prioritized over other ethically salient considerations. The harm principle involves the provider identifying a harm threshold above which no reasonable parent would decline treatment. This principle is based on allowing the parent to make decisions regarding their child as long as those decisions are not deemed to be neglectful or creating an unnecessary risk for the patient.

The AAP recommends that minors should receive effective medical treatments if such treatments are "likely to prevent substantial harm, serious disability, or death." This is true even when parents object to such treatments,

including objections based on their religious beliefs. These situations can often be mitigated by using hospital resources, such as social workers, specialist consultations, second opinions, ethics consultations, and counselors. In situations where a common agreement cannot be reached, or if a child is in immediate danger, health care providers have an obligation to involve the legal system, including child protective services and/or the court system.

Minors Providing Consent

In the United States, the Health Insurance Portability and Accountability Act delineates four circumstances under which the parent or guardian would not be the personal representative of the minor patient: (1) when state or other applicable law gives the minor the right to consent to care; (2) when the minor is receiving care under court order; (3) when the patient, parent, and provider agree that the provider and patient may have a confidential relationship; and (4) in situations where treating a person as a personal representative poses the risk of abuse, neglect, and endangerment. State law gives minors the ability to consent when they are declared to be emancipated minors (a rare case in most clinical practices) or under certain clinical conditions, like when the minor seeks treatment for a sexually transmitted infection or substance use.

Confidentiality

In 2021, the federal government implemented the 21st Century Cures Act. This regulation includes a stipulation that patients or their legally empowered caregivers should have access to medical records, while specifying the types of clinical notes that must be immediately shared with patients and caregivers. However, the release of information to caregivers can potentially create a situation in which the confidentiality between a health care provider and an adolescent patient can be compromised. The 21st Century Cures Act does provide for exceptions that allow for information blocking, including the "Preventing Harm Exception" and the "Privacy Exception." The preventing harm exception applies when the contents of a note present a risk for the patient to physically harm themself or for a caregiver to harm the patient. The privacy exception applies when a legal decision maker requests that certain information not be released. This may then enable health care systems to comply with state laws regarding patient privacy.

Pearls and Pitfalls

- When a minor can consent, it is not necessary to treat the parent or guardian as a personal representative for the patient.

- A confidentiality agreement between the patient, parent, and provider can make it possible to give confidential care under the 21st Century Cures Act.
- The clinical conditions under which a minor can consent vary from state to state.
- In some cases, a patient younger than 18 years can give consent.
- A patient as young as 7 years of age may be able to give assent.

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CHAPTER 33

Palliative Care

Introduction

Pediatric palliative care (PPC) offers physical, emotional, psychological, social, and spiritual support to children with serious illnesses. The emphasis of PPC is to maximize quality of life and goal-concordant decision-making through interdisciplinary collaboration to address the burden of pain and suffering. The American Academy of Pediatrics recommends that PPC be instituted from the time of diagnosis of a life-threatening or serious illness and be continued throughout all subsequent phases of therapy, regardless of whether the expected outcome is cure, life extension, comfort, or care.

The growing population of children with medical complexity, many with life-threatening conditions requiring multiple hospitalizations, provides an opportunity for pediatric hospitalists to engage both families and palliative care teams. An interdisciplinary team consisting of physicians, nurses, social workers, case managers, psychologists, physical and occupational therapists, speech pathologists, child life specialists, music/art therapists, and spiritual care providers can provide PPC. This PPC team can then collaborate with the primary medical teams, the medical home, and specialty providers to participate in the care of these vulnerable patients.

Indications for PPC

Pediatric palliative care is appropriate for patients of any age and at any stage of a life-threatening or life-limiting disease, including those receiving curative treatment. The overarching goal is to improve quality of life and reduce suffering in a manner that aligns with the patient's and family's goals, values, and understanding. Specific triggers for PPC consultation are given in Box 33–1.

Introducing PPC to Patients and Families

The introduction of PPC to a family may be challenging. Families may equate PPC with hospice or view PPC involvement as a signal that death is imminent or that the care team has "given up" on their child. Therefore, it is critically important, at the beginning of building the relationship, to share that PPC will be provided by an interdisciplinary team that collaborates with primary and specialty medical services. The process will ensure that extra support is given to patients and families who are facing serious illness. Informing families that PPC emphasizes goal-directed care, which is integrated with life-prolonging and even curative treatment, may offer reassurance that the medical team is

Box 33–1. Triggers for Pediatric Palliative Care Consultation

Condition-Focused Triggers

An acute or chronic diagnosis with a potentially life-threatening or life-limiting prognosis
Significant symptom burden related to a life-threatening, life-limiting, or serious illness
Decision-making when considering new medical technology, such as a feeding tube, tracheostomy, or ventilator support
Frequent hospital admissions or extended periods of feeling unwell
A serious fetal diagnosis
Progression or relapse of a life-threatening or life-limiting disease
End-of-life and bereavement support

Family-Focused Triggers

Changes in quality of life
Concerns about suffering
Changes in baseline status
Acknowledgment of the need for psychological, social, spiritual, and emotional support for a patient and/or a family
Confusion around the understanding of a prognosis and/or available treatment options

not "giving up" on their child. Emphasize that the medical services in your institution often consult the PPC team for patients with serious illness when the care plan is complex or when there is prognostic uncertainty. Box 33–2 provides an example of wording the physician might use to bring up PPC with the family.

Goals of Care

The goals of care are different for each patient and family. To help identify these goals, invite families (and when appropriate, the child or any person who plays a vital role in decision-making in the family) to a meeting with a small group of the medical team with whom they have a good relationship. Often, it is useful for the medical providers to meet first, so that all members of the team agree on the diagnosis, prognosis, and recommended treatment plans. To determine the patient's and family's goals, ask the following key questions:

- What is your understanding of your (child's) condition?
- What do you expect in the future?
- What are the most important things you desire (for your child) right now?

Box 33–2. Example for the Introduction of Pediatric Palliative Care

To provide the best care for your child and family, we believe it would be helpful to have the PPC service visit with you. Our PPC team partners with families and other health care teams. They are experts at improving your child's quality of life by helping to manage symptoms, such as pain, nausea, and fatigue, as well as providing support to your child and family. They also can help you work through decisions as they arise. Our goal is for all of the teams to work together to provide your child and family with the best care possible.

Abbreviation: PPC, pediatric palliative care.

- What are you hoping for?
- What are your (child's) greatest needs right now?
- What most worries you? What keeps you awake at night?

Spiritual Assessment

A spiritual assessment may also be helpful to better understand the patient's and family's goals. The acronym **HOPE** is a useful tool for assessing the patient's and family's spiritual status and needs.

- **H**ope: What are your sources of hope, strength, comfort, and peace? What do you rely on during difficult times? What or who sustains you and keeps you going?
- **O**rganized religion: Are you a part of a religious community? How is this helpful to you?
- **P**ersonal spirituality and practices: Do you have other personal spiritual beliefs that are helpful to you? What aspects of your spirituality are most helpful (eg, prayer, meditation, music, nature)?
- **E**ffects on medical care and end-of-life issues: Has your (child's) health condition affected your spiritual practices? Are there conflicts between your beliefs and the medical situation? Would it be helpful to speak to a spiritual leader?

Continuity of Care

Pediatric palliative care emphasizes interdisciplinary collaboration among the patient's primary medical team, specialty services, family, and community-based care providers, with the intention of enhancing communication and improving continuity of care. In addition, this continuity of care encompasses end-of-life care, whether in the hospital or at home, as well as the provision of bereavement resources for long-term support to families.

Language Selection

Communication is a key component of successful PPC. Language choices have meaningful effects on patients and families, and it is important to choose words carefully (Table 33–1).

Pain Management

Use the World Health Organization 4-step "ladder" for pain management.

- Step 1: For mild pain, use nonopioids, such as acetaminophen or ibuprofen, with or without adjuvant therapy.

Table 33–1. Appropriate Language Selection

Language to Avoid	Therapeutic Language
Diagnosis-first language (eg, "the leukemic")	Person-first language (eg, "the child with leukemia")
Your child failed therapy.	Unfortunately, our treatments were not successful in curing your child's disease.
I know how you feel. I know how difficult this situation is for you.	I see how difficult this situation is for you.
Do you want us to do everything we can to keep your child alive?	I would like to talk about how to best care for your child if they get sicker or have a sudden event. Have you thought about what would be important to you and your family if that were to happen?
Are you ready to sign the do not resuscitate orders?	I have heard you say that you want to protect your child from painful interventions such as cardiopulmonary resuscitation and intubation. Together we will complete paperwork to ensure that those wishes are honored, both here in the hospital and in the community.
Withdrawal of care	Stopping life support machines

- Step 2: For mild to moderate pain, use a "weak" opioid with or without adjuvant therapy.
- Step 3: For moderate to severe pain, use a "strong" opioid with or without adjuvant therapy.
- Step 4: If there is no pain relief or the pain is increasing, use invasive and minimally invasive treatments.

When discussing analgesics with patients and families, use the term "opioid medication" rather than "narcotic," which may raise concerns about misuse, addiction, or diversion of these medications. Be prepared to engage in open and honest conversations about the indications for using opioid medications. Outline the safety parameters that are recommended and available to mitigate common risks (eg, pill counts, lock boxes, urine drug screens).

Titrate opioid medications based on clinical response. The "right dose" is that which best controls the pain with the fewest side effects. Increase the base dosage as a percentage of the current dose: 30% increase for mild pain, 50% increase for moderate pain, and 100% increase for severe pain. For continuous, nonincidental pain, prescribe long-acting opioid medications (eg, morphine extended release, methadone, fentanyl patch) to provide more continuous pain coverage, together with as-needed short-acting opioid medications.

When using opioid medications, titrate a bowel regimen (osmotic agent and/or stimulant) to prevent and treat constipation.

See Chapter 103, Pain Management, for a more complete discussion.

Nonpharmacologic Symptom Management

Use integrative therapies (eg, relaxation, meditation, breathing exercises, hypnosis, guided imagery, Reiki, biofeedback, yoga, massage, acupuncture/acupressure, art/pet/play/music therapy) to help manage pain and other symptoms.

Fatigue: Consider contributing factors, such as anemia, depression, and medication side effects. Sleep, attending to hygiene needs, and gentle exercise may be helpful interventions.

Dyspnea: Use mindfulness and relaxation exercises, repositioning, a fan, and gentle suctioning. Minimize hydration/avoid overhydration. First-line pharmacologic therapy consists of low-dose, short-acting opioid medications.

Nausea: Attempt dietary modifications (eg, bland/soft foods, timing/volume of intake). Use aromatherapy (peppermint or lavender oils), ginger, and acupuncture/acupressure.

Limit painful procedures and address depression and anxiety through counseling and psychopharmacologic agents, as needed.

Support for Families

Provide respite care when feasible, such that families have time away from caring for the affected patient. Child life specialists and volunteers may provide support for siblings. In addition, enlist case management and social work teams to explore appropriate community-based resources.

Provider Fatigue

Providing PPC to children and families is most often highly rewarding, but it can be overwhelming, leading to frustration, stress, hopelessness, and burnout. To avoid or ameliorate these adverse emotional responses, it is critical for providers to maintain open channels of communication with professional colleagues, other clinicians, and support services. Establish consistent forums for debriefing, with self-reflection and discussion, to provide a safe place for providers to share and reflect on their experiences.

Disposition and Follow-up

Hospice

The availability of pediatric hospice services varies greatly across the country. If a patient enrolls in hospice, it is helpful for the child, family, and primary care team to connect with providers from the hospice agency prior to hospital

discharge. Important topics to address include the symptom management plan, preferred location of death, goals related to resuscitative efforts outside of the hospital, and identifying the physician of record for the hospice agency. Most hospice medical directors are trained in adult medicine, so they may feel uncomfortable caring for children. As such, PPC physicians and community pediatricians often provide medical support to hospice agencies for their patients. A provision of the Patient Protection and Affordable Care Act of 2010 mandates that children enrolled in either Medicaid or children's health insurance programs be eligible for concurrent care, allowing those patients who meet hospice eligibility to receive hospice-based services while also continuing to receive disease-directed therapies. Commonly, children with private insurance are not eligible for this benefit, and many patients and families find themselves at risk of losing important services (eg, home-based shift nursing) or treatment options (eg, blood transfusions) if they enroll in hospice. It is therefore necessary to consider all of the benefits and burdens of adding hospice to the child's care.

Home Care

The philosophy of PPC may be successfully implemented in the home. A PPC provider may be on call to provide support in the home and can serve as a link among the medical home, hospital, specialists, and community caregivers. This PPC provider can help to prevent or facilitate hospital admissions, as well as organize and supervise the provision of respite care and increased home services, as needed. Patients and families benefit from knowing how to obtain help quickly when clinical conditions change (eg, pain flares, behavior changes, breathing difficulties, patient's color changes).

If the patient is being discharged home with goals of care that limit resuscitative measures, complete an out-of-hospital do not resuscitate form and/or a physician/medical orders for life-sustaining treatment form (see Chapter 31, Do Not Resuscitate/Do Not Intubate). These forms are state specific and may be found online through the individual state's department of public health and national organizations. The do not resuscitate form protects a patient from aggressive interventions, such as cardiopulmonary resuscitation and intubation, in the event that emergency medical services are called. Even if the family has signed the form, they may still choose full resuscitative measures at any time.

Pearls and Pitfalls

- The goals of PPC are to maximize quality of life, minimize suffering, and support decision-making through interdisciplinary collaboration.

- If your hospital does not have a dedicated interdisciplinary PPC team, identify key stakeholders and PPC allies to advocate for creating one.
- In the absence of a dedicated PPC team, palliative care may be provided by using primary skills and competencies required of all physicians and health care professionals.
- The role of the hospitalist may be challenging when PPC concepts and end-of-life discussions have not been addressed with a patient and family prior to admission. However, all hospitalists can readily learn the primary skills and competencies of PPC to provide compassionate care that aligns with patients' and families' values and goals.

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Gastroenterology

Acute Hepatitis

Introduction

Acute hepatitis is defined as inflammatory liver injury in a patient with no previous history of chronic liver disease.

The cause of acute hepatitis in children varies according to age. Overall, when a cause can be identified, a viral etiology is the most common (hepatitis A, Epstein-Barr virus). In a neonate, hepatitis can be multifactorial, and infectious and metabolic hepatitis are more frequent. In children older than 1 year of age, viral hepatitis, drugs, and indeterminate causes are the most common etiologies, followed by autoimmune conditions and Wilson disease (rare). Acetaminophen overdose is an important cause in adolescents that has increased in frequency during and immediately following the COVID-19 pandemic.

Clinical Presentation

History

The typical presentation is a flulike illness with symptoms that include anorexia, vomiting, abdominal pain, malaise, and lethargy, with or without fever. This will be followed by progressive jaundice over days to weeks. In rare cases, encephalopathy may occur within hours and will manifest as confusion, somnolence, or altered consciousness. However, encephalopathy may not be detected in infants and young children until they develop severe hepatitis.

Ask about exposure to sick persons with infectious hepatitis (common viruses and hepatitis-causing viruses), a history of blood transfusion, and medications (both prescribed and over the counter) that the child receives or might have taken. A history of developmental delay, failure to thrive, or seizures raises the concern for a metabolic disease or drug side effects. There may be a family history of liver disease, autoimmune conditions, metabolic conditions like α1-antitrypsin deficiency, or Wilson disease.

An adolescent making a suicide attempt or gesture might take a medication (often acetaminophen), with or without other drugs and/or alcohol. In addition, it is important to specifically ask about acetaminophen use, because toxicity can occur from dosing errors during a prolonged therapeutic course.

Physical Examination

Priorities include the growth parameters (young infants) and skin evaluation for jaundice, bruises, and petechiae. Perform an abdominal examination for

hepatomegaly, splenomegaly, and ascites, and look for peripheral edema. A thorough neurologic examination is also essential. Assess mental status, which may range from mild confusion (excessive crying in infants) to coma with hyperreflexia and decorticate/decerebrate rigidity (late stages). The patient may also have signs of hypoglycemia (pallor, diaphoresis), cerebral edema, and/or signs of increased intracranial pressure. In contrast to adults, children with acute liver failure (ALF) do not present with asterixis and fetor hepaticus.

Complications

Hepatitis can progress and lead to anorexia, hypoglycemia, coagulopathy, and, in the worst-case scenario, ALF.

Laboratory Workup

Obtain laboratory studies in a tiered fashion, addressing the most common etiologies first. Initially, obtain a complete blood cell count and electrolyte, glucose, calcium, and phosphorus levels, and perform liver function tests (LFTs), including alanine transaminase (ALT), aspartate transaminase (AST), γ-glutamyltransferase, albumin, and total and direct bilirubin levels. Assess the degree of coagulopathy with prothrombin time (PT) and international normalized ratio (INR). Other initial tests include fibrinogen, ammonia, lipase, and amylase levels. Base further workup on the most likely suspected etiologies. However, the early identification of conditions that are amenable to treatment is the priority for early diagnosis.

If a viral etiology is suspected, send serologic samples for hepatitis A (anti–hepatitis A virus immunoglobulin [Ig] M), B (surface antigen of the hepatitis B virus, antibody to the hepatitis B core antigen), C (anti–hepatitis C virus), and D (anti–hepatitis D virus RNA). Mycoplasma, cytomegalovirus (CMV), and Epstein-Barr serology may be warranted, based on the history.

Obtain a serum acetaminophen level in an adolescent or if accidental ingestion is suspected (see Chapter 68, Toxic Exposures). If the time of ingestion is unknown, the acetaminophen level may be very low, despite markedly increased ALT and AST levels (> 3,500 IU/L]). See Chapter 43, Inborn Errors of Metabolism, for the laboratory evaluation of a suspected metabolic disorder.

If an autoimmune disease is a possibility, obtain immunoglobulin (IgG, IgA, IgM), antinuclear antibody, anti–smooth muscle antigen, and liver–kidney microsomal antibody levels, and complement component tests (C3 and C4).

Obtain serial LTFs to monitor and manage progression or improvement. Consult with a gastroenterologist if the patient is not improving or a coagulopathy develops.

Radiology Examination

Abdominal and Doppler ultrasonography are useful to assess liver size and texture, identify ascites and/or a liver mass, and establish the patency and flow in the hepatic portal circulation (eg, allowing exclusion of Budd-Chiari syndrome, portal vein thrombosis).

Differential Diagnosis

The differential diagnosis for acute hepatitis is broad and includes viral hepatitis, metabolic disease, accidental or nonaccidental ingestion of hepatotoxic agents, autoimmune hepatitis, anatomic abnormalities including biliary atresia, and nonalcoholic fatty liver disease. Severe hypotension caused by trauma, hemorrhage, cardiomyopathy, or heart failure can lead to acute hepatitis. Increases of liver transaminase levels (ALT and/or AST) may be a consequence of hemolysis, muscle injury or myositis, pancreatitis, and/or myocardial injury.

Consider nonhepatic causes, such as congestive heart failure, myopathy, or storage diseases (see Table 34–1).

Treatment

Most patients with ALF will have a spontaneous recovery, without the need for any specific therapy. Liver transplant may be necessary if the patient progresses to liver failure.

Otherwise, the treatment of hepatitis varies, based on the etiology. Treat viral hepatitis with supportive care, including intravenous hydration, adequate nutrition, serial monitoring of LFTs, accurate measurements of input and output, and monitoring for progression and complications. Monitor serial PT and INR as necessary, and supplement vitamin K if a coagulopathy is noted.

Table 34–1. Etiologies of Acute Hepatitis

Etiology	Examples
Bacterial infection	Leptospirosis, *Salmonella*, syphilis
Drug	Acetaminophen (most common), anticonvulsants
Metabolic disease	α1-Antitrypsin deficiency Wilson disease Other inborn error of metabolism
Viral infection	Hepatitis A (most common), hepatitis B Adenovirus, coxsackievirus, cytomegalovirus, enterovirus, Epstein-Barr virus, herpes simplex, HIV, varicella
Other	Autoimmune hepatitis, cardiomyopathy, systemic lupus erythematosus Indeterminate

Antiviral treatment is indicated in newborns with congenital CMV or an immunocompromised patient with hepatitis due to CMV. Contact a gastroenterologist for treatment of autoimmune hepatitis with immune suppression. Treat acetaminophen toxicity with *N*-acetylcysteine (see Chapter 68, Toxic Exposures).

Disposition

- **Intensive care unit transfer:** Acute liver failure, coagulopathy
- **Discharge criteria:** Able to maintain hydration and nutrition orally with laboratory studies suggesting improved liver function

Follow-up

- Primary care or gastroenterologist/hepatologist in 1 to 2 weeks

Pearls and Pitfalls

- Early identification of conditions that are amenable to treatment is a critical priority.
- Always consider acetaminophen poisoning, especially in an adolescent. There may be marked increase of transaminase levels, with a normal or minimal increase in the total bilirubin level.
- Coagulopathy is an excellent tool for monitoring the patient's status, progression, and prognosis. In contrast, transaminase levels do not correlate with severity of disease.
- Alkaline phosphatase to bilirubin ratio less than 2 can differentiate fulminant Wilson disease from other causes of acute liver failure.
- An ammonia sample (when indicated) must be obtained from a free-flowing sample, placed on ice, and rapidly transported to the laboratory.
- A patient with hepatitis B can return to school or day care when the activity level returns to normal. In contrast, a patient with hepatitis A cannot return to school or day care until 1 week after the beginning of symptoms, due to viral shedding.

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CHAPTER 35

Constipation

Introduction

Constipation is defined as a delay or difficulty in defecation for at least 4 to 7 days' duration. It is a common pediatric problem, affecting all age groups. While most cases of constipation can be addressed and treated as an outpatient, some patients require hospitalization for removal of the stool (cleanout) and workup for the cause of the constipation. Often, the first step is to differentiate between functional constipation, constipation without an identified pathologic cause, and constipation from an organic etiology.

Clinical Presentation

History

Delayed passage of meconium stools and irregular bowel movements since birth suggest an organic cause. This is more likely if the patient has had a poor response to stool softeners and laxatives. In addition, poor growth or failure to thrive, vomiting, or feeding difficulties suggest an organic cause.

Functional constipation typically occurs during transition periods such as diet changes, toilet training, or attending school, when withholding behaviors develop in response to painful stools or embarrassment. The family may report soiling of underwear due to encopresis or blood streaks on stool, which may be hard or pellet-like. A low-fiber diet or poor liquid intake also predispose children to constipation.

Physical Examination

With a significant stool burden, the abdomen is distended and full, with active bowel sounds. Palpate the abdomen looking for hard, tubular structures, which indicate impacted stool. Pain and tenderness are usually periumbilical but may localize to a lower quadrant. Concerning findings include a rigid abdomen, rebound tenderness, bilious emesis, and absent bowel sounds.

Perform a rectal examination and note the anal position, skin tags, rectal fissure, and rectal tone. Check for stool in the rectum and note the characteristics of the stool. Also check the motor strength and reflexes of the lower extremities. As listed in Table 35–1, concerning findings include the lack of stool in the rectum, muscle weakness, absent reflexes, paraesthesias, and the absence of the anal wink reflex.

Table 35–1. Differential Diagnosis of Constipation

Diagnosis	Clinical Features
Anterior displaced anus	Anogenital index Males: 1/2 of the distance between scrotum and sacrum Females: 1/3 of the distance between vagina and sacrum
Cystic fibrosis	Meconium ileus at birth Poor growth despite adequate nutrition Concurrent pulmonary infections
Functional constipation	Painful defecation Stool retentive behaviors Onset during transition periods Lack of other findings
Hirschsprung disease	Failure to pass meconium in first 48 hours after birth Abdominal distention Lack of stool in rectum
Hypothyroidism	Doughy skin Brittle hair Cold intolerance Poor weight gain
Intestinal obstruction	Bilious emesis Rebound tenderness Rigid abdomen Loss of bowel sounds
Medication side effects Opiates Barbiturates Anticholinergics	History of pain medications History of phenobarbital for seizures History of diphenhydramine for allergies
Neuropathic conditions Tethered cord Spinal cord mass Demyelinating process	Neurologic changes to lower extremities Muscle weakness Loss of reflexes (anal wink) Decreased sensation

Laboratory Workup

Send testing, such as thyroid hormone and free thyroxine levels, sweat chloride, or medication levels, only if clinically indicated.

Radiology Examinations

If obtained, an initial abdominal radiograph will confirm a moderate to severe stool burden within the colon, along with a dilated rectum (short- and ultrashort-segment Hirschsprung disease are exceptions). If polyethylene glycol (PEG) cleanout is planned, obtain a second abdominal radiograph to confirm placement of the nasogastric tube.

Additional testing, such as barium enema, anorectal manometry, or rectal suction biopsy, can help to identify some uncommon organic causes of

constipation. They are not necessary during the initial hospitalization and can be performed at follow-up visits.

Differential Diagnosis

The differential diagnosis of constipation is summarized in Table 35–1.

Treatment

Polyethylene Glycol Cleanout

Most often, previous outpatient regimens have not been effective. If impacted rectal stool is noted, order 1 saline enema 10 mL/kg (60–240 mL maximum, based on age). Once there has been some response to the enema, insert a nasogastric tube and start an infusion of PEG at 10 mL/kg/h. Increase the rate by 10 mL/kg/h, every hour, until the goal rate of 40 mL/kg/h is reached, but do not exceed 500 mL/h. Treat significant nausea with intravenous ondansetron 0.1 mg/kg every 6 hours (maximum, 4 mg per dose), as needed. If the patient vomits, stop the infusion and restart 30 minutes later at the previous lower rate. Continue the PEG until the effluent is clear twice, which usually takes 24 to 48 hours. A repeat abdominal radiograph is not required to determine when cleanout is complete.

Laxatives

Osmotic laxatives are first-line therapy. Polyethylene glycol is more palatable than other osmotic laxatives, with better tolerance and increased stooling. The maintenance dose of oral PEG is 0.5 mg/kg/d (maximum 17 g/d), with a goal of soft, daily stools. Lactulose (1 mL/kg/d, maximum 60 mL/d) and magnesium hydroxide (100 mg/kg/d, maximum 1,200–2,400 mg/d, based on age) are both less effective and have more side effects.

Nonosmotic laxatives, such as senna (anthraquinones; 4.4–50 mg/d, based on age) and bisacodyl (diphenylmethane; 5–15 mg/d, based on age), stimulate intestinal motility and contractions. They are second-line medications because of cramping and abdominal pain.

Lubricants

Lubricants are also second-line therapy, with the primary disadvantage of oily stools and leakage. The dose of mineral oil is 1 to 3 mL/kg/d (maximum, 45 mL/d), and the dose of docusate is 50 to 360 mg/d, based on age.

Discharge

At discharge, initiate a daily bowel regimen with adequate nutrition, hydration, and a laxative. For a patient 2 years or older, ensure that the dietary fiber

intake is equal to the patient's age (in years) plus 5 g (maximum 30 g), per day. Do not prescribe fiber supplements or probiotics. Also, educate the family about a high-fiber diet, toilet time, and the stooling medication regimen for a goal of daily stools with soft-serve ice cream consistency.

Indications for Consultation

- **Endocrinology:** Hypothyroidism
- **Gastroenterology:** Cystic fibrosis, necrotizing enterocolitis, inflammatory bowel disease, Hirschsprung disease
- **Neurology/neurosurgery:** Tethered cord, spinal cord mass, demyelinating process
- **Nutrition:** Low-fiber diet or poor liquid intake
- **Surgery:** Gastrointestinal obstruction or perforation, Hirschsprung disease

Disposition

- **Intensive care unit transfer/surgery:** Intestinal perforation with peritonitis or septic shock
- **Discharge criteria:** Stool effluent clear twice, tolerating adequate oral intake with improved abdominal pain

Follow-up

- **Primary care:** 1 week
- **Gastroenterology clinic:** 1 month

Pearls and Pitfalls

- The stool effluent will initially be clear due to PEG going around stool. A full cleanout takes 24 to 48 hours.
- During cleanout, a lack of stool with worsening abdominal pain or vomiting may indicate obstruction.
- Dietary education and home stooling regimen are important to prevent recurrence of functional constipation.
- An osmotic laxative is the first-line medication for maintaining regular stools at home.

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CHAPTER 36

Failure to Thrive

Introduction

Failure to thrive (FTT) is generally defined as a weight, or weight for height, lower than the 3rd or 5th percentile on a growth chart, or a change in weight that has crossed down 2 major percentile lines over 3 to 6 months. Failure to thrive is caused by inadequate calorie intake, excessive calorie losses, or increased calorie requirements.

The most common cause, found in most cases, is inadequate calorie intake, which may be associated with significant psychosocial difficulties. However, this view is too narrow, as inadequate nutrition reflects a complex interaction among a child's medical, nutritional, emotional, and social issues. Therefore, a thorough psychosocial evaluation is an important part of patient and family assessment.

Indications for hospitalization include failure of outpatient therapies, severe FTT or malnutrition, serious infections, and a concern regarding parental neglect or patient safety. Implementation of a multidisciplinary team providing services for parental education, support, and coordination is best performed in the inpatient setting.

Clinical Presentation

History

A detailed history is critical to assigning the diagnosis. Compile a thorough dietary history, including feeding/breastfeeding patterns, foods and formulas (preparation, frequency), juice/water intake, behaviors at mealtime, and the duration of feedings. Attempt to quantify the daily caloric intake. If feasible, it is best to do a 24-hour diet recall or to have the family keep a 3-day diet log. Inquire about secondary gastrointestinal (GI) signs and symptoms (vomiting or spitting up, rumination, difficulty swallowing or eating), stool production (pattern, frequency, consistency, diarrhea, bloody, mucoid), respiratory issues (difficulty breathing, chronic cough, snoring), and recurrent infections. Pregnancy and birth history, including place of birth, birth weight, corrected gestational age, and a complete medical history and review of symptoms, are essential. Document the developmental milestones for an infant, and confirm the newborn screening results.

As noted earlier, FTT can be organic or psychosocial. A complete assessment of the family and social situation is important, including who is caring for the

child. Assess the parents' economic status and risk of food insecurity, mental health and intellectual capacity, and parent–child interaction. Try to determine whether there are other stressors in the home, family dysfunction, prior involvement with social services or child protective services, and behavior consistent with child maltreatment or neglect. Obtain a complete family history, focusing on systemic diseases (inflammatory bowel disease, asthma, cystic fibrosis, renal tubular acidosis, thyroid disease), FTT, and short stature (note the height and weight of both parents and calculate a midparental height).

Review of the growth charts and trends in growth is crucial. Inadequate nutrition leads to poor weight gain initially, which will be followed, over time, by decreased height velocity. Head circumference is typically normal unless the problem is severe.

Physical Examination

The vital signs and general appearance (dysmorphic features, cachexia, general activity) are priorities. Examine the oropharynx for a cleft palate, poor suck or swallow, dental caries, and enlarged tonsils. Assess the work of breathing, auscultate for a murmur, and palpate the abdomen for hepatomegaly. Note any loose skin, edema, poor hygiene, rash, or bruises and other evidence of trauma. Perform a neurologic examination for muscle tone, reflexes, social interaction, and developmental milestones. A priority is to observe the parent–child interaction and feeding routine.

Laboratory Workup

Limit the use of laboratory tests and evaluations to those suggested by the history and physical examination, because without specific evidence for organic disease, laboratory testing is rarely helpful in determining the etiology of FTT. When indicated, screening tests may include a complete blood cell count; comprehensive chemistry evaluation (including electrolyte levels, blood urea nitrogen/creatinine ratio, and calcium, phosphorus, magnesium, and albumin levels); liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels); erythrocyte sedimentation rate; urinalysis; and stool samples for occult blood, pH level, and reducing substances (Table 36–1). Other tests to consider, *only if indicated* by the findings in the history and physical examination, are thyroid function tests, ammonia level, lactate level, HIV, tuberculosis testing, sweat chloride, stool for ova and parasites, and bone age.

Table 36–1. Differential Diagnosis of Failure to Thrive

Diagnosis	Clinical Features	Initial Laboratory Tests and Evaluations
Inadequate Caloric Intake		
Breastfeeding failure Feeding problem	Uncoordinated suck/swallow Mother feels milk supply is inadequate	Observe infant feeding Weigh infant pre- and postfeeding Consult lactation care provider (if breastfeeding)
Excess juice consumption	Dietary history	None
Incorrect formula preparation	Dietary history History of economic pressures	CBC, electrolyte levels
Oromotor dysfunction	Observation of feeding	Speech/swallow consult
Psychosocial: insufficient food	Stressors in the home (poverty, food insecurity)	CBC, electrolyte levels Family psychosocial screening
Inadequate Caloric Absorption/Usage		
Celiac disease	Family history Diarrhea	CBC, albumin levels Antitissue transglutaminase level Stool pH level, reducing substances, fecal fats
Cystic fibrosis	Family history Abnormal newborn screening results Respiratory symptoms Diarrhea	Review newborn screening results Sweat test Stool pH level, reducing substances, fecal fats
Gastroesophageal reflux	Vomiting history Arching of the back	Response to treatment with/without swallowing study or pH level probe
Increased intracranial pressure	Vomiting history Cushing triad Abnormal neurologic examination finding Rapidly increasing head circumference	Head computed tomography Neurology consult
Inflammatory bowel disease	Family history Diarrhea, bloody stools	CBC, erythrocyte sedimentation rate and C-reactive protein level, albumin level Stool occult blood
Liver disease	Jaundice Diarrhea	Liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels) Hepatitis serologic studies
Milk protein allergy	Family history Vomiting history Diarrhea, bloody stools Eczema	Stool occult blood GI consult Possible endoscopy
Increased Caloric Requirements		
Adrenal diseases	Vomiting, diarrhea Hyperpigmentation Hypotension	Chemistry assessment Glucose level

Continued

Table 36–1. Differential Diagnosis of Failure to Thrive, continued

Diagnosis	Clinical Features	Initial Laboratory Tests and Evaluations
Blood disorders	Fatigue Pallor	CBC
Cardiopulmonary diseases	Fatigue, especially with feedings Respiratory illnesses	Chest radiography Electrocardiogram and echocardiogram
Diabetes mellitus	Polydipsia, polyuria, polyphagia	Chemistry assessment, fasting glucose level Urinalysis
Genetic diseases	Family history Dysmorphic features	Specific for suspected diseases
Hyperthyroidism	Fatigue, increased sweating, polyphagia Nervousness, sleep disturbance Diarrhea Tachycardia, exophthalmos	Thyroid studies
Renal tubular acidosis	Normal anion gap metabolic acidosis	Venous blood gas analysis and urinalysis (compare serum and urine pH levels)

Abbreviations: CBC, complete blood cell count; GI, gastrointestinal.

Differential Diagnosis

Establishing the etiology of FTT is challenging. Perform a comprehensive review of the growth chart trends and identify chronic illnesses and syndromes that alter growth. In contrast to a patient with an endocrinologic or chromosomal disorder, a child with FTT will fall off the weight curve before falling off the height/length curve, with the weight having deteriorated to a lower percentile than the height. Base the differential diagnosis on caloric intake and expenditure (Table 36–1).

The etiology may be secondary to inadequate caloric intake, inadequate caloric absorption/usage, or increased caloric requirements (excess metabolic demand as occurs in chronic diseases). Inadequate caloric intake is by far the most common cause of FTT. However, some diseases, such as congenital heart disease or bronchopulmonary dysplasia, appear with a mixed picture of inadequate intake and a hypermetabolic condition at presentation.

Physiological causes of short stature and symmetrically small growth that are not considered to be FTT include a history of prematurity or small size for gestational age, familial short stature, and constitutional growth delay.

Treatment

The treatment for FTT is to provide adequate nutrition for catch-up growth (Box 36–1). Therefore, the patient will typically require 100% to 150% of the

usual maintenance calories to transition from a negative to a positive nitrogen balance. In a case of poor caloric intake, daily requirements will lead to weight gain within 2 to 3 days. Once adequate nutrition is delivered, typical rates of weight gain are as follows: 0 to 4 months of age, 23 to 34 g/d; 4 to 8 months of age, 10 to 16 g/d; 8 to 12 months of age, 6 to 11 g/d; and 12 to 24 months of age, 4 to 9 g/d. However, there is often a lag of several days before weight gain finally begins.

Encourage the breastfeeding mother to continue nursing, with the goals of increasing the milk supply and/or improving the milk transfer. Consult with a breastfeeding-trained pediatrician and/or a lactation care provider. The severity of the poor weight gain will determine if, and how much, supplementation is needed for the breastfeeding infant.

For an exclusively breastfed infant, supplement with expressed breast milk if the breast milk volume is adequate. If weight gain remains low despite adequate intake, add fortification. As a general estimate, adding a teaspoon of a powdered formula to 100 mL of breast milk will increase the caloric density to about 24 kcal/oz. If a formula-fed infant does not gain weight with a regular formula (20 kcal/oz) but no secondary cause is suspected, increase the caloric intake gradually (24–30 kcal/oz) while monitoring for weight gain. If a formula concentration greater than 24 kcal/oz is needed, request a nutrition consult. One option is to add 0.4 mL of medium-chain triglycerides to 1 ounce of the 24-kcal/oz formula.

For a patient older than 1 year, consult with a nutritionist and use behavioral modification and high-calorie foods. Recommend the "rule of threes" (3 meals, 3 snacks, and 3 choices) and high-calorie liquids (fortified whole milk or commercial formulas that contain $>$ 20 kcal/oz). Hypercaloric feedings are usually, but not always, hyperosmolar, which may cause side effects (eg, osmotic diarrhea) if the feedings are advanced too quickly.

In a case of severe malnutrition, marasmus, or kwashiorkor, reintroduce intake slowly to avoid refeeding syndrome (rare). This occurs when such a patient begins to receive adequate nutrition too quickly, triggering insulin release. Manifestations may include hypophosphatemia (most common), hypokalemia, and hypomagnesemia, as well as edema and volume overload. To prevent refeeding syndrome in a patient at risk, prior to initiating feeds, correct all electrolyte abnormalities and rule out any infections. Begin feeding slowly, starting with less than 50% of the caloric needs orally with the rest given as intravenous fluids, then increase the oral intake by 10% to 20% of the daily calories every 3 to 4 days. Closely monitor the vital signs, daily weights, and physical examination (for edema). Check the electrolyte levels (comprehensive chemistry assessment with magnesium and phosphorus levels) daily at first, but if refeeding syndrome is suspected,

evaluate electrolyte levels 2 to 3 times a day and correct any abnormalities. If there are serious derangements, transfer the patient to an intensive care unit (ICU) for closer monitoring.

Assess growth with calorie counts and daily weights. Use nasogastric or transpyloric tube feedings when a patient cannot manage adequate oral intake because of increased energy needs and/or physiological impairment while the GI tract is fully or partially functioning. Transpyloric or pyloric (nasoduodenal or nasojejunal) tube feeding is useful when a nasogastric feeding is not indicated, such as when there are congenital upper GI anomalies, inadequate gastric motility, high aspiration risk, severe gastroesophageal reflux, or upper GI obstruction.

See Table 36–2 for the details on starting continuous tube feeding. The overall rate is determined by the kilocalories per day necessary, based on the catch-up growth formula described in Box 36–1. Transition to bolus nasogastric feedings (Table 36–2) once continuous maintenance intake is tolerated, but do not use bolus feeding with a nasoduodenal or nasojejunal tube. Make one change, either volume or concentration, when adjusting enteral feedings, and monitor the patient for tolerance. If the patient does not tolerate a full-strength formula, decrease the volume and slowly increase as tolerated. If the patient will be on a combination bolus and continuous feeding schedule (day/nocturnal feedings), wait 2 hours from the end of the continuous schedule to initiate the bolus schedule.

Box 36–1. Nutrition for Catch-up Growth

$$\text{kcal/kg required} = \frac{[\text{IBW in kg (50th percentile wt/ht)}] \times [\text{kcal/kg/d (DRI for age)}]}{[\text{actual weight (kg)}]}$$

Abbreviations: DRI, Dietary Reference Intake (available at https://www.nal.usda.gov/legacy/fnic/dri-calculator/); ht, height; IBW, ideal body weight; wt, weight.

Table 36–2. Enteral Feeding Guidelines

Age	How to Start	How to Advance	Tolerance Volume
Continuous Feeding			
0–12 mo	1–2 mL/kg/h	1–2 mL/kg every 2–8 h	6 mL/kg/h
1–6 y	1 mL/kg/h	1 mL/kg every 2–8 h	1–5 mL/kg/h
> 7 y	25 mL/h	25 mL every 2–8 h	100–150 mL/h
Bolus Feeding			
0–2 mo	10–15 mL/kg every 2–3 h	10–30 mL per feeding	20–30 mL/kg every 4–5 h
1–6 y	5–10 mL/kg every 2–3 h	30–45 mL per feeding	15–20 mL/kg every 4–5 h
> 7 y	90–120 mL every 3–4 h	60–90 mL per feeding	330–480 mL every 4–5 h

Adapted from Yi DY. Enteral nutrition in pediatric patients. *Pediatr Gastroenterol Hepatol Nutr*. 2018;21(1):12–19.

Indications for Consultation

- **Child protection team:** Concern for child abuse or neglect
- **Gastroenterology:** Severe gastroesophageal reflux or milk protein allergy, inflammatory bowel disease, cystic fibrosis, celiac disease
- **Lactation care provider:** Breastfeeding failure
- **Nutritionist:** All patients admitted for FTT
- **Social work:** Assessment of family dynamics, emotional health, resources, and ability to adhere to outpatient plan
- **Speech therapy:** Cleft palate, oromotor dysfunction

Disposition

- **ICU transfer:** Critical malnutrition (bradycardia, hypothermia, severe dehydration, altered mental status), severe electrolyte disturbances (hypophosphatemia, hypokalemia, hypomagnesemia, hypocalcemia) secondary to refeeding syndrome
- **Discharge criteria:** Adequate, consistent weight gain demonstrated for 2 to 3 consecutive days; any underlying disease identified and treatment initiated; feeding regimen with adequate calories established; family demonstrates understanding of nutrition recommendations, proper feeding techniques, and growth expectations; relevant social and emotional issues have been adequately addressed

Follow-up

Primary care: Weekly to monitor long-term weight gain and development

Pearls and Pitfalls

- Failure to thrive is often multifactorial and requires a multidisciplinary approach.
- Most cases of FTT are failure to (adequately) feed, so compiling a detailed feeding history is critical.
- Use a disease-specific growth curve to plot data for a child with a congenital or genetic disease.
- Laboratory testing is usually not helpful in determining an etiology.
- Red flags for possible child abuse or neglect include multiorgan system involvement, previous evaluations at multiple institutions or providers, a convoluted history, or numerous reported allergies.

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CHAPTER 37

Gallbladder Disease

Introduction

Gallbladder disease includes cholelithiasis (gallstones), choledocholithiasis (stones in the common bile duct), calculous or acalculous cholecystitis (inflamed gallbladder with or without stones), biliary dyskinesia, and hydrops of the gallbladder (acute distention without inflammation). The incidence of gallstones is rising because of increasing rates of obesity and the more frequent diagnosis of asymptomatic gallstones via ultrasonography (US). Patients with certain risk factors have a higher incidence of gallbladder disease, with a prevalence of 40% among adolescents with sickle cell disease. In up to 80% of patients, gallstones are asymptomatic, although pancreatitis can occur in 5% to 10% of patients.

Historically, up to 50% of the cases of cholecystitis in children were acalculous and developed from biliary dyskinesia or acquired biliary stasis secondary to compression of the cystic duct by edema, lymph node, or congenital malformation. Recently, more cases have occurred secondary to gallstone disease.

Hydrops of the gallbladder occurs in up to 20% of children with Kawasaki disease, as well as in patients with other infections or inflammatory conditions, such as scarlet fever, Epstein-Barr virus, and Henoch-Schönlein purpura.

Biliary dyskinesia is a functional gallbladder disorder in which there is abnormal gallbladder motility, without obstruction, stones, or sludge. This is uncommon in children and often a diagnosis of exclusion.

Clinical Presentation

The presentation of biliary tract disease is summarized in Table 37–1.

History

A patient with gallbladder inflammation, distention, or biliary colic will report nausea, vomiting, anorexia, and abdominal pain. The biliary colic may be described as a constant right upper quadrant pain that radiates to the right shoulder. There may be a history of previous episodes of cholecystitis. An older child or adolescent may describe the pain as postprandial, especially if the meal was fatty. The patient may have light-colored stools and dark urine, which raises a suspicion for obstructive jaundice. The presentation of hydrops is similar to that of cholecystitis.

Inquire about the following predisposing risk factors: hemolytic disease, obesity, family history of gallstones, pregnancy, recent delivery, recent total parenteral nutrition (TPN), as well as ceftriaxone, cyclosporine, or furosemide

Table 37–1. Presentation of Biliary Tract Diseases

Diagnosis	Clinical Features
Acalculous cholecystitis	Fever and pain Leukocytosis with normal transaminase levels US: thickened gallbladder wall with no gallstones
Asymptomatic gallstones	No pain, nausea, or vomiting Incidental finding at US
Biliary dyskinesia	No defined/accepted pediatric criteria Chronic or recurrent epigastric or right upper quadrant pain Absence of gallstones
Calculous cholecystitis	Fever and pain Leukocytosis with normal transaminase levels US: gallstones in the gallbladder
Cholangitis	Charcot triad: fever, jaundice, right upper quadrant pain May have acholic stools and dark urine (in infants) Leukocytosis
Choledocholithiasis	Jaundice (↑ direct bilirubin level) and pain US: no gallstones in the gallbladder, but stones may be present in the common bile duct ↑ Alkaline phosphatase and γ-glutamyltransferase levels
Hydrops	Normal gallbladder wall but dilated lumen
Pancreatitis	Pain may radiate to the patient's back ↑ Amylase and/or lipase levels

Abbreviation: US, ultrasonography.
↑ indicates increased.

use; cystic fibrosis; bowel resection; ileal disease; Down syndrome; Gilbert syndrome; artificial heart valve; and bronchopulmonary dysplasia. Additional risk factors include prolonged fasting, infective endocarditis, opiate use, and infection (streptococcal and gram-negative sepsis, leptospirosis, Rocky Mountain spotted fever, typhoid fever, ascariasis, and *Giardia lamblia*). Other parasitic, candidal, and viral infections can cause acalculous cholecystitis in an immunocompromised host.

Symptoms of complications of gallstones may include pain that radiates to the patient's back in pancreatitis. There may be fever and malaise in cholecystitis, or fever and jaundice in cholangitis.

Physical Examination

In calculous or acalculous cholecystitis, there will be right upper quadrant abdominal pain with a positive Murphy sign (pain during inspiration while palpating the right upper quadrant). Hepatomegaly is uncommon in primary gallbladder disease but may be present if there has been long-standing obstructive cholestasis causing cirrhosis. Jaundice and scleral

icterus occur when a gallstone is obstructing the common bile duct. With bacterial cholangitis or cholecystitis, the patient has fever, tachycardia, and tachypnea. Perforation of the gallbladder appears with peritoneal signs at presentation, such as abdominal guarding, rebound tenderness, and a firm or distended abdomen.

Laboratory Workup

If gallbladder disease is suspected, obtain a complete blood cell count with differential; liver function panel with alkaline phosphatase, amylase, γ-glutamyltransferase, and total and direct bilirubin levels; and, if the patient is febrile, a blood culture.

Radiology Examinations

Ultrasonographic examination is the preferred initial imaging study for gallbladder disease, with a sensitivity of up to 96% for cholelithiasis and 81% for cholecystitis. Order abdominal US to look for stones, sludge, or a thickened gallbladder. Give the patient nothing by mouth for at least 4 hours before the study. The US findings may be normal if the stone is in the common bile duct or the patient has gallbladder dyskinesia.

Cholescintigraphy is more sensitive for cholecystitis (96%) but is less readily available and exposes the patient to radiation. Order this test when there are no gallstones in the gallbladder at US but there is still concern for extrahepatic biliary disease or obstruction of the common bile duct (good hepatic uptake but delayed or no gallbladder filling). If the findings are equivocal, order computed tomography or magnetic resonance (MR) imaging.

If a patient has signs of cholecystitis or cholangitis but no stones in the gallbladder at US, order MR cholangiopancreatography (MRCP), which can demonstrate stones in the common bile duct and allow assessment of the biliary tree anatomy for congenital malformations. Arrange endoscopic retrograde cholangiopancreatography (ERCP) for therapeutic removal of an obstructive stone during imaging.

Differential Diagnosis

The differential diagnosis of right upper quadrant pain is presented in Table 37–2.

Treatment

Acute Cholecystitis

Give the patient nothing by mouth, provide maintenance intravenous hydration with 5% dextrose in one-half normal saline with 20 mEq/L

Table 37–2. Differential Diagnosis of Right Upper Quadrant Pain

Diagnosis	Clinical Features
Appendicitis	Atypical location of the appendix (especially in pregnancy)
Fitz-Hugh-Curtis syndrome	Sexually active female subject ↑ C-reactive protein level/ESR Possible vaginal symptoms or (+) nucleic acid amplification test
Gastroenteritis	Patient may also have diarrhea
Hepatitis	↑ Alanine transaminase (serum glutamic pyruvic transaminase) and aspartate transaminase (serum glutamic oxaloacetic transaminase) levels
Musculoskeletal pain	Afebrile May have point tenderness Normal alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, total and direct bilirubin levels, ESR, ultrasonographic findings
Peptic ulcer disease	(+) Guaiac stool Pain relieved by eating meals or taking antacids or histamine$_2$ blockers
Pleural effusion	Decreased breath sounds (+) Chest radiographic findings
Pneumonia	Localized rales or decreased breath sounds (+) Chest radiographic findings
Pancreatitis	↑ Lipase level

Abbreviation: ESR, erythrocyte sedimentation rate.
+ indicates a positive finding; ↑, increased.

(20 mmol/L) of potassium chloride, and correct any additional electrolyte abnormalities or fluid deficits. Although cholecystitis is typically an inflammatory disease, secondary infection can occur, so empirical antibiotic administration is indicated if the patient is febrile. Cover for gram-negative bacilli and anaerobes, with ampicillin/sulbactam (300 mg/kg/d, divided into doses administered every 6 hours; maximum, 12 g ampicillin/d) *or* piperacillin/tazobactam (337.5 mg/kg/d, divided into doses administered every 8 hours; maximum, 12 g piperacillin/d or 3.375 g every 6 hours for weight > 40 kg), *or* the combination of ceftriaxone (50–75 mg/kg/d, divided into doses administered every 12–24 hours; 4-g/d maximum) *and* metronidazole (30 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum).

Analgesia is a priority. Start with a nonsteroidal anti-inflammatory drug (NSAID), such as ketorolac (0.5 mg/kg administered every 6 hours for 5 days; 120-mg/d maximum). However, the patient may require an opiate, such as morphine sulfate (0.05–0.10 mg/kg per dose administered every 2–4 hours; maximum of 2 mg per dose for infants, 4–8 mg per dose for children, and 15 mg per dose for adolescents).

Consult with a surgeon, because an acute cholecystectomy may be necessary if supportive care does not relieve the pain or if there are signs of

peritonitis, sepsis, or worsening distress. Otherwise, if the patient improves quickly, elective surgery (preferably laparoscopic cholecystectomy) is indicated 6 to 12 weeks after resolution of the symptoms. However, instruct the patient to return to the hospital immediately for urgent cholecystectomy if the symptoms of cholecystitis recur.

Cholelithiasis

Manage asymptomatic cholelithiasis on an outpatient basis, with a follow-up US study performed in 6 months. However, if the patient has a hemolytic disease, consult with a surgeon to plan a cholecystectomy.

Choledocholithiasis

In addition to supportive care, consult a gastroenterologist and surgeon. Arrange for the patient to undergo MRCP or ERCP. However, if cholecystectomy is planned, cholangiography is usually also performed to confirm the presence or absence of an obstructing stone.

Acalculous Cholecystitis

Treat the underlying condition, such as by discontinuing the implicated medication or administering antibiotics for the inciting bacterial infection.

Hydrops of the Gallbladder

This is usually self-limited, so no specific treatment is necessary.

Indications for Consultation

- **Gastroenterology or surgery (depending on the availability of ERCP):** Choledocholithiasis
- **Hematology or other subspecialists:** As needed for underlying disease
- **Surgery (urgent):** Cholecystitis or hydrops of the gallbladder, with perforation, empyema, or necrosis

Disposition

- **Intensive care unit transfer:** Sepsis or peritonitis
- **Discharge criteria:** Patient afebrile and maintaining adequate oral hydration and pain control

Follow-up

- **Primary care:** 1 week
- **Surgery:** 3 to 5 days (if the patient underwent cholecystectomy); 1 to 2 weeks to arrange for elective cholecystectomy in the next 2 to 3 months

Pearls and Pitfalls

- Consider cholangitis and consult a surgeon if fever and jaundice accompany cholecystitis.
- Ultrasonography is the primary imaging modality for disorders of the gallbladder.
- While NSAIDs are the first-line analgesics, opiates are not contraindicated.

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CHAPTER 38

Gastroenteritis

Introduction

Gastroenteritis is an intraluminal inflammation of the gastrointestinal (GI) tract that involves any region from the stomach to the colon. Infectious gastroenteritis may be caused by bacteria, viruses, parasites, or preformed toxins produced by bacteria. Viral causes are the most common.

Clinical Presentation

History

Complete a thorough history to help determine the possible etiology, assess the severity of dehydration, and rule out other serious illnesses that can appear with vomiting and/or diarrhea at presentation. Determine the character of the vomiting and/or diarrhea, including the duration of symptoms, number of episodes, and presence of bile or blood in the vomitus or of blood or mucus in the stools. Ask about fever, abdominal pain, prior history of GI and other illnesses, rotavirus vaccine status, injuries, medications (especially antibiotics), recent contact with sick persons, contact with animals (specifically farm animals or reptiles), travel history, juice intake, and potential exposure to contaminated food or water. In addition, assess the hydration status and severity of the illness and determine recent oral intake, urine output, acute weight loss (if known), and any change in mental status.

Viral Gastroenteritis

Symptoms of viral gastroenteritis typically manifest 2 to 4 days after exposure, usually beginning with vomiting, followed by frequent loose or watery diarrhea. However, diarrhea may be the only symptom. Depending on the virus, fever may or may not be present, and complete resolution of symptoms typically occurs within 7 days. Some viral infections, such as enteric adenovirus, can be more prolonged, lasting up to 7 to 10 days. A patient with acute COVID-19 disease may also experience diarrhea and/or vomiting, with or without respiratory symptoms.

Bacterial Gastroenteritis

Signs and symptoms typically overlap with viral gastroenteritis but may cause a more significant colitis associated with diarrhea with gross blood and/or mucus, fever, myalgia, abdominal pain, and tenesmus.

Extraintestinal manifestations may accompany specific bacterial infections, such as *Campylobacter* (erythema nodosum, glomerulonephritis, reactive arthritis), *Escherichia coli* (hemolytic uremic syndrome [HUS]), *Salmonella*

(erythema nodosum, reactive arthritis), *Shigella* (encephalopathy, glomerulonephritis, reactive arthritis, seizures), and *Yersinia* (erythema nodosum, glomerulonephritis, hemolytic anemia, reactive arthritis) infections.

Nontyphoidal *Salmonella*–associated gastroenteritis typically causes fever and watery diarrhea and may result in a more severe inflammatory colitis. The illness may also be complicated by bacteremia, especially in a patient who is immunocompromised or younger than 1 year. Ask about exposure to potential sources of *Salmonella* bacteria, including reptiles and contaminated food products, such as eggs and milk products.

Salmonella typhi and *Salmonella paratyphi* are usually acquired outside the United States and cause a systemic infection, with remitting fever that becomes sustained. Other complaints include abdominal pain and constitutional symptoms, such as headache, malaise, anorexia, and lethargy. The patient may progress to having a blanching, macular rash on the trunk and an altered mental status. *S typhi* can also cause intestinal perforation that appears as peritonitis or septic shock at presentation, although this is rare in a child.

Shigella infection causes symptoms that range from mild, watery stools to dysentery. Certain species of the bacteria may also produce the Shiga toxin that causes endothelial damage and HUS, as well as seizures. *Shigella* bacteria are more resistant to acid when compared with other bacteria and can transmit disease through the stomach. Because as few as 10 to 100 organisms may cause disease, *Shigella* infection is highly contagious.

Gastroenteritis caused by *Yersinia* infection is relatively uncommon in the United States. A known risk factor is eating chitterlings (pig intestines). In a younger child, *Yersinia* infection may present as a mild, self-limited disease, whereas an older patient may have more prominent symptoms, including abdominal pain and tenderness caused by mesenteric adenitis.

Campylobacter-associated infection is characterized by fever, chills, crampy abdominal pain, and bloody, mucoid diarrhea. It can also cause frank rectal bleeding. The source of *Campylobacter* infection is primarily food, such as poultry and eggs.

E coli, which has several identified groups, can cause the full spectrum of diarrheal illness. The enterohemorrhagic *E coli* O157:H7 organism, in particular, produces a Shiga-like toxin that may cause HUS. Other groups of the bacteria include enterotoxigenic *E coli,* which causes watery diarrhea and is seen in developing countries, and enteroinvasive *E coli,* which typically manifests in foodborne outbreaks of dysentery due to undercooked ground beef, raw milk, and, occasionally, raw vegetables. The enteropathogenic form of the bacteria causes acute and chronic diarrhea in infants, and the enteroaggregative form causes acute and chronic watery diarrhea.

Clostridioides difficile is found in cases of antibiotic-associated diarrhea, particularly after treatment with β-lactam antibiotics and clindamycin. As with other bacterial sources of diarrhea, symptoms can range from mild diarrhea to life-threatening enterocolitis.

Parasitic Gastroenteritis

Protozoan gastroenteritis may appear as watery diarrhea at presentation but can also cause a protracted diarrhea that lasts 2 to 4 weeks. *Giardia intestinalis* (formerly *Giardia lamblia* and *Giardia duodenalis*) is the leading cause of waterborne disease in the United States. Typical infections are characterized by explosive, foul-smelling, watery diarrhea with abdominal cramps and bloating.

Physical Examination

The priority at physical examination is accurate assessment of the patient's hydration status. Categorize the dehydration status as minimal (< 3% of body weight), moderate (3%–9% of body weight), or severe (> 9% of body weight), which will then guide rehydration protocols. The standard of reference for this calculation is based on the patient's acute weight change, although this information is not always available. Assess the patient's general appearance, mental status, subjective thirst level, heart rate, pulse rate and quality, orthostatic vital sign changes, respiratory effort, potentially sunken eyes, tear production, mucous membrane moistness, skin turgor, capillary refill, mottled appearance of extremities, and urine output. Hypotension is a late finding indicating severe dehydration. As noted earlier, extraintestinal manifestations noted at physical examination may provide clues to the etiology of infection.

Laboratory Workup

According to guidelines from the U.S. Centers for Disease Control and Prevention and the American Academy of Pediatrics, laboratory testing for uncomplicated acute gastroenteritis with mild or moderate dehydration is not needed. Laboratory evaluation is indicated for patients who exhibit severe dehydration and may have electrolyte imbalances. If there is concern for certain extraintestinal manifestations, such as HUS, obtain a complete blood cell count (CBC), peripheral blood smear, electrolyte levels, and blood urea nitrogen (BUN) and creatinine levels. Perform a CBC and blood culture if there is concern for a serious bacterial illness. If there is suspicion for a urinary tract infection in an infant, perform a catheterized urine culture.

If the patient has dysentery (blood, pus, and mucus in the stools), send stool samples for culture. Routine stool cultures will typically include testing for *Shigella*, *Salmonella*, and *Campylobacter*, although some laboratories

require specific notification to test for *Yersinia*. If the stools are bloody, specifically order testing for *E coli* O157:H7. Obtain a blood culture for a high-risk patient, including a patient younger than 1 year, or if the patient is immunocompromised or septic. Evaluation for *C difficile* toxin is indicated if the patient has severe, persistent diarrhea or predisposing conditions, such as receipt of recent or multiple courses of antibiotics, has an underlying GI disorder or immunodeficiency, or has recently been hospitalized. However, do not routinely test a patient younger than 1 year, because false-positive *C difficile* results are frequent. Also, there is no need to test for a cure, because the toxin can remain after symptoms resolve. At some institutions, multiplex gastrointestinal pathogen panels are replacing stool cultures. These panels offer increased sensitivity and a shorter turnaround time, but they cannot distinguish infection from shedding or colonization. Send stool samples for ova and parasite evaluation, as well as stool antigen tests for *Giardia* and *Cryptosporidium*, if the patient has a pertinent travel history, has had contact with untreated water, or has experienced prolonged GI symptoms.

Differential Diagnosis

While the patient will most often have viral gastroenteritis, the priority is to ensure that the diagnosis is not serious or even life-threatening (Table 38–1). This is particularly true if the child presents with vomiting without diarrhea, a toxic appearance, prolonged symptoms, or signs of shock, or if the patient required excessive fluid resuscitation. Similarly, if the patient has an altered mental status that does not respond to fluid intake, consider toxic ingestion, encephalitis, intussusception, or increased intracranial pressure as a potential cause.

Treatment

Oral rehydration therapy (ORT) is the mainstay of management of mild and moderate dehydration for a patient who can tolerate oral intake. An oral rehydration solution (ORS) is a glucose electrolyte solution that has an appropriate balance of sodium (45–90 mEq/L [45–90 mmol/L]) and glucose (2%) to promote water absorption through the sodium-glucose transporter in cells lining the small intestine. Fluids high in glucose content and low in sodium, such as sports drinks and fruit juices, are ineffective rehydration solutions because of the creation of an osmotic load that causes more fluid secretion. However, Pedialyte, other oral electrolyte solutions, and the World Health Organization ORS are acceptable alternatives.

A patient most often requires intravenous (IV) fluids because of a failure of ORT, an inability to take adequate oral intake to replace deficit and keep up

Table 38–1. Differential Diagnosis of Gastroenteritis

Diagnosis	Clinical Features
Adrenal insufficiency	Unopposed vomiting Weakness, fatigue, anorexia Previous steroid exposure Elevated potassium, decreased sodium
Appendicitis	Abdominal pain that precedes vomiting Minimal or no diarrhea Signs of acute abdomen (abdominal guarding, rebound)
Diabetic ketoacidosis	History of weight loss/polydipsia/polyuria but no diarrhea Deep (Kussmaul) breathing Mental status change out of proportion to the vomiting frequency
Increased intracranial pressure	History of trauma or hydrocephalus Headache, cranial nerve abnormalities Unopposed vomiting May have Cushing triad (decreased heart rate with increased blood pressure)
Inflammatory bowel disease	Chronic symptoms and poor overall growth and/or pubertal delay Extraintestinal symptoms: rash, arthritis, uveitis, microcytic anemia
Poisoning, toxic ingestion Inborn errors of metabolism	Acute onset Mental status change out of proportion to the vomiting frequency
Intussusception	Sudden onset of severe, crampy pain and inconsolability Patient draws up legs when in pain Patient may have altered mental status Guaiac (+) or "currant jelly" stools (late finding)
Malabsorption syndromes (celiac disease)	Chronic diarrhea and weight loss Diet-related onset
Myocarditis	Usually no diarrhea Tachycardia out of proportion to dehydration level Gallop cardiac rhythm
Peritonitis	Fever (may be high) Worsening abdominal pain Rebound and guarding at abdominal examination
Small-bowel obstruction	Persistent, bilious vomiting Abdominal distention History of previous abdominal surgery
Urinary tract infection	Dysuria, urgency, frequency (+) Urinalysis

+ indicates a positive finding.

with ongoing losses, severe dehydration, or an underlying metabolic or renal disorder. Give isotonic IV fluids, such as normal saline or lactated Ringer solution, for the initial fluid resuscitation, and add dextrose and potassium to ongoing fluids. Consider enteral hydration for a patient who refuses oral intake but does not have ongoing emesis. Enteral hydration is as effective as IV hydration and has many advantages, such as reduced cost, fewer

complications, and faster recovery. Calculate the total 4-hour fluid goal and administer the ORS at a tolerated rate over 4 hours. Order contact precautions, and do not use antimotility agents.

Moderate Dehydration

Replace the fluid deficit with 75 to 100 mL/kg of an ORS over 3 to 4 hours, given in frequent, small (5–10 mL) aliquots. Afterward, encourage continued fluid intake to maintain hydration and an age-appropriate diet and continue appropriate replacement of fluid losses as done for mild dehydration.

Severe Dehydration

Correct severe dehydration with 1 to 3 20-mL/kg IV boluses of an isotonic fluid, either normal saline or lactated Ringer solution, until the patient no longer has hypotension or orthostatic vital sign changes, with improved peripheral perfusion and mental status. However, it may take several hours before the patient has normal urine output (1 mL/kg/h). Unless the patient has renal disease, sickle cell disease, or diabetes, the urine output is a good gauge as to whether subsequent boluses are needed. Once the patient is stabilized and has appropriate mental status, begin ORT. If the patient does not void after 3 fluid boluses, insert a bladder catheter and obtain electrolyte, BUN, and creatinine levels. Poor perfusion despite multiple boluses occurs with distributive shock secondary to sepsis. Treat with broad-spectrum antibiotics and vasopressors and transfer the patient to an intensive care unit (ICU) setting.

Frequent reassessments, including input and output (stool and urine assessment with specific gravity), vital signs, and physical examination are crucial for both tracking ongoing fluid losses and diagnosing an underlying illness other than a viral gastroenteritis. Be particularly suspicious of an alternative diagnosis if the patient has an inadequate response to fluid administration, persistent inability to tolerate oral intake, severe abdominal pain, or persistent altered mental status.

Diet

There is no indication for gut rest. As soon as oral intake can be tolerated, resume an unrestricted age-appropriate diet, including complex carbohydrates, lean meat, fruits, vegetables, milk products, or human milk and/or infant formula. If the patient has persistent nausea and/or vomiting that is distressing, administer a dose of oral (sublingual) or IV ondansetron (0.15–0.3 mg/kg, as needed, up to every 6 hours; 8-mg maximum). Do not use ondansetron if there is unopposed vomiting without diarrhea, any concern about a surgical abdomen (acute abdomen that will likely require surgical intervention), or other underlying medical problems, such as long QT syndrome.

Probiotics

Although probiotics had been recommended as a safe adjunctive therapy, the most recent guidelines from the North American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition state that there is minimal evidence to support probiotic use.

Antibiotics

The antibiotic treatment of bacterial gastroenteritis is summarized in Table 38–2.

Use metronidazole for *Giardia* infection (15 mg/kg/d, divided into doses administered 3 times a day for 5 days; 750-mg/d maximum).

Indications for Consultation

- **Gastroenterology:** Persistent diarrhea (> 14 days), significant GI bleeding, or suspected inflammatory bowel disease
- **Infectious disease:** Unusual or resistant pathogen isolated, multiple recurrences of *C difficile*
- **Surgery:** Possible acute abdomen

Disposition

- **ICU transfer:** Decompensated shock, patient not responsive to fluid boluses, concern for acute adrenal insufficiency, diabetic ketoacidosis, increased intracranial pressure, or myocarditis
- **Discharge criteria:** Dehydration resolved, oral intake adequate to maintain hydration, oral antibiotics (if indicated) tolerated

Follow-up

- **Primary care:** Advise the family to seek care for worsening symptoms or decreased oral intake after discharge. Telemedicine follow-up visits are acceptable.

Pearls and Pitfalls

- Viral gastroenteritis typically presents with vomiting and diarrhea without blood or mucus.
- Bacterial gastroenteritis may appear as dysentery at presentation, with bloody, mucoid stools.
- Vomiting without diarrhea may be caused by a non-GI disease.
- The presence of diarrhea does not rule out appendicitis.
- Consider enteral hydration over IV hydration in mild to moderate dehydration.

Table 38–2. Treatment of Bacterial Gastroenteritis

Indications	Antibiotics
***Salmonella* (Nontyphoidal) Infection**	
Unproven benefit Risk factors for an invasive infection include Age < 3 mo Chronic GI disease Hemoglobinopathy Malignancy HIV infection Immunosuppressive illnesses or therapies See the American Academy of Pediatrics *Red Book* for additional treatment issues	*In areas with susceptible strains, treat with* TMP-SMX (20 mg/kg/d, divided into doses administered every 6–8 h; 640-mg/d maximum) for 3–7 d *In areas of increased resistance, treat with* Azithromycin (12 mg/kg/d, 500-mg/d maximum) for 3–5 d *or* Ciprofloxacin (20–30 mg/kg/d, divided into doses administered every 12 h; 800-mg/d maximum) for 3–5 d *In a patient with localized invasive disease or bacteremia associated with immunosuppression, treat with* Ceftriaxone (50 mg/kg/d, 4-g/d maximum) for 3–7 d
***Shigella* Infection**	
Culture-positive *Shigella* bacteria High suspicion for *Shigella* bacteria while awaiting culture results if patient has Severe disease or dysentery *or* Underlying immunosuppressive disorder Treat symptomatic family members and close contacts, as well	Antimicrobial susceptibilities are warranted given resistance patterns *For ampicillin and TMP-SMX–resistant or unknown strains (dosing as above), treat with* Azithromycin (3 d) *or* Ciprofloxacin (3 d) *or* Ceftriaxone (2–5 d)
***Campylobacter* Infection**	
Treatment can shorten the duration of illness and prevent relapse when administered early during infection	*Treat with* Azithromycin (10 mg/kg/d, 500-mg/d maximum) for 3 d *or* Erythromycin (40 mg/kg/d, divided into doses administered every 6 h; 2-g/d maximum) for 5 d
***Escherichia coli* Infection**	
Treatment is not indicated for O157:H7 enteritis or a clinical or epidemiologic picture strongly suggestive of Shiga toxin–producing *E coli* infection, given unclear increased risk of HUS	No antibiotics
***Clostridioides difficile* Infection**	
Discontinue the offending antibiotic	*Treat with* Metronidazole (30 mg/kg/d PO or IV, divided into doses administered every 6 h; 2-g/d maximum) for 10 d *or* Vancomycin (40 mg/kg/d PO, divided into doses administered every 6 h; 2-g/d maximum) for 10 d if unresponsive to metronidazole, severe disease, or multiple recurrences

Abbreviations: GI, gastrointestinal; HUS, hemolytic uremic syndrome; IV, intravenous; PO, per os (oral); SMX, sulfamethoxazole; TMP, trimethoprim.

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CHAPTER 39

Gastrointestinal Bleeding

Introduction

Gastrointestinal (GI) bleeding is a complaint that requires prompt evaluation. The presentation and differential diagnosis are broad, with a spectrum that ranges from an occult, self-limited bleed to a severe, rapidly progressive, life-threatening hemorrhage that can originate from either the upper GI (UGI) or lower GI (LGI) tract. A systematic approach is critical, beginning with the confirmation of actual blood that originates from the GI tract, an assessment of the severity of the bleeding, and the initiation of appropriate resuscitation. Once the patient is stabilized, the priorities are determining the exact cause and site of the bleeding (UGI vs LGI) and planning for subsequent treatment.

Clinical Presentation

History

Ask about the duration of bleeding, associated symptoms, and the estimated amount of blood loss, measured in terms understandable to nonmedical caregivers, such as teaspoons. Document the presence of fever, lethargy, and weight loss, as well as the location, intensity, and pattern of any abdominal pain. Determine if there have been any prior episodes of bleeding or a family history of disease.

Obtain a thorough history regarding the patient's diet, medications, and possible ingestions, because certain foods and drugs can give the false appearance of blood. Any food with a red skin (beets, tomatoes, apples) or red food coloring (candy, drinks, gelatin) can be mistaken for frank blood if vomited. Likewise, medications that contain flavoring syrups (antibiotics, certain preparations of acetaminophen) can resemble hematemesis. Spinach, blueberries, plums, grapes, and medications that contain iron or bismuth can cause melena-like stools. For a breastfeeding infant, ask if the mother's nipples are cracked or bleeding.

Inquire about a choking episode prior to the suspected bleeding. Ingested foreign bodies can lead to GI bleeding if they are sharp or caustic (button batteries) or if they become lodged in the GI tract mucosa.

Aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids increase the risk of GI bleeding by directly damaging gastric mucosa. Anticoagulants (heparin, warfarin, aspirin, NSAIDs) can affect coagulation and increase the risk of mucocutaneous bleeding. In addition, some medications (doxycycline, aspirin, NSAIDs) can cause esophagitis.

UGI Bleeding

By definition, UGI bleeding originates proximal to the ligament of Treitz and can present as hematemesis, which can be coffee ground or bright red in appearance, depending on the source, severity, and chronicity of the bleed. A slow UGI bleed may also appear with melena at presentation or, if the bleeding is brisk enough, hematochezia (bright red or dark blood that passes through the rectum). Ask about a history of lesions or active disease in the nose, mouth, pharynx, larynx, or lungs, which can lead to swallowed blood and mimic a UGI bleed. Ask about a history of prematurity and possible umbilical artery line insertion. Document symptoms of vomiting and retching (Mallory-Weiss tear) and itching and jaundice (liver disease and portal hypertension). Also inquire about a history of abdominal trauma, which can lead to duodenal injury.

LGI Bleeding

Ask about the quality, consistency, and frequency of the patient's stool. A slow LGI bleed can appear with melena at presentation but more commonly presents with hematochezia. Hard stool that is blood streaked on the outside occurs with bleeding in the rectal vault or anal canal. Bloody diarrhea suggests colitis, most often secondary to an infectious etiology, as does the presence of mucus mixed with the stool, whereas "currant jelly" stool is a classic finding of intussusception. Ask about weight loss, rash, joint pain, atopy in the family or patient, or tenesmus, which, along with a family history of chronic bleeding or GI or autoimmune disorders, can suggest inflammatory bowel disease (IBD).

Physical Examination

The patient can appear ill as a result of the underlying condition causing the GI bleed or as a consequence of the bleeding itself. Carefully assess the patient's vital signs (including orthostatic changes), growth parameters, general appearance, perfusion, and mental status to determine if aggressive resuscitation or urgent specialty consultation is needed.

Examine the patient's eyes for scleral icterus (indicative of liver disease) and the oral and nasal mucosa for freckles (associated with polyps), ulcers (associated with IBD), or evidence of bleeding or trauma. Examine the abdomen for distention, bowel sounds, tenderness, ascites, masses, hepatosplenomegaly, or signs of acute abdomen. Epigastric tenderness is nonspecific but may indicate peptic ulcer disease (PUD), gastritis, or esophagitis, while hepatosplenomegaly in conjunction with caput medusae is highly suggestive of portal hypertension with esophageal varices. Cutaneous hemangiomas raise the suspicion for other vascular lesions within the GI tract (upper and/or lower). Perform a careful

anal and rectal examination to look for fissures, skin tags, fistulas, occult blood, impacted stool, or polyps. Rectal bleeding without tenderness suggests a Meckel diverticulum, while a lower right quadrant mass may be noted with intussusception.

Laboratory Workup

The goals of the diagnostic evaluation are to first confirm the presence of blood and then determine the source and severity of the bleed. Perform a complete blood cell count (CBC), a stool guaiac test for both UGI and LGI bleeds, and a gastric occult blood and pH test for a UGI bleed. If the bleeding is either hemodynamically significant or ongoing, repeat the CBC at least every 6 to 12 hours. If there is evidence of liver dysfunction or coagulopathy (easy bruising or a history of recurrent bleeding, liver disease, or anticoagulant use), obtain a comprehensive chemistry profile, with liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels) and a prothrombin time (PT)/partial thromboplastin time/international normalized ratio. Also obtain a C-reactive protein level and/or erythrocyte sedimentation rate if the clinical picture suggests an inflammatory process based on findings such as weight loss, fatigue, fever, arthralgia or arthritis, purpura, or a prior history of such symptoms.

If the patient has hematochezia, testing for infectious etiology is not always indicated, but when symptoms are excessive (high fever, prolonged diarrhea, systemic symptoms), obtain stool for bacterial culture for common pathogens (*Salmonella*, *Shigella*, *Yersinia enterocolitica*, *Campylobacter jejuni*). If suggested by the clinical presentation, also test for *Escherichia coli* O157:H7 and *Clostridioides difficile* toxin A and B. If indicated by a recent travel history to endemic areas, send stool for *Entamoeba histolytica* and *Trichuris trichiura* testing. Perform a urinalysis if the initial test results are consistent with hemolytic uremic syndrome (anemia, thrombocytopenia, evidence of hemolysis on a peripheral smear, and renal impairment). For hemodynamically significant bleeds, order a type and screen in anticipation of obtaining blood products.

Nasogastric or orogastric lavage is not routinely indicated, unless the source of a GI bleed is uncertain or the bleeding is clinically significant. If the lavage returns fresh blood, blood-tinged secretions, or coffee-ground secretions, a UGI or nasopharyngeal source of bleeding is confirmed. The lavage may have falsely negative findings if the bleeding has stopped or if the source is distal to a closed pylorus. A lavage with bilious fluid may indicate an open pylorus and/or a small-bowel obstruction. Use warm saline, because cold solutions may cause hypothermia in an infant or young child, while using water may lead to electrolyte imbalances.

Radiology Examinations

Radiologic tests, such as abdominal imaging with anteroposterior abdominal radiography (commonly referred to as "KUB"), ultrasonography (US), computed tomography (CT), or barium enema, may be useful for locating the source of the bleeding and determining the appropriate next step in evaluation (ie, upper vs lower endoscopy) and treatment.

Perform abdominal Doppler US when there is evidence of liver disease that is suggestive of portal hypertension and may be associated with esophageal varices. Abdominal CT with intravenous contrast material, abdominal magnetic resonance imaging, or a UGI series can be used to further evaluate the patient for esophageal varices. If esophagogastroduodenoscopy (EGD) is not readily available, perform a UGI series to identify a radiopaque foreign body and gastric and duodenal ulcers. However, defer radiographic imaging until the patient is hemodynamically stable.

If further visualization of a potential UGI bleed site is needed, EGD performed by a gastroenterologist is the next best plan of action. An EGD can help identify sites of active bleeding so that therapeutic interventions may be initiated, when indicated. Perform emergency EGD when bleeding is considered to be life-threatening. Otherwise, it is best performed in a controlled setting with anesthesia.

If an infant or younger child has an LGI bleed plus vomiting, perform KUB with either an upright or a cross-table lateral view to look for intestinal obstruction, pneumatosis intestinalis, or findings consistent with an intussusception or volvulus. If intussusception is strongly suspected, perform an air-contrast enema, which will be both diagnostic and therapeutic. A UGI series is indicated for possible volvulus. However, perform abdominal CT or US if an ischemic process is suspected in an older child.

When a Meckel diverticulum is suspected, perform a Meckel scan with technetium 99m (^{99m}Tc) to identify ectopic gastric tissue seen in either the diverticulum or intestinal duplications. The ^{99m}Tc is absorbed by ectopic gastric mucosa, which is seen as areas of increased uptake on the scan.

In select cases, capsule endoscopy, exploratory laparoscopy, or laparotomy is necessary to be able to identify the source. If the diagnosis remains uncertain, a slow bleed may be identified with a "bleeding scan" performed with ^{99m}Tc-labeled red cells, and more active bleeding may be detected with angiography.

Differential Diagnosis

The presence of hematemesis, melena, or hematochezia can help narrow the differential diagnosis when evaluated in the context of the patient's age. Hematemesis reflects bleeding proximal to the ligament of Treitz, and melena is secondary to bleeding proximal to the transverse or descending

colon, with a slow intestinal transit time that allows bacteria to denature the hemoglobin. Hematochezia usually (but not always) reflects bleeding distal to the transverse colon. Table 39–1 summarizes the most common causes according to age group and location of the bleed.

Treatment

The priority for treatment of a GI bleed is hemodynamic stabilization, including correction of any coagulopathies or blood product deficits. Once stabilization has begun, treat active bleeding with empirical gastric acid–reduction therapy with a proton-pump inhibitor until a UGI bleed has been ruled out (Table 39–2). If PUD is suspected, treat the patient with a cytoprotective agent, such as

Table 39–1. Most Common Causes of Gastrointestinal Bleeding

Patient Age	UGI Bleed	LGI Bleed
Neonate	Coagulopathy (vitamin K deficiency, thrombocytopenia) Milk protein sensitivity Swallowed maternal blood Vascular malformations	Allergic colitis (allergy to cow milk protein) Anorectal fissure Coagulopathy (vitamin K deficiency, thrombocytopenia) Necrotizing enterocolitis Swallowed maternal blood Vascular malformation
1 month to 2 years of age	Esophageal varices Esophagitis Gastritis Ingestion (toxin, foreign body) Stress gastritis or ulcer Vascular malformation	Anorectal fissure Infectious colitis Allergic colitis (allergy to cow milk protein) Intussusception Meckel diverticulum Polyps Vascular malformations
2–5 years of age	Esophageal varices Esophagitis Gastritis Ingestion (toxin, foreign body) Mallory-Weiss tear Reflux esophagitis Stress ulcer Vascular malformation	Anorectal fissure Henoch-Schönlein purpura Infectious colitis Inflammatory bowel disease Intussusception Meckel diverticulum PUD Polyps Vascular lesion
Older child or adolescent	Esophageal varices Gastritis IBD Mallory-Weiss tear Reflux esophagitis Ulcer Vascular malformation	Henoch-Schönlein purpura Infectious colitis IBD Meckel diverticulum PUD Polyp Vascular lesion

Abbreviations: IBD, inflammatory bowel disease; LGI, lower gastrointestinal; PUD, peptic ulcer disease; UGI, upper gastrointestinal.

Table 39–2. Initial Treatment of Active Gastrointestinal Bleeding

Indication	Drug Name (Class)	Dose
Active bleeding	Lansoprazole (PPI)	≤ 30 kg: 15 mg orally once daily > 30 kg: 30 mg orally once daily orally
	Esomeprazole (PPI)	Infants: 0.5 mg/kg IV once daily ≤ 55 kg: 10 mg IV once daily > 55 kg: 20 mg IV once daily Continuous infusion: bolus of 1 mg/kg (80-mg maximum), followed by infusion of 0.1 mg/kg/h (8-mg/h maximum) for 72 hours
	Pantoprazole (PPI)	≤ 40 kg: 0.5–1.0 mg/kg IV once daily Patient > 40 kg: IV 20–40 mg every day Continuous infusion: bolus of 1 mg/kg (80-mg maximum), followed by infusion of 0.1 mg/kg/h (8-mg/h maximum) for 72 hours
	Octreotide (somatostatin analog, vasoactive agent)	1-mcg/kg bolus (50-mcg maximum) followed by 1 mcg/kg/h; titrate infusion rate to response (maximum, 2.5 mcg/kg/h) May increase every 8 h to 4 mcg/kg (maximum, 250 mcg every 8 h) Taper by 50% for 1–2 d when bleeding is controlled
	Vasopressin (antidiuretic hormone, vasoactive agent)	0.002–0.005 U/kg/min for 12 h, then taper for 1–2 d (maximum, 0.2 U/min)
PUD Bleeding ulcer	Sucralfate (mucosal adhesive)	40–80 mg/kg/d orally, divided into doses administered every 6 hours (4-g/d maximum)
Liver disease Prolonged PT Hemorrhagic disease of the newborn	Vitamin K	IM, IV, SC 1–2 mg every day SC administration route preferred Severe reactions resembling anaphylaxis or hypersensitivity have rarely occurred after IV or IM administration

Abbreviations: IM, intramuscular; IV, intravenous; PPI, proton-pump inhibitor; PT, prothrombin time; PUD, peptic ulcer disease; SC, subcutaneous.

sucralfate. If liver disease or a prolonged PT is discovered or if hemorrhagic disease of the newborn is suspected, treat with vitamin K.

Consult a gastroenterologist if there is severe bleeding. Therapeutic options may include octreotide or vasopressin, vasoactive agents that are infused to control severe bleeds from varices or bleeding ulcers. Furthermore, treatment for specific lesions found at endoscopy or surgical exploration can be accomplished through electrocoagulation; use of a heater probe, multipolar probe, endoscopic hemoclips, or band ligation; sclerotherapy (injection or laser); or ligation and resection of the lesion.

Indications for Consultation

- **Gastroenterology:** Severe bleeding, endoscopy needed, suspicion of liver disease, portal hypertension, or IBD

- **Surgery:** Possible surgical abdomen (volvulus, intussusception, perforation), abdominal trauma, suspicion of a duplication cyst or Meckel diverticulum, exploratory laparotomy needed

Disposition

- **Intensive care unit transfer:** Hemodynamic instability
- **Discharge criteria:** Cause of the bleeding identified and controlled, anemia adequately treated, and nutrition optimized

Follow-up

- **Primary care:** 1 to 2 weeks
- **Gastroenterology and/or surgery:** Depending on the source and expected chronicity of the bleed

Pearls and Pitfalls

- Swallowed blood (from cracked maternal nipples in a breastfed infant), coughing, tonsillitis, lost teeth, epistaxis, genitourinary bleeding, or menarche may give the false appearance of GI bleeding.
- Medications (bismuth subsalicylate [Pepto-Bismol], iron, liquid acetaminophen [Tylenol]), and foods (red juice, beets) can falsely give the physical and chemical appearance of blood.
- Artificial devices (nasogastric or orogastric tubes; tracheostomy tubes; gastrostomy, gastrojejunal, or jejunal tubes) in which the device tip is causing mucosal irritation can lead to ulceration and bleeding.
- Radiologic contrast material may interfere with an EGD, so consult with a gastroenterologist before choosing between imaging or EGD as the next step.

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CHAPTER 40

Inflammatory Bowel Disease

Introduction

Inflammatory bowel diseases (IBDs), including ulcerative colitis (UC) and Crohn disease (CD), cause chronic intestinal inflammation characterized by clinical exacerbations and remissions. Inflammatory bowel disease affects children of all ages. Disease in the first 2 years after birth is referred to as infantile-onset IBD, while very early–onset IBD occurs in patients between 2 and 6 years of age.

Specific symptoms are dependent on the extent and location of inflammation, with significant individual variability in disease severity. Crohn disease can affect any portion of the gastrointestinal (GI) tract but frequently involves the colon and terminal ileum. Ulcerative colitis affects the rectum and colon in a continuous pattern. Pediatric IBD most commonly manifests during adolescence, although it can occur in younger children. A patient with IBD is often admitted to the hospital to control a symptomatic flare of their disease; they can also experience rare, but serious, complications.

Clinical Presentation

History

A patient with new onset or an exacerbation of IBD classically presents with abdominal pain, bloody diarrhea, weight loss, and increased stool frequency, including nocturnal bowel movements. There may also be fever, fatigue, slowed growth velocity, and delayed puberty. However, the onset of IBD may be subtle, appearing solely with growth delay. At some point, about one-third of patients with IBD have extraintestinal manifestations, including arthralgia or arthritis, skin eruption (erythema nodosum, pyoderma gangrenosum), aphthous stomatitis, and ophthalmologic inflammation. Other extraintestinal manifestations and complications include cholelithiasis, nephrolithiasis, primary sclerosing cholangitis, and osteoporosis. On occasion, these extraintestinal manifestations are the sole presenting signs or symptoms of the disease.

Physical Examination

Perform a complete physical examination, including perianal and digital rectal examinations. Review the patient's height, weight, and body mass index, and assess the Tanner stage. Common findings include abdominal tenderness, inflamed rectal skin tags, perianal fissures, and drainage from

enterocutaneous fistula. A mass is sometimes palpable when there is significant intestinal inflammation or an abscess.

Laboratory Workup

If IBD or an IBD exacerbation is suspected, obtain a complete blood cell count, C-reactive protein (CRP) level and/or erythrocyte sedimentation rate (ESR), a comprehensive metabolic panel, and stool for guaiac, culture, ova and parasite testing, and *Clostridioides difficile* testing. Also check the amylase and lipase levels if the patient has midepigastric pain. These studies, in addition to fecal calprotectin or lactoferrin, can help differentiate relapse from other causes of abdominal pain. Findings can include anemia, leukocytosis and thrombocytosis, increased ESR and CRP levels, hypoalbuminemia, and guaiac-positive stools, although all of these results can be normal. Given the lack of diagnostic predictive value and high cost, do not use an IBD serology panel as a screening test. Obtain blood cultures if a patient with IBD who is receiving immunosuppressive medications is febrile (> 38.3°C [> 101.0°F], or > 38°C [> 100.4°F] for more than an hour or twice over 12 hours).

Radiology Examinations

If the patient presents with severe abdominal pain, order an abdominal radiograph to look for small-bowel obstruction (air-fluid levels) or perforation (free air). In severe acute colitis, toxic megacolon can also be identified on a plain-film radiograph (transverse colon dilatation). If a patient known or suspected to have CD presents with persistent or escalating abdominal pain, persistent fever, bilious emesis, cutaneous fistulae, or persistent rectal bleeding without a source at endoscopy, order an upper GI series with small-bowel follow-through, computed tomographic (CT) enterography, or magnetic resonance (MR) enterography to evaluate the patient for internal disease (stricture, fistula, abscess). If there is concern for extraluminal disease, but both MR and CT enterography are unavailable or the patient is unable to tolerate enteral or rectal contrast material or lying still, perform CT with contrast material. For perianal disease, order MR imaging with contrast material.

Diagnostic Procedures

Endoscopy and colonoscopy with biopsy are needed to assign a diagnosis of IBD, but defer them until the patient is clinically stable. These procedures may also be indicated intermittently to evaluate the extent of relapsing disease before changing therapy. Both upper endoscopy and colonoscopy are required because CD may affect any site in the GI tract, from the mouth to the anus. Findings that distinguish CD from UC are disease location, patchy

inflammation (skip lesions), and noncaseating granulomas. Though these granulomas are pathognomonic for CD, they are found in less than 30% of biopsies. In UC, there is continuous chronic inflammation that starts in the rectum and extends proximally. However, in some cases, pediatric CD can also appear with pancolitis at presentation, with or without granulomas.

Differential Diagnosis

Infectious colitis may mimic the acute presentation of IBD. Perform stool cultures and *C difficile* toxin A and B assay or polymerase chain reaction. However, the presence of *C difficile* does not rule out IBD, because a patient with IBD is at increased risk for non–antibiotic-associated *C difficile* infection. The differential diagnosis of IBD is summarized in Table 40–1.

Table 40–1. Differential Diagnosis of Inflammatory Bowel Disease

Diagnosis	Clinical Features
Bloody Diarrhea	
Allergic colitis	Patient usually < 5 y of age No extraintestinal manifestations Peripheral eosinophilia
Infectious colitis (*Campylobacter, Clostridioides difficile,* cytomegalovirus, *Entamoeba histolytica, Escherichia coli, Salmonella, Shigella,* or *Yersinia* infection)	Usually more acute presentation Extraintestinal manifestations are rare, other than fever and arthritis
Henoch-Schönlein purpura	Usually more acute presentation Purpura on legs and buttocks May have hematuria Extraintestinal manifestations are rare, other than arthritis
Abdominal Pain, Diarrhea, and Weight Loss	
Celiac disease	Nonbloody diarrhea Positive celiac serologic findings Biopsy: villous blunting and intraepithelial lymphocytes
Constitutional Symptoms (Weight Loss, Fever, Fatigue, Increased CRP Level/ESR)	
Behçet disease	Patient can have genital ulcers Biopsy does not show chronic inflammation
HIV, other immunodeficiencies	Recurrent infections Leukopenia
Juvenile idiopathic arthritis Other connective tissue disorders	GI symptoms are usually less prominent
Malignancy	Patient may have pancytopenia Patient may have tumor lysis
Tuberculosis	Bloody stools are rare

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal.

Serious Complications

The most common serious complications of CD are a result of stricturing and penetrating disease, including perforation and peritonitis, abdominal and perirectal abscesses, fistula, and small-bowel obstruction. A patient with refractory UC may develop toxic megacolon, leading to perforation and/or sepsis, whereas a patient with IBD is at increased risk of thrombosis and venous thromboembolism (VTE) due to a hypercoagulable state. In addition, many medications used to treat IBD cause immunosuppression, leading to a risk of community-acquired and opportunistic infections. See Table 40–2 for other important potential side effects of IBD treatment.

Treatment

The goals of inpatient treatment are to stabilize the patient, treat complications, and improve symptoms, while ideally inducing a disease remission. Therapy for IBD is individualized and therefore best guided by a gastroenterologist. Acute management may include fluid resuscitation, packed red blood cells (10–15 mL/kg) for symptomatic or significant anemia in the setting of continued blood loss, and 25% albumin infusion (1 g/kg, 25-g maximum) if the serum albumin level is lower than 2 g/dL. Maximize nutrition intake with oral or tube feedings. In a patient with severe malnutrition or weight loss, be vigilant for refeeding syndrome when starting enteral feeds. If enteral nutrition is not feasible, initiate parenteral nutrition. Try to minimize opioid use, because it can lead to side effects such as ileus (leading to nausea, vomiting, and constipation symptoms), toxic megacolon in UC, and narcotic bowel syndrome (a paradoxical increase in abdominal pain). Depending on severity of disease and additional risk factors, consider VTE prophylaxis, including mobilization, mechanical prophylaxis, and prophylactic pharmacologic

Table 40–2. Medication Adverse Effects[a]

Medication	Adverse Effects
6-Mercaptopurine	Hepatotoxicity, immunosuppression, lymphoma, pancreatitis
Corticosteroids	Adrenal suppression, glaucoma, hyperglycemia, hypertension, mood disturbance, immunosuppression, pseudotumor cerebri, poor wound healing, psychosis, osteopenia, and fractures
Calcineurin inhibitors (cyclosporine)	Hypertension, immunosuppression, lymphoma, renal impairment
Anti–tumor necrosis factor α (infliximab, adalimumab)	Anaphylaxis, immunosuppression, lymphoma, reactivation of latent diseases (tuberculosis, hepatitis B, histoplasmosis, coccidioidomycosis)
Mesalamine	Myocarditis/pericarditis, nephritis, pancreatitis
Methotrexate	Hepatotoxicity, immunosuppression, pneumonitis

[a] Only severe effects are included here; this is not a comprehensive list.

anticoagulation (see Chapter 49, Thrombocytopenia). The treatment of IBD complications is summarized in Table 40–3.

Indications for Consultation

- **Gastroenterology:** All patients
- **Hematology:** Suspected complication of hypercoagulable state

Table 40–3. Treatment of IBD Complications

Complication	Treatment
Complications of Crohn Disease	
Complex fistula	IV antibiotics*: Regimen A–D[abcd] Surgery consultation
Intra-abdominal abscess	IV antibiotics*: Regimen A–D[abcd] Surgery consultation
Perianal abscess	IV antibiotics*: Regimen E–F[ef] Surgery consultation
Small-bowel obstruction	NPO Decompression with a nasogastric tube Urgent surgery consultation
Complications of Both Crohn Disease and Ulcerative Colitis	
Perforation	IV antibiotics*: Regimen A–D[abcd] Urgent surgery consultation NPO Treat disseminated intravascular coagulation, electrolyte abnormalities, and hypotension
Toxic megacolon	IV antibiotics*: Regimen A–D[abcd] Urgent surgery consultation NPO Correct electrolyte abnormalities
Sepsis	IV antibiotics*: Regimen A–D[abcd] Hemodynamic support
Thrombosis or thromboembolism	Consult with a hematologist and possibly a vascular surgeon and neurologist Possible anticoagulation, thrombolysis, or surgery

Abbreviations: IBD, inflammatory bowel disease; IV, intravenous; NPO, nil per os (nothing by mouth).

* Choose empirical antibiotics based on local resistance patterns and likely organism. Use broader coverage for critically ill patients and narrow coverage based on identification and sensitivities, if available. Note: Add vancomycin 45 mg/kg/d, divided into doses administered every 8 hours, if methicillin-resistant *Staphylococcus aureus* is a concern.

[a] Regimen A: Cefoxitin 100–160 mg/kg/d, divided into doses administered every 4–6 hours, with or without gentamicin 7.5 mg/kg/d, divided into doses administered every 8 hours.

[b] Regimen B: Cefotaxime 100–200 mg/kg/d, divided into doses administered every 6–8 hours and metronidazole 30 mg/kg/d, divided into doses administered every 8 hours.

[c] Regimen C: Piperacillin/tazobactam 300 mg/kg/d, divided into doses administered every 8 hours.

[d] Regimen D: Meropenem 60 mg/kg/d, divided into doses administered every 8 hours.

[e] Regimen E: Metronidazole 30 mg/kg/d, divided into doses administered every 8 hours and/or ciprofloxacin 20–30 mg/kg/d, divided into doses administered every 12 hours.

[f] Regimen F: Cefotaxime 100–200 mg/kg/d, divided into doses administered every 6–8 hours and metronidazole 30 mg/kg/d, divided into doses administered every 8 hours.

- **Infectious diseases:** Immunosuppressed patient with a high fever or not improving with appropriate antibiotic therapy
- **Surgery:** Suspected perforation, small-bowel obstruction, or toxic megacolon; abscess, stricture, or fistula; intractable bleeding; UC that has failed to respond to medical management
- **Nutrition:** Malnutrition, inability to tolerate oral feedings, use of exclusive enteral nutrition as therapy

Disposition

- **Intensive care unit transfer:** Shock, impending respiratory failure, peritonitis, life-threatening electrolyte abnormalities, severe postoperative complications, thrombotic complications
- **Discharge criteria:** Patient tolerating maintenance oral or tube diet, intravenous (IV) medications discontinued, pain well controlled, no or minimal blood in stools, stable hemoglobin level with no symptoms of anemia

Follow-up

- **Gastroenterology:** 1 to 2 weeks
- **Primary care:** 2 to 4 weeks

Pearls and Pitfalls

- Abdominal distention may be caused by obstruction, ileus, perforation, or toxic megacolon.
- A patient with known IBD may have another etiology for acute abdominal symptoms, such as appendicitis or pancreatitis. Pursue a careful differential diagnosis for each presentation.
- In severe acute UC, IV steroids are the first-line therapy. If there is no response to treatment after 5 to 7 days, escalate therapy to infliximab or cyclosporine and discuss the need for possible colectomy.
- Take caution with repeat imaging, because a patient with IBD may be exposed to high levels of ionizing radiation from repeat CT scans.
- Coordinate the timing of imaging with the gastroenterologist, as some contrast material can interfere with endoscopy.

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CHAPTER 41

Pancreatitis

Introduction

Pancreatitis is an acute, recurrent, or chronic inflammatory condition of the pancreas. Approximately 25% of pediatric cases of acute pancreatitis are idiopathic. Other causes include trauma, systemic illness, structural abnormalities, medications or toxins, infections, and metabolic or autoimmune disorders (Table 41–1).

Pancreatitis can lead to abnormal endocrine or exocrine function, which usually resolves completely. Rarely, it can progress to necrotizing pancreatitis, with potential pancreatic insufficiency. Some patients will have recurrent pancreatitis, with the potential for persistent inflammation and chronic pancreatitis within the ductal system. Severe cases of chronic or hereditary (autosomal dominant) pancreatitis may cause pancreatic insufficiency or insulin-dependent diabetes.

Clinical Presentation

History

The patient typically presents with acute abdominal pain, vomiting, fever, and, rarely, shock. The abdominal pain is continuous, typically epigastric or in the upper quadrants, and may radiate to the patient's back or shoulders. Pain is worsened by oral intake and may be relieved with bending forward. Nausea and vomiting tend to occur as the inflammation progresses.

Table 41–1. Etiology of Acute Pancreatitis

Category	Examples
Abdominal trauma	Abdominal injuries from motor vehicle accidents, handlebar injuries
Genetic/metabolic origin	Cystic fibrosis, hypercalcemia, hypertriglyceridemia
Idiopathic	(none)
Infectious	Mumps, mycoplasma
Medications/toxins	Azathioprine, valproic acid
Obstruction	Cholelithiasis Abdominal masses or intestinal strictures obstructing the pancreatic duct
Systemic illnesses	Burns, sepsis, shock
Structural abnormalities	Pancreas divisum
Toxins	Alcohol Scorpion and spider bites

Inquire about predisposing factors, including trauma, exposures to drugs or medications, recent illnesses, and family history of hyperlipidemia, gallstones, or pancreatitis.

Physical Examination

The patient may appear restless because of the pain. There may be abdominal rigidity, guarding, and hypoactive or absent bowel sounds. An epigastric mass secondary to a pseudocyst may be palpable. In severe cases, findings may include diminished breath sounds because of pleural effusions, toxic appearance, periumbilical ecchymoses (Cullen sign), or flank ecchymoses (Grey-Turner sign). Mild jaundice can occur with any etiology of pancreatitis, but moderate to severe jaundice is typically associated with common bile duct obstruction from gallstones or edema of the pancreatic head.

Laboratory Workup

If pancreatitis is suspected, obtain a serum lipase level. While an amylase level increases within hours of pain onset, it is not indicated because of its low sensitivity (75%). Elevation of the lipase level typically occurs 72 hours after symptom onset, and it is more sensitive (90%) and specific (90%) for pancreatic inflammation. However, the degree of lipase, or amylase, increase does not necessarily correlate with disease severity. Also obtain electrolyte (including calcium), glucose, blood urea nitrogen, and creatinine levels, along with liver function tests (aspartate transaminase, alanine transaminase, alkaline phosphatase, γ-glutamyl transpeptidase, albumin, and total bilirubin tests), and a fasting lipid panel (specifically triglycerides).

Radiology Examinations

Radiologic studies are not required to diagnose pancreatitis but may be useful for determining the etiology. Order an abdominal ultrasonographic (US) examination to evaluate the patient for the presence of gallstones or ductal dilation, characterize pancreatic anatomy, document the presence of cysts or abscesses, and rule out other potential causes of abdominal pain. If US examination is unavailable, or visualization is inadequate, computed tomography (CT) with contrast can reveal peripancreatic fluid collections or pseudocysts. However, CT is not routinely indicated, nor is it required for initial diagnosis of pancreatitis. If evaluating for potential complications, delaying the CT scan for at least 96 hours after symptom onset leads to higher yield. Abdominal magnetic resonance (MR) imaging is an alternative if intravenous contrast for a CT is contraindicated.

If the patient has recurrent or chronic pancreatitis because of pancreatic duct obstruction, arrange for evaluation of the biliary system with MR

cholangiopancreatography (MRCP) and/or endoscopic retrograde cholangiopancreatography (ERCP). ERCP may be therapeutic for ductal abnormalities if stone removal or stent placement is performed. These are typically performed electively, after the resolution of acute inflammation, unless there is obstructive jaundice and/or cholangitis. Magnetic resonance cholangiopancreatography is preferable if a therapeutic procedure will not be necessary.

Differential Diagnosis

Standardized definitions and diagnostic criteria for the various clinical presentations of pancreatitis have been developed.

- *Acute pancreatitis*. The patient has at least 2 of the following: characteristic abdominal pain, serum lipase greater than or equal to 3 times the upper limit of normal, and imaging findings consistent with pancreatitis.
- *Acute recurrent pancreatitis.* The patient has had at least 2 discrete episodes of acute pancreatitis in the absence of evidence of irreversible, structural changes in the pancreas. The acute pancreatitis must resolve after the first episode.
- *Chronic pancreatitis*. There is evidence of irreversible damage to the pancreas, along with at least one of the following: periods of consistent abdominal pain or lipase greater than 3 times the upper limit of normal, exocrine pancreatic insufficiency, or endocrine pancreatic insufficiency.

As noted above, an increased serum amylase level is not specific for pancreatitis and can occur in other conditions, including salivary gland inflammation, diabetic ketoacidosis, perforated gastric ulcer, gallbladder disease, ruptured fallopian tube, and renal failure. The differential diagnosis of pancreatitis is summarized in Table 41–2. In these alternative diagnoses, lipase levels are generally normal.

Treatment

Permit no intake by mouth, and insert a nasogastric tube for suction if the patient has repeated vomiting or significant abdominal distention. Provide aggressive fluid resuscitation with isotonic crystalloid fluids (normal saline [NS] or lactated ringer [LR]), replacing any volume deficit if the patient appears dehydrated. Subsequently, start intravenous fluids with dextrose 5% NS solution with 20 mEq/L (20 mmol/L) of potassium chloride or LR at 1.5 to 2 times maintenance. Monitor the vital signs every 4 hours and perform serial abdominal examinations, because the patient is at risk for third-spacing fluid (peritoneal or pleural cavity) and intravascular depletion. In particular, closely monitor cardiac, respiratory, and kidney function due to the risk of systemic

Table 41–2. Differential Diagnosis of Pancreatitis	
Diagnosis	**Clinical Features**
Acute gastroenteritis	Diarrhea is commonly present Pain is generalized and mild and not associated with eating Pain is not relieved by leaning forward
Appendicitis	Pain is constant Pain classically migrates from the periumbilical area to the right lower quadrant
Cholelithiasis	Right upper quadrant colicky pain Pain may worsen with meals
Intussusception	Pain is cramping and intermittent May be associated with drawing up the legs Hematochezia may be present
Peptic ulcer	Epigastric pain, worse before meals, is not relieved by leaning forward May improve by taking antacids Pancreatic enzyme levels are typically normal but may be increased with severe ulcer or perforation
Viral hepatitis	Pain is localized to the right upper quadrant Liver enzyme levels are typically elevated, although they may be normal during the acute phase

inflammatory response syndrome (SIRS), respiratory distress, or decreased urine output due to third-spacing of fluids. Monitor electrolyte levels and urine output until normal, and address abnormalities with electrolyte-specific correction and fluid replacement.

Provide adequate nutrition early during the hospitalization, ideally within 48 hours of admission. Normalization of the pancreatic enzyme levels is not necessary before resuming feedings. Enteral feedings are preferred, particularly once the patient's pain is resolving and bowel sounds are present. Jejunal feeding is an alternative for a patient with no signs of bowel obstruction or ileus. If the patient is unable to tolerate enteral feeding, provide total parenteral nutrition, without intralipids if severe hypertriglyceridemia is present.

For analgesia, administer morphine (0.05–0.10 mg/kg every 2–4 hours as needed; maximum, 15 mg per dose), as there is no evidence that opiates interfere with biliary drainage. For severe pain, order patient-controlled analgesia (see Chapter 103, Pain Management); usually just interval dosing without a basal rate will suffice. Acetaminophen and other nonsteroidal anti-inflammatory drugs, such as ibuprofen, ketorolac, and diclofenac, are effective for less severe pain.

Antibiotics are generally not indicated for acute or chronic pancreatitis, except when it is associated with common bile duct obstruction or for necrotizing pancreatitis. In such cases, treat bacterial superinfection with either piperacillin/tazobactam (patient weight < 41 kg: 100 mg/kg of piperacillin

every 8 hours with a maximum of 4 g; patient weight ≥ 41 kg: 3 g of piperacillin every 6 hours) or imipenem (15–25 mg/kg every 6 hours, 2–4g/d maximum) to cover enteric gram-negative organisms.

Most pediatric patients have mild pancreatitis that is not associated with organ failure or local/systemic complications and that resolves within 1 week of presentation. Abdominal imaging (CT or MR imaging) is indicated if the patient has ongoing severe pain requiring opioids, continuing fever, or a persistent leukocytosis. This will identify any pancreatic fluid collections or necrosis. Consult a pediatric surgeon or gastroenterologist for possible drainage if an enlarging pseudocyst or pancreatic abscess is present. Treat the primary or underlying cause of the pancreatitis when applicable.

Indications for Consultation

- **Gastroenterology:** Recurrent or chronic pancreatitis, pancreatic complications, pancreatic insufficiency, need for ERCP
- **Genetics:** Hypertriglyceridemia, hereditary pancreatitis
- **Pain service:** Uncontrolled or prolonged pain
- **Surgery:** Pseudocyst, abscess, or necrotizing pancreatitis

Disposition

- **Intensive care unit transfer:** Shock, suspected sepsis, SIRS, severe respiratory distress caused by pleural effusions, organ failure or dysfunction (severe pancreatitis)
- **Discharge criteria:** Patient tolerating a low-fat diet, electrolyte abnormalities corrected, and pain controlled with oral medications

Follow-up

- **Primary care:** 2 to 3 days
- **Pediatric gastroenterologist:** 2 to 3 weeks if complicated hospital course or consultation is required

Pearls and Pitfalls

- Early initiation of enteral feedings as tolerated, aggressive fluid hydration, electrolyte level correction, and pain control are the keys of treatment.
- The degree of amylase and lipase level increase does not indicate the severity of pancreatitis. Therefore, trending of enzyme levels is unnecessary. Also, normalization of the pancreatic enzyme levels is not necessary before resuming feedings.

- Approximately 15% to 35% of patients will have a recurrence of pancreatitis. These patients may go on to develop acute recurrent pancreatitis or chronic pancreatitis.
- Arrange genetic testing for a patient with recurrent pancreatitis to identify potential causes.

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Genetics and Metabolism

CHAPTER 42

Genetics

Introduction

Hospitalists are caring for an increasing number of patients with genetic conditions. At the same time, genetics is having a greater influence on clinical decision-making, as there is now increased access to a wider range of more complex testing. Therefore, hospitalists must be able to identify patients whose clinical presentation or family history warrants *immediate*, inpatient genetic evaluation and consultation.

Clinical Presentation

History

In assessing a potentially heritable disorder, the family history is the first and most cost-effective "genetic test." Construct a multigenerational pedigree of at least 3 generations, which will provide a visual representation of the family history and aid in identifying patterns of occurrence. Online tools, such as "My Family Health Portrait" (http://kahuna.clayton.edu/jqu/FHH/html/index.html), can help in the development of a robust pedigree.

Pay attention to conditions or diseases that run in the family, particularly malignancies, cardiac disease, neurodegenerative disorders, epilepsy, developmental disabilities, and dermatologic disorders, as well as sudden death. Other useful information includes difficulties with reproduction, such as infertility, birth defects, or problems with pregnancy; early onset of disease, disability, or death; consanguinity; and ethnicity. A family history that includes "too" or "two" descriptors may indicate a genetic condition (eg, too tall or short, too young, too many, 2 tumors, 2 birth defects, or 2 generations). Sometimes, a pattern of inheritance does not reveal itself in a patient suspected of having a genetic disorder. This may be secondary to a complex multifactorial disease process or a de novo mutation in the patient.

Important findings in the patient's medical history include intrauterine growth restriction or small size for gestational age, abnormal stature, failure to thrive, brain malformation, seizures, vision loss, deafness, developmental delays, autism spectrum disorder, and special health care needs.

Physical Examination

A thorough physical examination increases the chances of diagnosis and helps guide the testing strategy. Look for signs of growth abnormalities,

such as disproportionate growth, overgrowth, short stature, or Marfanoid habitus. Likewise, evidence of congenital abnormalities, including dysmorphic features, limb or skeletal malformations, and internal malformations, such as tracheoesophageal fistula, diaphragmatic hernias, and renal agenesis, can suggest a genetic disorder—especially in combination. Neurologic abnormalities, such as hyper- or hypotonia, spasticity, or micro- or macrocephaly, encompass the widest category of findings that can point to a genetic basis. There may be dermatologic findings consistent with a neurocutaneous disorder (eg, café au lait macules, ash leaf spots) or an oncologic process (eg, multiple lipomas). Other important findings include cardiomyopathy without viral cause, clotting abnormalities, and multifocal or bilateral malignancies, such as Wilms tumor or retinoblastoma.

Laboratory Workup

Genetic testing is indicated to confirm a diagnosis in a symptomatic patient, identify carrier status, or identify a late-onset disorder in a presymptomatic patient. Once the decision for testing has been made, consult an organ-specific or genetic specialist to determine test selection, as the breadth of commercially available tests is increasingly complex. Additionally, more than one test may be required to arrive at a final diagnosis. The general approach to genetic testing is to select the most cost-effective test that will provide results in the timeliest manner. The "correct" test, or tests, depends on the disease or phenotype and the gene or genes suspected. Genetic tests are summarized in Table 42–1.

Chromosomal microarray (CMA) is the standard, first-line genetic test in a patient with an unknown diagnosis of suspected genetic etiology. Chromosomal microarray is more sensitive than the karyotype and combines 2 technologies (comparative genomic hybridization and single-nucleotide polymorphism), which elucidates copy number variants (CNVs). With ongoing improvements in the cost and capability of next-generation sequencing (NGS) to detect CNVs and highly repetitive sequences, CMA may eventually be eclipsed as first-line testing. Defer to the genetic specialist to choose subsequent testing, depending on whether the phenotype matches a particular syndrome and the degree of associated genetic heterogeneity. When the diagnosis remains elusive, the ultimate testing step (for the geneticist) is whole-genome sequencing (WGS). It is important to note that reinterpretation of previously negative sequencing may be very helpful as genetic databases expand and variants of unknown significance (VUS) are reclassified.

Table 42–1. Specific Genetic Testing		
Test	**When to Consider**	**Detects/Examples**
Chromosomal microarray	Global developmental delay or intellectual disability of unknown etiology Multiple congenital anomalies	Microdeletion/microduplications CNV > 1000 base pairs Regions of homozygosity (consanguinity)
Fluorescence in situ hybridization	Suspected disorders due to deletion at targeted locus	Deletions in chromosomes in metaphase/interphase (DiGeorge Syndrome 22q11.2)
Karyotype	Suspected disorders due to whole chromosome abnormality Family history suggests balanced translocation (recurrent miscarriages/infertility)	Aneuploidy (trisomy 21, Turner syndrome) Structural rearrangements such as inversions, ring chromosomes, translocations and large deletions (cri du chat syndrome 5p-)
Methylation analysis	Suspected disorder of imprinting and hypermethylated trinucleotide repeats	Southern blot using methylation dependent digestion (Beckwith-Wiedemann syndrome, Angelman syndrome) Southern blot using methylation inactivated digestion (fragile X syndrome)
Non-NGS gene panels	Test for specific mutations associated with suspected disorder Rapid mass screening such as newborn screening for CF	Most common mutations associated with a disorder
mtDNA	Suspected mitochondrial disorder	NGS of mtDNA and nuclear DNA important to mitochondrial function (Leigh syndrome, Kearns-Sayre syndrome, MELAS)
Next-generation Sequencing		
Single/multiple gene panels	Selected gene(s) associated with a phenotype	Examples: cardiomyopathy, DNA repair defects, epilepsy, hearing loss, X-linked intellectual disability
WES	Genetic diagnosis unclear	Exon or coding region sequencing
WGS	Genetic diagnosis unclear Negative WES results	Entire genome (exons and introns)

Abbreviations: CF, cystic fibrosis; CNV, copy number variant; MELAS, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; mtDNA, mitochondrial DNA; NGS, next-generation sequencing; WES; whole-exome sequencing; WGS, whole-genome sequencing.

Ethics and Testing

Genetic testing is rapidly expanding, and misuse can have significant ethical, psychological, social, legal, and financial consequences for the patient and family. These tests, although potentially diagnostic for a patient's specific condition, may reveal incidental findings of known or unknown significance. Therefore, base all decisions regarding genetic testing on the best interests of the child. In close collaboration with a geneticist or genetic counselor, discuss the risks and benefits with the patient and parents/guardians, and, ideally, obtain the minor's assent. Testing for therapeutic purposes is acceptable, as

well as predictive testing in an asymptomatic child at risk for a childhood-onset illness. However, defer predictive testing for adult-onset conditions for which there are no interventions during childhood. Likewise, do not perform carrier testing when no medical benefits would arise from the results.

Direct-to-consumer (DTC) genetic testing has become more readily available to the public in the past few years. Consumers receive results that are unaccompanied by interpretation from a qualified medical provider, without the benefit of genetic counseling prior to testing. This can lead to myriad complications, including psychosocial stress and pursuing further inappropriate testing. The American Academy of Pediatrics and the American College of Medical Genetics and Genomics strongly discourage the use of DTC testing.

Management

While a genetic diagnosis may be confirmed, often there is no potential curative treatment. However, families often report that a diagnosis provides validation to help guide advocacy for their child, as well as a framework for discussing expectations, goals of care, and even future family planning. Families are also better able to seek out support groups once a diagnosis is assigned. Hospitalists and the primary care physician can help guide families to the appropriate services, whether these are subspecialists, rehabilitation staff, or palliative/supportive care.

In rare cases, a curative treatment may be identified after a genetic diagnosis is determined. For example, a patient with cystic fibrosis (CF) and a specific CF transmembrane conductance regulator (CFTR) gene mutation is eligible to receive a medication that essentially makes their CFTR protein functional; or, a child with a rare glycogen storage disorder could be cured with a liver transplant. Ongoing gene therapy studies have led to successful treatment of certain patients with disorders such as X-linked chronic granulomatous disease, sickle cell disease, and spinal muscular atrophy. Defer such treatment to the appropriate subspecialist.

Indications for Consultation

- **Genetics and genetic counseling:** Suspected or diagnosed genetic disorder; prior to, during, and after next-generation testing; for family counseling
- **Organ-specific subspecialist:** Organ-specific disorder, when considering specific next-generation panel sequencing
- **Nutrition:** Inborn errors of metabolism
- **Palliative and supportive care:** To establish patient and family goals of care and facilitate discussions of end-of-life care

Pearls and Pitfalls

- Testing costs and insurance coverage are variable across institutions and health management plans. Determine whether the patient's insurance will cover these costs.
- Do not perform whole-exome sequencing or WGS without input from a genetics specialist.
- An initial negative genetic test result does not rule out a genetic disorder. Review of sequencing results at a later time can yield new diagnostic considerations, particularly as VUS become reclassified.
- Not every variant is pathologic, and VUS are the rule and not the exception.

Online Resources

Centers for Disease Control and Prevention and Surgeon General's Family Health History: https://cdc.gov/genomics/famhistory/

Genetic Testing Registry: https://ncbi.nlm.nih.gov/gtr

National Organization for Rare Disorders: https://rarediseases.org

Online Mendelian Inheritance in Man: https://ncbi.nlm.nih.gov/omim

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CHAPTER 43

Inborn Errors of Metabolism

Introduction

Inborn errors of metabolism (IEMs) encompass deficiencies of enzymes or cofactors that normally aid in the breakdown of carbohydrates, proteins, fats, and other molecules. These defects can cause a buildup of potentially toxic metabolites and a defect in energy production, most commonly leading to hypoglycemia, hyperammonemia, and/or anion gap metabolic acidosis. State newborn screening programs aid in the early diagnosis and treatment of many, but not all, of these illnesses. A patient with an IEM is at highest risk for morbidity or mortality when caloric intake (especially glucose) is poor or when there is an intercurrent illness. They are then dependent on catabolism of stored sugar (glycogen), protein, or fat for energy. A patient with an IEM may be admitted preventively, at the first signs of any illness or prior to a surgical procedure to avoid a metabolic decompensation.

Many IEMs can be identified by the newborn screen. However, there is much variability among the states, so a negative screen does not rule out an IEM.

Urea Cycle Defects

The urea cycle metabolizes ammonia from protein breakdown into urea, which is excreted in the urine. Urea cycle defects (UCDs) are caused by an enzyme deficiency in the pathway, leading to hyperammonemia, which presents with vomiting, lethargy or somnolence, chronic liver disease, and neurodevelopmental delay. Triggers for hyperammonemic crises include acute illnesses, physiologic changes such as puberty, excessive protein intake, and decreased caloric intake.

Fatty Acid Oxidation Disorders

Fatty acids are shuttled to the inner mitochondria by a molecule called carnitine, where they are metabolized when needed for energy into acetyl coenzyme A and then ketone bodies. Different enzymes are responsible for breaking down fatty acids at different stages of the process. An enzyme deficiency in this β-oxidation process or in the carnitine transportation process leads to hypoketotic hypoglycemia in a fasted or catabolic state.

Amino Acidemias and Organic Acidemias

Amino acidemias are caused by a proximal defect in an amino acid metabolic pathway (eg, maple syrup urine disease). Organic acidemias are caused by

more distal defects in metabolic pathways of many compounds. These disorders include methylmalonic acidemia, propionic acidemia, and isovaleric acidemia. Along with specific enzymes, some organic acid breakdown pathways require vitamin cofactors, such as biotin and vitamin B_{12}. Several organic acidemias may cause hyperammonemia when a patient is acutely ill.

Clinical Presentation

History

If a patient with an established diagnosis of an IEM is acutely ill, they will often be referred to the hospital by a metabolic geneticist or primary care pediatrician. The patient may present with normal examination findings or appear ill, with possible neurologic symptoms such as seizures, decreased alertness, or irritability. Ask about prior hospitalizations, and obtain a detailed diet history, including prescribed formulas, supplements, and medications. Ask whether the family has a "sick plan," which may include a "sick formula" with more calories than the normal day formula recipe, as well as increased doses of current home medications (eg, carnitine in fatty acid oxidation [FAO] disorders). Determine how the diagnosis was assigned and whether appropriate follow-up has been conducted with a metabolic geneticist and a metabolic nutritionist.

A patient with an undiagnosed IEM may present with unexplained poor feeding, failure to thrive, or persistent vomiting, associated with a rapid onset of lethargy or coma. There may be a family history of unexplained infant death, which is highly suspicious for an FAO disorder. Storage diseases can present at any age, often with multisystem involvement, including hypotonia, cardiomyopathy, seizures, and failure to thrive with or without developmental delay. Other possible features are coarse facies and organomegaly.

Physical Examination

The priority is evaluation of the cardiorespiratory, hydration, glycemic, and mental status. The patient may be acutely hypotonic, lethargic, or irritable from hyperammonemia or hypoglycemia. With a UCD, hyperammonemia can stimulate the respiratory center and cause central hyperventilation. The neurologic examination findings in an older child with acute hyperammonemia may be significant for somnolence, excessive sleepiness, word-finding difficulties, or combativeness.

Aside from possible failure to thrive or hypotonia, a patient with an undiagnosed IEM may appear normal until stressed by an acute illness. Some patients with storage disease present with abnormal neurologic findings of strabismus or irritability. Plot the growth measurements to assess the patient

for chronic malnutrition. Listen for murmurs or gallops suggestive of cardiomyopathy and assess the patient for hepatosplenomegaly. Examine the skin for pallor or bruising as possible signs of pancytopenia.

Laboratory Workup

For a patient with a known diagnosis of an IEM, perform routine chemistry tests and a venous blood gas analysis to assess for hypoglycemia and metabolic acidosis, respectively. Beyond this, individualize the laboratory evaluation to the type of disorder or the diagnosis and clinical scenario. See Table 43–1 for the approach in a patient with a suspected but not previously diagnosed IEM. Table 43–2 lists the common laboratory abnormalities in various types of IEMs.

For a patient with a suspected but undiagnosed IEM, the *critical* laboratory tests to perform before introducing dextrose-containing fluids are a complete metabolic panel, complete blood cell count, venous blood gas analysis, and ammonia level, as well as a urinalysis for ketones. There are approaches for a comprehensive evaluation, but this can be streamlined depending on the initial abnormality or presenting symptom (Tables 43–1 and 43–2).

Table 43–1. Initial Laboratory Evaluations When an Inborn Error of Metabolism Is Suspected

Clinical Scenario/ Indication	Initial Laboratory Evaluations
Comprehensive evaluation	Complete blood cell count with differential, CMP, creatine kinase, venous blood gas Ammonia, lactate, creatine kinase, amino acid levels Free and total carnitine, acylcarnitine profile If there are neurologic symptoms: homocysteine level Urine: urinalysis, reducing substances, organic acids test, orotic acid
Anion gap metabolic acidosis	Serum: lactate to pyruvate ratio Amino acid levels, acylcarnitine profile, total and free carnitine levels Urine: urinalysis (ketones), organic acids test
Chronic metabolic encephalopathy	Serum: lactate to pyruvate ratio CMP, ammonia, carnitine, and amino acid levels; acylcarnitine profile Urine: urinalysis, reducing substances, organic acids test
Hyperammonemia: neonate	Amino acid levels Urine: organic acids test, urine orotic acid
Hyperammonemia: infant/child	Amino acid levels, acylcarnitine profile, total and free carnitine levels Urine: organic acids test, urine orotic acid
Hypoglycemia	Acylcarnitine profile, total and free carnitine levels, plasma amino acids Urine: urinalysis (ketones), organic acids test

Abbreviation: CMP, comprehensive metabolic panel.

Data from Burton BK. Inborn errors of metabolism in infancy: a guide to diagnosis. *Pediatrics.* 1998;102(6):e69.

Table 43–2. Inborn Errors of Metabolism Laboratory Findings

Laboratory Finding	Urea Cycle Defects	FAO Disorders	Organic Acidemias
Acidosis	–	+/–	+
Cytopenias	–	–	+/–
↑ Creatine kinase level[a]	–	+	–
Hyperammonemia	+	–	+/–
Hypoglycemia[a]	–	+	+/–
Ketonuria[a]	–	–	+
Lactic acidosis	–	+/–	+/–
Transaminitis	+/–	+	–

Abbreviation: FAO, fatty acid oxidation.
+ indicates a positive finding; –, a negative finding.
[a]Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis.* 2012;7:32.

In addition, obtain a total plasma homocysteine evaluation and a lactate level (suggestive of a mitochondrial disorder) in any patient who presents with abnormal neurologic examination findings.

Differential Diagnosis

In a neonate, a new-onset IEM can be confused with sepsis, heart disease (congestive heart failure, cardiomyopathy), chromosomal disorders, or liver disease. In an older infant or child, the differential diagnosis also includes child abuse, pyloric stenosis, allergy to milk protein, acute psychosis, porphyria, cerebral palsy, and developmental delay.

Treatment

If an IEM is being considered, *immediately stop all feedings,* introduce intravenous (IV) fluids that contain 10% dextrose (D10) and appropriate electrolyte levels at a high glucose infusion rate (GIR), and perform the critical laboratory tests. Fluids containing D10 provide a protein-free, fat-free caloric source and stimulate insulin secretion, which switches the metabolism from catabolic to anabolic state. For a patient younger than 12 years who weighs less than 50 kg, start with a GIR of 10. For an older or larger patient, start with 10% dextrose administered at 1.5 times the maintenance rate.

$$\text{GIR (mg/kg/min)} = \frac{\text{IV fluid rate (mL/h)} \times \text{\% dextrose}}{6 \times \text{body weight (kg)}}$$

Once the laboratory values have normalized and the patient is tolerating a regular diet, deescalate care by tapering the GIR over 12 to 24 hours or according to the recommendations of the metabolic geneticist.

In addition, individual IEMs require different combinations and doses of medications during a metabolic crisis. Review dosing with the metabolic geneticist before administration, because these treatments can be highly toxic.

Disposition

- **Intensive care unit transfer:** Severe hypoglycemia (< 50 mg/dL [< 2.78 mmol/L]), hyperammonemia (> 200 mcg/dL [> 142.8 µmol/L]), severe acidosis (pH level < 7.2)
- **Discharge criteria:** Able to maintain homeostasis without IV fluid administration

Follow-up

- **Primary care:** 1 to 2 days
- **Metabolic geneticist:** 1 to 2 weeks, but encourage phone follow-up sooner if the patient has not recovered fully

Pearls and Pitfalls

- Ketonuria may clear quickly once the patient receives IV fluids with dextrose.
- To prevent a falsely increased ammonia level, obtain a free-flowing sample that is immediately put onto ice and taken to the laboratory.
- If the serum ammonia level is over 500 mcg/dL (> 357 µmol/L), urgently consult a nephrologist because dialysis may be necessary. In this scenario, contact interventional radiology and/or surgery, as advanced intravenous access will be needed. This is typically done in the intensive care unit setting.
- When evaluating a patient for a new diagnosis of an IEM, always check that a newborn screening was performed and verify that the results were normal.
- Galactosemia testing (urine-reducing substances) will only yield a positive result if the patient has recently been receiving galactose in the diet.

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Hematology

Anemia

Introduction

Anemia is a hemoglobin concentration or red blood cell (RBC) mass below the normal range for a patient's age and sex. Red blood cell mass is maintained by a homeostatic balance between RBC production and RBC destruction. When that balance is upset by decreased RBC production, increased RBC destruction, or significant blood loss, the result is anemia. Mild to moderate anemia is typically managed in the outpatient setting, but severe or acute-onset anemia that overwhelms a patient's physiologic ability to compensate may require inpatient evaluation and/or treatment. Anemia can also occur as a comorbidity in a child admitted to the hospital for some other medical condition.

Clinical Presentation

History

Symptoms of anemia include pallor, fatigue, weakness, decreased energy, headache, and shortness of breath. Palpitations and a sensation of lightheadedness may also occur. A very young or preterm infant may present with feeding difficulty, lethargy, or apnea.

Obtain a thorough history, looking for indications of decreased RBC production and increased RBC loss or destruction. Ask about dietary intake including type and quantity of milk; foods rich in iron, vitamin B_{12}, and folate; and vitamins or supplements. Inquire about pica, as it can be both a symptom and a cause of anemia. Check for recent or chronic illnesses and medication exposures that could affect RBC homeostasis. Note whether there has been bleeding from the gums or nose, note any blood found in the urine or stool, and take a careful menstrual history, if relevant. Note the patient's ethnic or geographic background and any family history of anemia, and review the newborn screening results, if available and relevant. Ask about dark urine or a personal or family history of neonatal jaundice, splenectomy, or cholecystectomy, which may suggest an underlying hemolytic anemia.

Physical Examination

The first priority is to assess the patient for hemodynamic instability, which requires immediate intervention. Signs include pallor, hypotension, persistent tachycardia, orthostatic changes, widened pulse pressure, and bounding pulses. A patient with severe uncompensated anemia may also present with hypoxia, signs of congestive heart failure, syncope, and altered mental status.

A systolic ejection murmur and increased prominence of the cardiac apical impulse may also be noted.

A common physical examination finding is pallor, which is best seen in the nail beds, palmar creases, conjunctivae, and mucosal surfaces. Jaundice, frontal bossing, hepatomegaly, and splenomegaly are features of a hemolytic process. Evidence of inflammation or systemic disease may be observed in anemia related to chronic disease.

Laboratory Workup

Obtain a complete blood cell count (CBC), reticulocyte count, and peripheral blood smear. If the patient has a clear source of blood loss, these values will serve as baseline measures. In cases of acute blood loss, the hemoglobin concentration and the reticulocyte count may initially be normal. The hemoglobin will drop as plasma volume is reaccumulated, and reticulocytes will rise as the bone marrow responds to the developing anemia.

If the cause of anemia is unknown, choose additional studies based on the results of the initial tests. It is important to weigh the value of each diagnostic test against the blood volume needed so as not to exacerbate the patient's anemia. If possible, obtain all blood samples prior to administering any transfusions so the patient's blood, and not the donor's, is evaluated.

Reticulocyte Count

Because the reticulocyte count represents a percentage of the total RBCs, it is important to correct for the degree of anemia by calculating the reticulocyte index:

$$\text{Reticulocyte index} = (\text{Measured reticulocyte count}) \times (\text{Measured hematocrit level} / \text{Normal hematocrit level for age and sex})$$

The reticulocyte index can indicate the underlying cause of a patient's anemia. Absence of an elevation of the reticulocyte index is consistent with decreased RBC production in the bone marrow. A high reticulocyte index shows that RBC production is intact and the bone marrow is responding appropriately to anemia caused by RBC loss or destruction.

Further Testing for Low-Reticulocyte Anemias

Assess the RBC morphology on the peripheral blood smear and CBC. Microcytosis most often suggests iron deficiency or anemia of chronic disease. Check the C-reactive protein level, iron level and total iron binding capacity, ferritin level, and liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels). Note that ferritin is also an acute-phase reactant and may demonstrate normal

levels in a patient with a chronic disease and an iron deficiency. Macrocytosis most often suggests vitamin B_{12} or folate deficiency or disorders of their metabolism, so obtain levels as appropriate. If the patient also has leukopenia and/or thrombocytopenia, check for parvovirus exposure, and consult with a pediatric hematologist/oncologist. Consider other causes of marrow suppression (see Differential Diagnosis) as a possible cause of aplastic anemia.

Further Testing for High-Reticulocyte Anemias

Order direct and, for a neonate, indirect antiglobulin (Coombs) tests to evaluate for antibody-mediated hemolytic anemia. Be aware that certain conditions, such as neonatal ABO incompatibility, are associated with low RBC antigens and can result in a positive indirect antiglobulin test result. Supportive laboratory findings for a hemolytic process include elevated aspartate transaminase, indirect bilirubin, and lactate dehydrogenase levels. A decreased haptoglobin level also indicates hemolysis, but be aware that it may be low if the patient is younger than 6 months or has liver disease.

Assess the peripheral blood smear for abnormal RBC morphologies including sickle cells, spherocytes, spiculated cells, poikilocytes, elliptocytes, target cells, and Heinz bodies. Additionally, check the other cell lines to evaluate platelet morphology and leukocyte abnormalities, especially the presence of malignant-appearing cells. Order a hemoglobin electrophoresis (HbEP) test when there is no clear etiology for a hemolytic process, when the newborn screening results are unavailable or abnormal, or when the family history supports a hereditary hemoglobinopathy. However, the HbEP will miss α-thalassemia trait and may miss β-thalassemia trait in the setting of iron-deficiency anemia. Spherocytes on peripheral smear and elevated mean corpuscular hemoglobin concentration suggest hereditary spherocytosis. Order incubated osmotic fragility testing to confirm the diagnosis.

To evaluate the patient for chronic blood loss, order a stool guaiac test and perform a urinalysis to look for evidence of renal pathology. In addition to obvious blood loss (eg, excessive menstrual bleeding, coffee-ground emesis, recurrent epistaxis), consider other occult sources of blood loss, such as intra-abdominal and intramuscular bleeding. In very young infants, intracranial bleeds can cause anemia.

Differential Diagnosis

The differential diagnosis of anemia is broad, but it can be divided into conditions caused by decreased RBC production, RBC loss, and increased RBC destruction. The reticulocyte index can help distinguish among these categories, as above. Table 44–1 presents a differential diagnosis of anemia sorted into these categories.

Table 44–1. Diagnosis of Anemia

Diagnosis	Clinical Features
Decreased RBC Production	
Aplastic anemia	Anemia with neutropenia and/or thrombocytopenia ↓ Reticulocyte levels
Chronic inflammation	History of chronic disease ↑ Erythrocyte sedimentation rate, C-reactive protein level, ferritin level ↓ Serum iron level, TIBC
Chronic renal disease	Uremia ↓ Erythropoietin level
Folate deficiency	Goat milk diet Maternal folate deficiency in a breastfeeding infant
Iron deficiency	History of inadequate iron in diet or malabsorption History of bleeding ↓ MCV, MCHC, serum iron level, ferritin level, reticulocyte level ↓↑ RBC distribution width
Liver disease	Jaundice, hepatomegaly ↑ Transaminase and bilirubin values, ↓ albumin level
Red cell aplasia (eg, Diamond-Blackfan anemia)	First year after birth Severe presentation Persistence of fetal hemoglobin Macrocytosis
Transient erythroblastopenia of childhood	Age: 6 mo to 3 y Neutropenia, normal platelet levels, ↓ reticulocyte levels
Vitamin B_{12} deficiency	Vegan diet or breastfed infant of vegan mother History of terminal ilium resection Hypersegmented neutrophils, macrocytosis
Blood Loss	
Acute blood loss	Overt bleeding Guaiac (+) stool or gastric output May not have reticulocyte level for 1–2 days
Chronic blood loss	May be the presentation of von Willebrand disease in menstruating girls May have guaiac (+) stool ↑ or ↓ Reticulocyte levels May have ↓ serum iron level, TIBC
RBC Destruction	
Autoimmune hemolytic anemia	Acute, severe presentation (+) Direct Coombs test result ↑ Haptoglobin, LDH, unconjugated bilirubin Hemoglobinuria
Hereditary spherocytosis	Spherocytes on smear ↑ Haptoglobin, LDH, unconjugated bilirubin ↑ MCHC (+) Osmotic fragility test

Table 44–1. Diagnosis of Anemia, continued

Diagnosis	Clinical Features
Inherited hemolytic anemia	Jaundice, organomegaly ↑ Bilirubin, reticulocyte levels Smear: RBC morphology (sickle cells, spherocytes) May have abnormal hemoglobin electrophoresis
Microangiopathic hemolytic anemia	Associated with hemolytic uremic syndrome/thrombotic thrombocytopenic purpura Schistocytes on smear Hemoglobinuria
Thalassemia major	Patient often of Mediterranean or African descent Presents during infancy Splenomegaly Severe anemia with ↓ MCV

Abbreviations: LDH, lactate dehydrogenase; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; TIBC, total iron binding capacity.
+ indicates positive finding; ↑, elevated level; ↓, decreased level.

Treatment

The treatment of anemia depends on its etiology and chronicity. Patients can tolerate very significant anemia if it develops sufficiently slowly, so there is no absolute hemoglobin level at which transfusion is indicated for all patients. A hemodynamically stable patient with symptoms of anemia such as fatigue, light-headedness, or exercise intolerance can be managed conservatively without transfusion, but a transfusion will speed their clinical recovery. Discuss the risks and benefits of a transfusion, and engage in shared decision-making with the patient and family. For a hemodynamically unstable patient with acute blood loss, provide urgent volume expansion with packed RBCs until their condition improves. For a critically ill but hemodynamically stable patient, transfuse packed RBCs if the hemoglobin level is below 7 g/dL (70 g/L) or if there are increasing cardiorespiratory symptoms, regardless of the hemoglobin level. The time course for a transfusion depends on the clinical situation, but in general, provide packed RBCs over a 4-hour period to avoid circulatory overload.

The treatment of a hemolytic anemia depends on the etiology and severity and typically involves consultation with a hematologist. In general, a patient with an inherited hemolytic anemia needs careful monitoring over time and may require occasional transfusions. For life-threatening autoimmune hemolysis, urgently consult with a hematologist to determine if treatment with high-dose steroids, intravenous immunoglobulin, plasmapheresis, or exchange transfusion is indicated. Long-term management may include splenectomy or immunosuppressant medications.

Treat iron deficiency anemia with oral elemental iron, 3 to 6 mg/kg/d, as well as a diet rich in iron and vitamin C. Intravenous iron sucrose 5 to 7 mg/kg/dose (maximum dose, 100 mg) every 1 to 7 days is a useful alternative if the patient is having difficulty tolerating oral iron. The reticulocyte count should increase within 2 to 4 days and the hemoglobin level within 2 to 4 weeks. Manage anemia of chronic disease and anemia secondary to excessive bleeding by treating the underlying cause.

Treat postoperative anemia conservatively if the patient is hemodynamically stable. However, a transfusion of packed RBCs may be necessary if the patient is tachycardic, hypotensive, hypoxic, excessively fatigued, in significant respiratory distress, or experiencing ongoing blood loss. Additionally, a transfusion may be indicated to promote postoperative healing of grafts or other injuries that may require a higher hemoglobin level than what is needed for cardiovascular stability.

For a patient with leukopenia and/or thrombocytopenia in addition to anemia, or if there are unusual immature cells on peripheral smear, delay all but lifesaving treatment until after consultation with a hematologist/oncologist. These findings are very concerning for possible malignancy, and transfusion or treatment with steroids can complicate the further workup and worsen the prognosis.

Indications for Consultation

- **Hematology/oncology:** Diagnosis unclear, intravascular hemolysis, condition refractory to treatment, concern for bone marrow failure, bone marrow aspirate required, long-term management considerations, suspicion of malignancy

Disposition

- **Intensive care unit transfer:** Hemodynamic instability
- **Discharge criteria:** Hemoglobin level stable, without acute physiological manifestations of anemia or ongoing excessive bleeding

Follow-up

- **Primary care:** 1 to 2 weeks, depending on condition at discharge
- **Hematology:** 1 to 2 weeks, depending on diagnosis and condition at discharge

Pearls and Pitfalls

- If possible, perform blood studies prior to transfusion of blood products.
- Be cautious about the volume of blood withdrawn from an anemic child because iatrogenic blood loss may acutely worsen the patient's anemia and cause clinical decline.

- Occult sources of internal blood loss are the abdomen, head (neonate), and thigh and chest (trauma victim). Except for a neonate, it is uncommon for intracranial hemorrhage to cause anemia in the absence of neurologic findings at physical examination.
- Steroid treatment can change the appearance of the bone marrow and lymph node morphology, which may then alter the subsequent treatment and prognosis of certain malignancies. Therefore, if there is any possibility of a malignancy (eg, generalized lymphadenopathy, hepatosplenomegaly, other cell lines affected), consult with a hematologist before starting steroid therapy in an anemic patient.

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CHAPTER 45

Complications of Cancer Therapy

Introduction

The survival rate for children with cancer continues to improve but is still associated with significant toxicities and late effects. Chemotherapy, which targets rapidly dividing cells, leads to significant cytotoxic side effects. Although the effects of radiation therapy are more localized, there can be profound consequences, including nausea, vomiting, pain, and skin changes. Surgery can lead to issues with wound care, infection, and pain.

Clinical Presentation and Diagnosis

Many chemotherapeutic agents share a number of side effects (see Table 45–1).

Adrenal Insufficiency

Steroids are used in treating pediatric cancers such as acute lymphoblastic leukemia and certain lymphomas, as well as for managing local edema surrounding brain tumors. Depending on the duration of the steroid course, a patient may be at risk for adrenal insufficiency (see Chapter 24, Acute Adrenal Insufficiency).

Signs of adrenal suppression can be subtle and hard to differentiate from chemotherapy-related toxicities, including dizziness, weakness, poor appetite, muscle aches, and persistent nausea. More commonly, severe adrenal insufficiency presents with hypotension, shock, or vital sign instability. Laboratory abnormalities may include hyponatremia, hyperkalemia, and metabolic acidosis with a normal anion gap.

Cytokine Release Syndrome

T-cell–activating immunotherapies, such as chimeric antigen receptor (CAR) T-cell therapy, can cause cytokine release syndrome (CRS). Mild CRS may present with flulike symptoms, including fever, arthralgias, headache, nausea, vomiting, and rash. In a more severe case there may be high fever and hypotension, progressing to systemic inflammatory response syndrome, shock, disseminated intravascular coagulation, acute respiratory distress syndrome, and multiorgan system failure. Note that fever may precede the onset of CRS by 1–3 days. Common laboratory abnormalities include elevated creatine and liver transaminase levels, elevated C-reactive protein, cytopenias, and abnormal coagulation studies. More severe cases may present with laboratory findings that resemble macrophage activating syndrome and hemophagocytic lymphohistiocytosis, including elevated ferritin and triglycerides. Interleukin-6 is elevated in patients with CRS following CAR T-cell therapy.

Table 45–1. Side Effects of Chemotherapeutic Agents

Onset	Common	Occasional	Rare
Pegylated *Escherichia coli*–Asparaginase			
Within 1–2 d	Diarrhea Local allergic reaction	Anaphylaxis Rash	Hyperuricemia
Within 2–3 wk	↑ Ammonia level Coagulation abnormalities	Hyperglycemia Pancreatitis	Disseminated intravascular coagulation/hemorrhage Thromboses
Bleomycin			
Within 1–2 d	High fever	Rash	Anaphylaxis Hypotension
Within 2–3 wk	Skin hyperpigmentation	None	Alopecia Onycholysis
About 3 mo	Raynaud phenomenon	Interstitial pneumonitis Pulmonary fibrosis	None
Carboplatin			
Within 1–2 d	Nausea/vomiting	Anaphylaxis Hypersensitivity reaction	Metallic taste
Within 2–3 wk	Myelosuppression	Hepatotoxicity Nephrotoxicity	Mucositis
After 2–3 wk	None	Ototoxicity	Peripheral neuropathy
CAR T-Cell Therapy			
Within 1–14 d	Coagulopathy Fever Headaches Myalgias	Capillary leak Hypotension Neurotoxicity (aphasia) Pulmonary edema Renal dysfunction	Cerebral edema Hemophagocytic lymphohistiocytosis Seizures
Cisplatin			
Within 1–2 d	Nausea/vomiting	↓ Magnesium level Metallic taste	Anaphylaxis
Within 2–3 wk	↓ Magnesium level High-frequency hearing loss Nephrotoxicity	↓ Calcium, potassium, sodium levels Peripheral neuropathy	Hepatotoxicity Seizures Vestibular dysfunction
Corticosteroids			
Within 1–2 d	Hyperphagia Insomnia	Gastritis	Hyperuricemia
Within 2–3 wk	Immunosuppression Personality changes Pituitary-adrenal axis suppression	Edema Hyperglycemia Hypertension Infections Poor wound healing	↑ Intraocular pressure Pancreatitis Psychosis

Table 45–1. Side Effects of Chemotherapeutic Agents, continued

Onset	Common	Occasional	Rare
Cytarabine (Cytosine Arabinoside)			
Within 1–2 d	Conjunctivitis Nausea/vomiting	Fever Flulike symptoms Rash	Acral erythema Anaphylaxis Cerebral/cerebellar dysfunction
Within 2–3 wk	Alopecia Myelosuppression Stomatitis	↓ Calcium, potassium, uric acid levels Diarrhea Pulmonary capillary leak	Hepatotoxicity Sinusoidal obstruction syndrome (venoocclusive disease)
Cyclophosphamide			
Within 1–2 d	Nausea/vomiting	Diarrhea	Anaphylaxis Transient blurred vision SIADH
Within 2–3 wk	Alopecia Myelosuppression	Hemorrhagic cystitis	Cardiac toxicity
Dasatinib/Imatinib			
During use	Diarrhea Nausea	Abdominal pain Chest pain Pericardial effusion Mucositis Myalgia	Severe tumor lysis Posterior reversible encephalopathy syndrome Cardiac dysfunction Gastrointestinal ulceration/stricture
Dinutuximab (Immunotherapy/Antibody Therapy)			
During infusion	Hives Pain (somatic and neuropathic) Cough Rash	Allergic reaction Dyspnea Blood pressure instability Numbness	Anaphylaxis Anemia Visual changes
Doxorubicin/Daunorubicin			
Within 1–2 d	Nausea/vomiting Pink/red body fluid discoloration	Hyperuricemia	Diarrhea
Within 2–3 wk	Alopecia Myelosuppression	Myocarditis-pericarditis syndrome Mucositis Radiation recall reactions	None
After 2–3 wk	None	None	Cardiomyopathy
Etoposide (VP-16)			
Within 1–2 d	Nausea/vomiting	Urticaria	Anaphylaxis Hypotension during infusion
Within 2–3 wk	Alopecia Myelosuppression	Diarrhea	Mucositis Peripheral neuropathy Stevens-Johnson syndrome

Continued

Table 45–1. Side Effects of Chemotherapeutic Agents, continued

Onset	Common	Occasional	Rare
Ifosfamide			
Within 1–2 d	Nausea/vomiting	CNS toxicity	↓ Potassium level Encephalopathy
Within 2–3 wk	Myelosuppression	Cardiac toxicity Hemorrhagic cystitis	Hepatotoxicity
After 2–3 wk	None	None	Fanconi-like syndrome Renal failure
Irinotecan			
Within 1–2 d	Cholinergic symptoms (profuse diarrhea) Nausea/vomiting	Headache	Anaphylaxis Dyspnea
Within 2–3 wk	Hepatotoxicity Myelosuppression		Colitis Renal failure
Isotretinoin			
During use	Dry eyes, mouth, skin Cheilosis Headache Blisters Hair loss ↑ Sensitivity to the sun	Blurred vision Tinnitus Hepatitis Seizure Mental status changes Anaphylaxis	None
Methotrexate			
Within 1–2 d	↑ Transaminase levels	Diarrhea Nausea/vomiting	Acral erythema Stevens-Johnson syndrome Toxic epidermal necrolysis
Within 2–3 wk		Mucositis Myelosuppression	CNS toxicity Renal toxicity
Mercaptopurine (6-MP)			
Within 1–2 d		Diarrhea Nausea/vomiting	Hyperuricemia Urticaria
Within 2–3 wk	Myelosuppression	Hepatotoxicity Mouth sores	Pancreatitis
Topotecan			
Within 1–2 d	Nausea/vomiting	Hypotension Rash	Anaphylaxis Rigors
Within 2–3 wk	Myelosuppression	Hepatotoxicity Mucositis	Paresthesia
Vinblastine			
Within 1–2 d	None	None	Jaw pain Seizure
Within 2–3 wk	Alopecia Myelosuppression	Constipation	Hemorrhagic enterocolitis Peripheral neuropathy Ototoxicity/vestibular dysfunction

Table 45–1. Side Effects of Chemotherapeutic Agents, continued

Onset	Common	Occasional	Rare
Vincristine			
Within 1–2 d	Abdominal pain Extremity pain	Headache Jaw pain	Bronchospasm Fever
Within 2–3 wk	Alopecia Constipation	Ptosis Vocal cord paralysis	Ptosis/diplopia Seizures SIADH
After 2–3 wk	Loss of deep tendon reflexes	Peripheral paresthesia	Autonomic neuropathy Sinusoidal obstruction syndrome

Abbreviations: CAR, chimeric antigen receptor; CNS, central nervous system; SIADH, syndrome of inappropriate antidiuretic hormone hypersecretion.
↑ indicates elevated level; ↓, decreased level.

Extravasation

Some chemotherapeutic agents may cause damage if they extravasate into surrounding tissue. Initially, local reactions include erythema and pain, but they may progress over days to weeks to blistering, ulcerations, and necrosis. Severe pain and loss of function may result if the necrosis extends to the nerves, ligaments, tendons, and bones.

Fever and Myelosuppression

Bone marrow suppression leads to anemia, thrombocytopenia, and leukopenia. Because granulocytes have a short life span and are the first line of defense against bacterial infection, oncology patients are at risk for neutropenia and subsequent infections. A patient with fever and neutropenia (absolute neutrophil count $< 500/\ mm^3$ [$< 0.5 \times 10^9$/L] or $< 1000/\ mm^3$ [$< 1.0 \times 10^9$/L] and expected to fall) requires immediate attention. Fever is defined differently at many centers, but commonly it is a temperature higher than 38.3 °C (101 °F) or several low-grade fever temperatures (37.8–38.3 °C [100–101 °F]) in a 24-hour period. However, a patient receiving steroids might not mount a febrile response. It is also critical to assess what type of indwelling catheter the child has (none, peripheral intravenous [IV] catheter, peripherally inserted central catheter, central venous catheter [CVC], tunneled or nontunneled CVC), because these carry differing risks of infection and the antibiotic coverage may differ.

Determine the date of the most recent chemotherapy administration to predict the expected direction of the white blood cell (WBC) trend. Most agents cause suppression 7 to 10 days after infusion, although platinum agents (carboplatin, cisplatin) can cause a delayed WBC suppression at 10 to 14 days. Also note the specific agents and doses administered, recent

blood transfusions (a transfusion reaction can cause fever), and a history of other infections, which may help guide antibiotic choices. Perform a thorough physical examination, with focus on the oropharynx and perianal region (looking for mucositis and perianal abscesses) and central venous line insertion sites, to assess for erythema, tenderness, or discharge. The patient may not be able to mount a typical inflammatory response if the WBC count is low.

A neutropenic patient is also at risk for neutropenic colitis (typhlitis), a potentially fatal complication. If suspected, perform a thorough abdominal examination, order imaging to assess for free air (perforation), consult with a surgeon, and initiate antibiotic therapy. Also, except in an emergency, do not permit rectal interventions (taking the patient's temperature or giving medications rectally) in a patient with neutropenia.

Hemorrhagic Cystitis

A patient receiving cyclophosphamide or ifosfamide may present with hematuria secondary to bladder wall irritation. In a patient undergoing heavy immunosuppression, such as those who have received a stem cell transplant, BK virus or adenovirus can also be etiologies.

Mucositis

Because chemotherapy affects any rapidly dividing cell, the gastrointestinal mucous membranes are at high risk of becoming inflamed and ulcerated. This can occur anywhere from the mouth to the anus. Signs and symptoms include exquisite pain, drooling, dysphagia, chest pain, abdominal pain, diarrhea, melena, or hematochezia. Mucositis can interfere with adequate oral hydration and, because of denuded mucosal barriers, also creates a portal of entry for infectious agents. A patient who has received high-dose cytosine arabinoside is at particular risk for a mucositis-related infection, including *Streptococcus mitis*, which can cause life-threatening sepsis.

Nausea and Vomiting

Nausea and vomiting can be caused by chemotherapy and radiation therapy or can occur postoperatively. Chemotherapy-induced nausea and vomiting (CINV) is either acute, occurring within the first 24 hours after receiving chemotherapy, or delayed, occurring more than 24 hours after chemotherapy administration and persisting for 1 week or longer. Breakthrough CINV is 3 or more episodes of retching or emesis despite proper prophylaxis. Finally, pediatric patients are uniquely at risk for anticipatory nausea/vomiting, a conditioned response to anxiety and treatment-related factors (eg, hospital,

clinic). The consequences of CINV include dehydration, electrolyte imbalance, anorexia, weight loss, and increased susceptibility to infections.

Skin Manifestations

Both radiation therapy and chemotherapy, such as methotrexate administration, can cause skin changes, such as acrodermatitis in a "stocking-glove" distribution. Erythema, swelling, and edema at the IV line site can be signs of infection in a neutropenic patient. Skin findings that are especially worrisome include blackened, purpuric spots or ulcerated/crusted lesions that could be signs of disseminated mold or fungal infection. Radiation therapy can induce skin breakdown and maceration, which can also be a significant nidus for infection. Carefully examine crevices and nonobvious skin folds in or near the radiation field. Chronic, diffuse hyperpigmentation may result from radiation therapy.

Tumor Lysis Syndrome

Tumor lysis refers to metabolic derangements caused by the rapid breakdown of tumor cells with subsequent release of intracellular contents, most often occurring in a patient with leukemia or lymphoma (particularly Burkett). Tumor lysis syndrome may occur prior to treatment in a patient with a very high WBC count at presentation or in those with rapidly growing tumors. Typically, however, it begins 12 to 72 hours after the induction of chemotherapy.

Metabolic derangements include hyperuricemia, hyperkalemia, hyperphosphatemia, and elevated creatinine. Because phosphorus precipitates with calcium, the patient can also develop hypocalcemia. Uric acid crystals and calcium phosphorus precipitates can obstruct the renal tubules, producing oliguria, acute kidney injury, and, sometimes, renal failure. Other clinical manifestations include nausea/vomiting, seizures, muscle cramping, tetany, and arrhythmias.

Treatment

Adrenal Insufficiency

Immediately initiate aggressive fluid and steroid replacement (see Chapter 24, Acute Adrenal Insufficiency). If the patient is hypotensive, administer 20 mL/kg 5% dextrose 0.9% normal saline (NS) boluses over 5 to 15 minutes until the blood pressure normalizes. Simultaneously, administer a stress dose of IV or intramuscular (IM) hydrocortisone (0 to 3 years of age, 25 mg; ≥ 3 to 12 years of age, 50 mg; ≥ 12 years of age, 100 mg), followed by 25 mg/m^2 or 1 mg/kg every 6 hours. Treat hypoglycemia (< 60 mg/dL [< 3.33 mmol/L]) with 2 to 4 mL/kg of 10% dextrose and recheck in 15 minutes. Also treat documented

hyperkalemia (see Chapter 89, Fluids and Electrolytes). Consult endocrinology for recommendations on ongoing steroid treatment and tapers.

Cytokine Release Syndrome

Consult oncology for any case of suspected CRS. Do not give steroids without oncology involvement for a patient who has received CAR T-cell therapy. Treat low-grade CRS with antipyretics and IV fluids. Because fever precedes the onset of CRS, closely monitor the patient for progression of the disease, which may require transfer to the intensive care unit.

Extravasation

If extravasation is suspected, immediately stop the infusion and institute measures to remove as much of the extravasated drug as possible. Apply warm or cold compresses, depending on the agent (Table 45–2). There are also specific antidotes for some medications.

Fever and Myelosuppression

If a neutropenic patient is febrile, obtain a complete blood cell count with differential and blood cultures. Some centers will require culture of all lumens of a central line, as well as peripheral sites. If a child is at risk for urinary tract infections (UTIs) (ie, prior history of UTI, presence of nephrostomy tubes or Foley catheter, < 2 years of age), perform a urinalysis and urine culture. Obtain stool cultures and order *Clostridioides difficile* toxin testing if abdominal symptoms or significant diarrhea are present. Culture any suspicious

Table 45–2. Treatment for Specific Agent Extravasation

Agent	Local Care	Antidote
Actinomycin D	Cold compress	Dimethyl sulfoxide[a]
Cisplatin	Cold compress	Sodium thiosulfate[b]
Daunorubicin	Cold compress	Dexrazoxane[c]
Doxorubicin	Cold compress	Dexrazoxane[c]
Etoposide	Warm compress	Hyaluronidase[d]
Idarubicin	Cold compress	Dexrazoxane[c]
Mechlorethamine	None	Sodium thiosulfate[b]
Mitomycin	None or cold compress	Dimethyl sulfoxide[a]
Paclitaxel	Cold compress	Hyaluronidase[d]
Vinblastine	Warm compress	Hyaluronidase[d]
Vincristine	Warm compress	Hyaluronidase[d]

[a] Dimethyl sulfoxide: Apply 4 drops/10 cm^2 of skin surface area topically to twice the area of the site 3–4 times a day for 7–14 days.
[b] Sodium thiosulfate: Administer 2 mL for each 100 mg of cisplatin extravasation or 2 mL for each 1 mg of mechlorethamine extravasation.
[c] Dexrazoxane: Administer 1,000 mg/m^2 per dose on days 1 and 2 and 500 mg/m^2 per dose on day 3, and administer each dose 24 hours apart.
[d] Hyaluronidase (150 U/mL): Administer 5 injections of 0.2 mL each, infiltrated around the extravasation.
↑ indicates increased level; ↓, decreased level.

lesions on the skin or near surgical or central line sites. Obtain a chest radiograph if there are respiratory symptoms.

Treat with broad-spectrum antibiotics that cover both gram-positive and gram-negative organisms (see Chapter 66, Sepsis), including *Pseudomonas aeruginosa*. Consult with the oncologist for the preferred regimen, as there are often center-specific guidelines. First-line treatment includes any of the following monotherapies:

- IV piperacillin/tazobactam (< 2 months of age, 480 mg piperacillin/kg/d, divided into doses administered every 6 hours; ≥ 2 to 9 months of age, 248 mg piperacillin/kg/d, divided into doses administered every 8 hours; ≥ 9 months of age, 300 mg piperacillin/kg/d, divided into doses administered every 8 hours; maximum, 16 g piperacillin/d)
- IV cefepime (150 mg/kg/d, divided into doses administered every 8 hours; maximum, 2 g/dose)
- IV meropenem (60 mg/kg/d, divided into doses administered every 8 hours; maximum, 1 g/dose)
- IV imipenem/cilastatin (60–100 mg/kg/d, divided into doses administered every 6 hours; maximum, 4 g/d)

Add a secondary agent, depending on the probable source of infection and local antibiograms. For example, add vancomycin if a central line infection with methicillin-resistant *Staphylococcus aureus* is suspected. Also expand coverage if the likelihood of other resistant organisms is high or if the patient appears septic or is clinically worsening. Add fungal coverage if the fever persists after 4 to 7 days of broad-spectrum antibacterial delivery without an identified source. If there are any respiratory symptoms, including coryza or cough, send a respiratory pathogen panel.

Transfusion Guidelines

Consult with an oncologist, because transfusion guidelines vary among treatment centers. Typically, packed red blood cell (RBC) transfusions are indicated if the patient is symptomatic from anemia or if the hemoglobin level is less than 7 to 8 g/dL (< 70–80 g/L). Prior to procedures and radiation therapy administration, some centers aim for a hemoglobin level closer to 9 to 10 g/dL (90–100 g/L). Ensure that all blood is irradiated, to prevent transfusion-associated graft-versus-host disease, and leukoreduced, to prevent transmission of cytomegalovirus, especially before and after a patient receives a bone marrow transplant.

Guidelines for platelet transfusions are also center specific. Generally, a transfusion is indicated if the platelet count falls below 10,000/ mm^3 (10×10^9/L) or there is active bleeding. However, maintain a higher count

(20,000–30,000/ mm^3 [20–30 $\times$ 10^9/L]) for a patient with residual brain tumor, unpredictable behavior/risk of falls, or undergoing bone marrow transplantation. If a patient will shortly be undergoing a procedure, is at risk for intracranial hemorrhage, or is taking concomitant anticoagulation therapy for a thrombosis, many centers will maintain the platelet count above 50,000/ mm^3 ($>$ 50 $\times$ 10^9/L).

Hemorrhagic Cystitis

Treatment is with vigorous hydration (per the specific chemotherapy protocol), correction of hematologic abnormalities (packed RBC or platelet transfusions, if indicated), and, if severe, bladder irrigation after placement of a double-lumen Foley catheter by a urologist. It is also important to rule out viral infections that may cause hemorrhagic cystitis. Prevention involves vigorous hydration to maintain a urine specific gravity below 1.010 or a urinary output of 2 to 3 mL/kg/h and the administration of sodium 2-mercaptoethane sulfonate (mesna) with cyclophosphamide or ifosfamide.

Mucositis

Treat mucositis with sponge-tipped applicators soaked in 0.9% sodium chloride for debridement; oral nystatin swish and swallow (100,000 U/mL) 5 mL 4 times a day; and "magic mouthwash" (2% viscous lidocaine plus liquid diphenhydramine plus liquid aluminum hydroxide with magnesium hydroxide) every 4 to 6 hours. For anal involvement, prescribe stool softeners (docusate sodium, 50–150 mg/d) and "butt paste" (nystatin cream, zinc oxide, and liquid aluminum hydroxide with magnesium hydroxide) for analgesia. The pain associated with mucositis is significant and can often require IV opioid therapy, IV fluid administration, or parenteral nutrition while the patient is taking nothing by mouth. A patient receiving an intensive regimen for treating acute myeloid leukemia or a hematopoietic stem cell transplant usually needs prophylactic antibiotics to prevent potentially fatal infections, resulting from oral flora entering the bloodstream.

Nausea/Vomiting

Check if the patient already has a specific antiemetic regimen prescribed so that those medications can be instituted or augmented. For acute nausea/vomiting, use oral or IV ondansetron (0.15 mg/kg administered every 8 hours). Higher doses up to a maximum of 16 mg per dose can be administered once in a 24-hour period, not to exceed a maximum daily dose of 24 mg. Other 5-HT_3 receptor antagonists are also available, including granisetron and palonosetron (longer acting). Dexamethasone can be used as an adjunctive antiemetic, but check with the oncologist because it is contraindicated in many cancers or in a patient receiving CAR T-cell therapy.

The natural killer cell receptor antagonists aprepitant and olanzapine are newer antiemetics that are especially useful for delayed or breakthrough CINV. Other adjunctive medications used frequently, but without strong evidence for their role as an antiemetic, include scopolamine patches, oral or IV diphenhydramine (1 mg/kg administered every 6 hours; maximum, 50 mg per dose); oral, IV, or IM phenergan (0.25–1.00 mg/kg administered every 4–6 hours; maximum, 25 mg per dose); or oral or IV hydroxyzine (1 mg/kg administered every 6 hours; maximum, 50 mg per dose). If the patient has continued nausea/vomiting, the addition of oral or IV lorazepam (0.04 mg/kg administered every 6 hours; maximum, 2 mg per dose) or oral or IV diazepam (0.2 mg/kg administered every 6–8 hours; 0.6-mg/kg/d maximum) can be effective. Benzodiazepines are also the treatment of choice for the anticipatory type of nausea/vomiting. Guidelines for managing nausea and vomiting are available from the Children's Oncology Group (https://childrensoncologygroup.org/downloads/COG_SC_Guideline_Document.pdf) and the Pediatric Oncology Group of Ontario (https://www.pogo.ca/healthcare/practiceguidelines/chemotherapy-induced-nausea-and-vomiting-cinv).

Skin Manifestations

Aspirate or biopsy (as appropriate) any new circumscribed or focal skin lesion. Perform a Tzanck smear and obtain a polymerase chain reaction test of any vesicular lesion that is suspicious for herpes or varicella. Treat radiation-induced skin changes with a lanolin-based ointment. Urgent dermatologic consultation is indicated for blackened, purpuric spots or ulcerated/crusted lesions that could be signs of disseminated mold or fungal infection.

Tumor Lysis Syndrome

Obtain serum electrolyte, calcium, phosphorus, blood urea nitrogen, creatinine, and uric acid levels prior to beginning chemotherapy and then every 4 to 6 hours thereafter. Closely monitor the patient's urine output and specific gravity, maintaining a specific gravity below 1.010.

The type of IV fluid used varies among institutions. Prior to starting chemotherapy, some centers prefer to alkalinize the urine with 5% dextrose one-quarter NS with 50 to 100 mEq/L (50–100 mmol/L) sodium bicarbonate at a 2-times maintenance rate to maintain a pH level of 7.0 to 7.5. Alkalinization is often discontinued once chemotherapy is started to prevent precipitation of calcium phosphorus stones. Administer allopurinol (50 mg/m^2 every 6 hours; maximum, 600 mg/d) to decrease the production of uric acid. Add rasburicase (50–100 U/kg administered once, but contraindicated in a patient with glucose-6 phosphate dehydrogenase deficiency) if the uric acid or creatinine level

remains increased and/or is increasing rapidly despite allopurinol administration and appropriate hydration.

Treat hyperkalemia (see Chapter 89, Fluids and Electrolytes). For hyperphosphatemia, administer an oral phosphate binder (ie, sevelamer). Calcium replacement for asymptomatic hypocalcemia is not warranted.

Dialysis is indicated for the persistence of hyperkalemia or hyperphosphatemia despite conservative measures and for renal failure with resulting uremia.

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CHAPTER 46

Deep Venous Thrombosis

Introduction

Deep venous thrombosis (DVT) is rare in children, with about 60 cases per 10,000 hospital admissions. A patient with DVT may have one or more of Virchow's triad (ie, blood flow stasis, endothelial lining injury, hypercoagulability). Prompt diagnosis is critical because an undiagnosed and untreated DVT can lead to a fatal pulmonary embolism (PE) or cause serious long-term morbidity. The most important risk factors for a DVT are a central venous line, altered mobility (for > 48 hours), local (osteomyelitis, skin and soft-tissue infections) or systemic infection, and a family history of DVT. More than 90% of pediatric DVT have more than 1 risk factor, with venous central lines present in more than 50% of cases of pediatric DVT.

Deep venous thrombosis primarily affects the lower extremities and is subdivided into 2 groups: distal (calf vein) and proximal (thigh vein) thrombosis. Up to 90% of PEs originate from a dislodged thrombus from one of the proximal lower-extremity veins. Involvement of the upper extremities is much less common and is almost always associated with some combination of a central line, total parenteral nutrition, dialysis, a hypercoagulable state, or chemotherapy. Although a PE can be found in up to 60% of patients with DVTs, most PEs are clinically silent. Nonetheless, maintain a high clinical suspicion for PE, because the mortality rate from clinically apparent PEs approaches 30%.

Clinical Presentation

History

Ask about a personal or family history of the risk factors and predisposing conditions listed in Box 46–1. The patient may report some combination of leg pain and swelling, pitting edema, warmth and erythema, dilated superficial veins, and, on occasion, a palpable cord in the calf, which is the thrombosed vein. The pain may result in a limp or a limitation of activity, and it may be worse during activity or when the affected limb is dependent because of swelling.

The most common symptoms of PE are sudden onset of dyspnea and pleuritic chest pain. Less frequently, the patient may complain of fever, cough, and hemoptysis.

Box 46–1. Risk Factors for Deep Venous Thrombosis	
Acquired Conditions	
Diabetes mellitus	Obesity (body mass index > 95th percentile for age)
Family or personal history of DVT	Pregnancy
Hyperosmolality > 320 mmol/kg (> 320 serum mOsm/kg)	Prosthetic cardiac valves
Immobilization (postsurgery, posttrauma)	Serious infections (osteomyelitis, sepsis)
Indwelling venous catheter (central, peripherally inserted central catheters)	Sickle cell disease
Inflammatory diseases (systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis)	Smoking
Malignancy	Spinal cord injury
Medications (estrogen use in the past 2 mo)	Trauma: > 1 lower-extremity fracture or a complex pelvic fracture
Nephrotic syndrome	
Inherited Hypercoagulable Conditions	
Antiphospholipid antibody syndrome	Protein S and C deficiency
Antithrombin deficiency	Prothrombin gene mutation
Factor V Leiden mutation	

Abbreviation: DVT, deep venous thrombosis.

Physical Examination

Carefully inspect the extremity, looking for swelling, erythema, tenderness, and dilated superficial veins. Palpate for a cord, which represents subcutaneous venous clots. Measure the circumference of the midportion of the affected limb segment (usually 10 cm below the tibial plateau) and compare it to that of the unaffected side. A difference greater than 3 cm is concerning for a DVT. Attempt to elicit the Homan sign, which is popliteal calf pain that occurs with forceful and abrupt dorsiflexion of the ankle while the knee is held in the flexed position. However, these findings are neither sensitive nor specific for DVT. If a lower-extremity DVT is a possibility, determine the Wells score (Table 46–1) based on signs, symptoms, and risk factors. There is a high probability of a DVT with a score greater than or equal to 3; moderate probability with a score of 1 or 2; and a low probability with a score of 0 or less.

Complications

Pulmonary embolism is the major complication of DVT and presents with tachypnea, dyspnea, fever, tachycardia, and hemoptysis. Rales and/or an S3 or S4 gallop rhythm may be detected.

Table 46–1. The Wells Score	
Clinical Feature	**Score**
Entire leg swollen	1
Calf swelling > 3 cm compared to other calf (measured 10 cm below the tibial tuberosity)	1
Localized tenderness along the distribution of the deep venous system	1
Pitting edema, greater in the symptomatic leg	1
Collateral superficial veins, not varicose	1
Active cancer, treatment ongoing or within previous 6 months of palliative treatment	1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	1
Patient recently bedridden for more than 3 d or major surgery performed within 4 wk	1
Alternative diagnosis as likely as or likelier than DVT	Subtract 2 points

Abbreviation: DVT, deep venous thrombosis.

Laboratory Workup

If a DVT is suspected, obtain a complete blood cell count (CBC), prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen level, and quantitative D-dimer level. If an inherited hypercoagulable condition is a concern in a patient with either no evident risk factors or recurrent DVTs, consult with a hematologist to determine if further testing is indicated (antithrombin III, protein C deficiency, protein S deficiency, factor V Leiden mutation, antiphospholipid antibodies, lupus anticoagulant, homocysteine, α2-antitrypsin, and prothrombin 20210 mutation).

Radiology Examinations

The noninvasive test of choice is Doppler ultrasonography (US) (US with Doppler imaging and compression of the major veins) of the affected limb. It is highly sensitive (89%–96%) and specific (94%–99%) for lower-extremity symptomatic proximal DVTs. It is much less sensitive in the upper extremity but remains the initial study of choice. If the Doppler US is negative but the clinical suspicion of DVT remains high, perform computed tomographic (CT) angiography or magnetic resonance venography of the limb. If PE is suspected, immediately order CT angiography (if available) or a high-resolution spiral CT.

Differential Diagnosis

A clotting activation marker, such as quantitative D-dimer, has a high sensitivity and negative predictive value, but a low specificity. The combination of low pretest probability or clinical decision rule (Wells score) and

a negative D-dimer result has an extremely high negative predictive value for venous thromboembolism (about 99%). However, a positive D-dimer result does not confirm the diagnosis of DVT. False-positive levels occur with malignancies, trauma, recent surgery, infections, pregnancy, and acute bleeding.

The differential diagnosis of suspected DVT (Table 46–2) includes a variety of disorders that can present in a similar fashion. It is essential to assign the correct diagnosis because an untreated DVT, or unnecessary anticoagulation, may have serious sequelae.

Treatment

If DVT is suspected, consult a hematologist. If the Doppler US is not immediately available, give a dose of low–molecular weight heparin (LMWH), as described below.

The goals of treating DVT are to prevent local extension of the thrombus and embolization (usually PE), reduce the risk of recurrent thrombosis, and minimize long-term complications (chronic venous insufficiency, post-thrombotic syndrome, or chronic thromboembolic pulmonary hypertension). There is no consensus on DVT management for children, so the treatment of choice is individualized to the specific circumstances of the patient and the preferences of the consultants. Options include thrombolytic therapy for a massive PE or symptomatic DVT, administration of anticoagulation therapy for at least 3 months, placement of a vena cava filter to prevent PE, surgical

Table 46–2. Differential Diagnosis of Deep Venous Thrombosis[a]

Diagnosis	Clinical Features
Muscle strain/sprain	Bruising and/or hematoma History of trauma Localized tenderness
Cellulitis	Clear demarcation between involved/uninvolved areas Constitutional symptoms (fever, malaise) Local area of skin with redness/warmth
Baker cyst	Palpable fluid-filled mass behind the knee Prior history of knee swelling and/or pain
Lymphedema	Cutaneous and subcutaneous thickening Insidious onset
Venous insufficiency	Chronic skin changes with possible ulceration Muscle cramping, numbness, tingling, or itching Visible dilated veins
Superficial thrombophlebitis	Palpable superficial veins

[a] In each case, the Homan sign will be negative, except with a calf muscle strain.

thrombectomy, and supportive care, including compressive stockings, use of a venous compressing pump, and management of skin ulcers.

Treat a symptomatic DVT and a submassive PE (acute PE in a normotensive patient, with associated right ventricular dysfunction or myocardial necrosis) with anticoagulation alone, without thrombolysis, thrombectomy, inferior vena cava filter, or antithrombin replacement therapy. However, if the patient has a PE associated with hemodynamic compromise, treat with thrombolysis followed by anticoagulation.

Low–Molecular Weight Heparin

In contrast to unfractionated heparin (UFH), LMWH offers several advantages, including superior bioavailability with a longer half-life and dose-independent clearance, which results in a more predictable anticoagulation response. Low–molecular weight heparin also has high specific activity against factor Xa and less activity against thrombin.

Low–molecular weight heparin can be administered subcutaneously, with minimal laboratory monitoring and dose adjustment. Prior to the institution of LMWH therapy, obtain a CBC, PT, aPTT, and platelet count. Do not give the patient salicylates, and avoid intramuscular injections and arterial punctures while the patient is receiving LMWH. Withhold LMWH for 24 hours prior to a major surgery, and resume the therapeutic dose 48 to 72 hours afterward. For a minor procedure or a lumbar puncture, withhold 1 dose before the procedure and resume the therapeutic dose immediately afterward.

The dose for DVT treatment is as follows: younger than 2 months, 1.5 mg/kg delivered subcutaneously every 12 hours; 2 months or older, 1 mg/kg delivered subcutaneously every 12 hours. Monitor LMWH therapy by obtaining anti–factor Xa levels 4 hours after the dose. The goal is 0.5 to 1.0 U/mL 4 hours after the last subcutaneous injection. Once this is achieved, follow the anti–factor Xa level weekly. For a DVT, treat with LMWH for 3 weeks to 6 months, as per the hematologist's recommendation.

Unfractionated Heparin

Use UFH specifically in a neurosurgical patient and when there is a risk of bleeding and rapid reversal may be needed. Because UFH has a short half-life, excessive levels can usually be controlled by stopping the infusion. Treat a symptomatic overdose with protamine (1 mg for each 100 units of UFH).

The loading dose of UFH is 75 U/kg delivered intravenously (IV) over 10 minutes, followed immediately by an infusion of 28 U/kg/h if younger than 1 year or 20 U/kg/h if older than 1 year. Use the aPTT to closely monitor therapy, and always obtain the sample from a different limb than that used

for the infusion site. Alternatively, monitor anti–factor Xa levels, aiming for a therapeutic range of 0.3 to 0.7 U/mL (laboratory dependent).

Obtain the aPTT 4 hours after administration of the UFH loading dose. When the aPTT is in the target range of 2 to 3 times the mean control value, repeat a CBC with platelet count. If the platelet count is less than 100,000/ mm^3 (100×10^9/L), consider the discontinuation of heparin and institution of an alternative therapy. The risk of heparin-induced thrombocytopenia is greatest after 5 to 7 days of treatment, so recheck the CBC on day 3 of therapy.

The usual duration of UFH therapy for DVT is 5 to 7 days before changing to a long-term medication. Institute warfarin therapy on day 1 or 2 (see next section) to facilitate the transition to long-term oral treatment. If the patient has a PE, administer the heparin therapy for 7 to 14 days and start the warfarin on day 5.

Warfarin

Use warfarin (oral vitamin K antagonist) to transition from IV heparin or LMWH administration to oral treatment for outpatient management. It is significantly less costly than LMWH but requires more frequent monitoring. The loading and maintenance dose is 0.1 to 0.2 mg/kg (10-mg maximum), delivered as single daily oral doses over 3 to 5 days. Base subsequent doses on the international normalized ratio (INR) response, measured every 3 to 5 days. When 2 INRs obtained 24 hours apart are between 2 and 3, discontinue the heparin. Continue to measure the INR weekly until stable, as well as after any medication change. The diet also must be stable. Prior to any surgery, consult with a hematologist to determine appropriate warfarin management.

Deep Venous Thrombosis Prophylaxis

While there is little evidence supporting the use of DVT prophylaxis in pediatrics, consider it for a patient with identifiable risk factors for DVT (Box 46–1). One of the major risk factors is altered mobility, defined as a patient who requires complete bed rest or is unable to move an extremity freely. Although there are no consensus pediatric protocols, do not initiate thromboprophylaxis in a patient younger than 14 years, unless they are at significantly high risk (> 4 DVT risk factors, particularly for a trauma patient). Treat an adolescent older than 14 years according to risk level (Table 46–3). Mobilization, in the form of early ambulation in coordination with physical therapy, is preferred for all risk categories. This is in addition to mechanical prophylaxis (use of compression stockings and sequential compression devices [SCDs]) for a moderate-risk patient and medical prophylaxis for a high-risk patient. Mechanical methods decrease venous stasis, but the effectiveness of an SCD is related to duration of use, with a goal of 18 hours per day.

Table 46–3. Deep Venous Thrombosis Categorization and Prophylaxis According to Risk

Risk Level	Criteria	Intervention
Low risk	Altered mobility[a] < 48 h No DVT risk factors	Encourage early ambulation
Moderate risk	Altered mobility[a] < 48 h *plus* ≥ 1 DVT risk factors *or* Altered mobility[a] > 48 h *plus* 0–1 DVT risk factor	Encourage early ambulation Mechanical prophylaxis: SCD (preferred) or compression stockings Goal of 18 h/d use
High risk	Altered mobility[a] > 48 h *plus* ≥ 2 DVT risk factors	Encourage early ambulation Mechanical prophylaxis: SCD (preferred) or compression stockings Goal of 18 h/d use Consult with hematologist for medical prophylaxis

Abbreviations: DVT, deep venous thrombosis; SCD, sequential compression device.

[a] Altered mobility definition: Patient requires complete bed rest or is unable to move an extremity freely.

Consult with a pediatric hematologist to initiate prophylactic anticoagulation with LMWH in a high-risk patient. Use half the DVT treatment dose (< 2 months of age, 0.75 mg/kg administered subcutaneously every 12 hours; > 2 months of age, 0.5 mg/kg administered subcutaneously every 12 hours). For UFH, titrate the dose to an aPTT of 1.2 to 1.5 times the control. Absolute contraindications to medical DVT prophylaxis include a known bleeding disorder, high risk of hemorrhage or active hemorrhage, and a platelet count not sustained at more than 50,000/ mm^3 (50×10^9/L).

Indications for Consultation

- **Hematologist:** All patients
- **Vascular surgeon:** Extensive thrombosis above the knee or elbow and involvement of any vessels of the chest or abdomen; ischemic changes

Disposition

- **Intensive care unit transfer:** Pulmonary embolism
- **Discharge criteria:** Therapeutic range of INR or anti–factor Xa achieved, parent/patient education completed (for DVT, anticoagulants, PE, and diet if the patient is taking warfarin), and patient stable

Follow-up

- **Primary care:** 1 week
- **Hematologist (depending on the outpatient anticoagulant choice):** Within 3 days if taking warfarin or after 1 week if taking LMWH
- **Vascular surgeon:** If involved, per the surgeon's request

Pearls and Pitfalls

- A positive D-dimer result does not confirm the diagnosis of DVT.
- Tailor the treatment to the clinical picture, because there is no consensus on pediatric DVT management.
- Do not initiate thromboprophylaxis in a patient younger than 14 years, unless they are at significantly high risk (> 4 DVT risk factors).
- Ensure that your institution's pharmacy stocks anticoagulants approved for pediatric use or can readily obtain them when needed.

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CHAPTER 47

Neutropenia

Introduction

Neutropenia may be transient, chronic, isolated, or a feature of a systemic disorder. It is defined by an absolute neutrophil count (ANC) (white blood cells × percent [mature + immature neutrophils]) below the normal reference range for a patient's age. In general, mild neutropenia is an ANC between 1,000 and 1,500 cells/mcL, moderate is 500 to 1,000 cells/mcL, and severe is < 500 cells/mcL. Mild and moderate neutropenia are typically addressed in the outpatient setting, while severe neutropenia may carry a significant risk of infection. However, the ANC only measures peripherally circulating neutrophils and does not reflect the status of the marginated pools or bone marrow reserves that constitute the majority (> 95%) of the total body neutrophil stores. Thus, when determining the clinical significance of a low ANC, recognize that neutropenia in the setting of normal reserves does not necessarily correlate with an increased risk of infection.

Clinical Presentation

History

Ask about any previous episodes of neutropenia, as well as any predisposing conditions (eg, drugs, medications, recent illnesses, poor diet). Obtain a thorough history of the patient's infectious diseases and antibiotic exposure, including the type, frequency, and duration, and note any patterns or periodicity. Specific signs and symptoms to elicit include fever, weight loss, cough, ear pain, sinus pressure, neck stiffness, headaches, abdominal pain, vomiting, diarrhea, perirectal pain, dysuria, skin infections (eg, cellulitis or furunculosis), and oral infections (eg, stomatitis or gingivitis). Although isolated neutropenia does not increase the risk of viral infections, several viruses can cause neutropenia, which makes viral syndromes relevant as well.

Determine if there is a family history of hematologic, autoimmune, or other systemic disorders with hematologic findings.

Physical Examination

Immediately assess the patient for evidence of hemodynamic instability that may indicate sepsis. Then, look for external signs of infection, such as erythema, warmth, tenderness, swelling, or meningismus. Frank pus or abscesses suggest adequate bone marrow reserve. A low marrow reserve results in an attenuated inflammatory response, in which case examination findings may be subtle or absent. Examine the skin and mucosal surfaces including the

oropharyngeal, perianal, and vulvar areas for signs of mucositis. Abdominal tenderness may indicate gastrointestinal mucosal involvement that includes typhlitis, also known as neutropenic enterocolitis. Examine the lungs, ears, and sinuses for evidence of bacterial infection. Generalized adenopathy, hepatosplenomegaly, or poor growth may point to an underlying systemic disease associated with neutropenia.

Avoid invasive examinations, such as digital rectal examinations, rectal temperature checks, or speculum examinations, as these may cause bacterial translocation and lead to invasive infection.

Laboratory Workup

For a stable patient with an incidental finding of neutropenia, repeat a complete blood cell count (CBC) with manual differential and peripheral smear to confirm the neutropenia and evaluate other cell lines. If the neutropenia is isolated and the history and examination findings are otherwise benign, arrange for the primary care provider to track the CBC in the outpatient setting.

If the initial history or physical examination findings have concerning features, consult a hematologist or oncologist to initiate further workup. Choose specific tests based on the clinical picture. These may include viral studies; antinuclear antibodies to assess for systemic autoimmune diseases; antineutrophil antibodies to screen for an immune-mediated neutropenia; erythrocyte sedimentation rate, C-reactive protein, and/or procalcitonin to evaluate for a deep-seated infection or systemic inflammatory condition; HIV screening and immunoglobulin levels to look for an underlying immunodeficiency; vitamin B_{12}, folate, and copper levels to evaluate for nutritional deficiencies; genetic testing; and bone marrow aspirate and biopsy with cytology.

If a neutropenic patient has a fever ($>$ 38.3 °C [$>$ 101 °F] or persistently $>$ 38 °C [$>$ 100.4 °F]), collect blood cultures and a clean-catch urinalysis with urine culture prior to antibiotic administration. Do not delay treatment if obtaining cultures proves to be difficult, but never catheterize a neutropenic patient. Order additional cultures and imaging as indicated by the history or physical examination.

Differential Diagnosis

The differential diagnosis of neutropenia is summarized in Table 47–1.

Treatment

In an asymptomatic patient with isolated mild to moderate neutropenia, watchful waiting without treatment is appropriate. This includes repeating the history, physical examination, and CBC. In more severe cases, or with a

Table 47–1. Most Common Causes of Neutropenia

Diagnosis	Clinical Features
Benign familial neutropenia	Yemenite Jewish, certain African populations including Ethiopian, and certain Arab populations ANC usually ≥ 1000 cells/mcL No risk of serious infections
Chronic idiopathic neutropenia	Mild but chronic neutropenia No predisposition to severe infections Diagnosis of exclusion
Acquired/Transient Neutropenia	
Viral postinfectious neutropenia	Most common cause of transient neutropenia in childhood Can start a few days before viral symptoms and persist up to 1 wk after symptoms resolve Etiologies: cytomegalovirus, Epstein-Barr virus, hepatitis A/B virus, HIV, influenza A/B virus, measles, respiratory syncytial virus, parvovirus B19, rubella, varicella, human herpesvirus 6
Bacterial postinfectious neutropenia	Endotoxin-mediated suppression, especially in newborn sepsis Neutropenia improves with treatment of infection Etiologies: *Staphylococcus aureus, Brucella, Rickettsia,* typhoid, tuberculosis, tularemia
Drug-induced neutropenia	Direct/immune mediated Abrupt onset 1–2 wk after first exposure or immediately with reexposure Lasts approximately 1 wk Toxic suppression Insidious onset, can occur months after drug initiation Lasts days to months Common etiologies: penicillins, sulfonamides, dapsone, ibuprofen, indomethacin, hydralazine, phenytoin, carbamazepine, valproate, clozapine, olanzapine, rituximab, phenothiazines, antithyroid medications
Primary Immune Disorders	
Autoimmune neutropenia of infancy	5–15 mo of age No risk of infections Spontaneous remission within 7–30 mo Low risk of recurrence
Chronic benign neutropenia Autoimmune neutropenia of childhood (primary)	Most common type of chronic neutropenia in children Appears as early as 6–12 mo of age, generally ≤ 3 y of age Mild mucocutaneous and upper respiratory infections Usually resolves spontaneously by 5 y of age but may persist into adulthood
Autoimmune neutropenia (secondary)	Patient often has another immune disorder (eg, autoimmune lymphoproliferative syndrome, systemic lupus erythematosus, Evans syndrome) Clinical course varies according to underlying diagnosis
Inherited/Syndromic Neutropenia	
Severe congenital neutropenia	Neurologic abnormalities can occur, such as developmental delay and seizures ANC ≤ 200 cells/mcL (can rarely increase to 500 cells/mcL) Autosomal dominant, X-linked, or autosomal recessive Severe infections (primarily skin, mouth, and rectum) in the first month after birth High risk of myelodysplastic syndrome and/or acute myeloid leukemia

Continued

Table 47–1. Most Common Causes of Neutropenia, continued	
Diagnosis	**Clinical Features**
Cyclic neutropenia	Periodic fever, painful oral ulcers, periodontal disease, lymphadenopathy, and recurrent infections Autosomal dominant Low ANC lasting 3–6 d, followed by a normal ANC for 14–28 d

Abbreviation: ANC, absolute neutrophil count.

diagnosis in which the neutropenia may not spontaneously resolve, consult a hematologist to initiate workup and guide management.

A patient with severe neutropenia who presents with fever is at high risk for sepsis. Treat with one of the following monotherapy regimens of broad-spectrum intravenous (IV) antibiotics:

- IV piperacillin/tazobactam (≤ 2 months of age, 320 mg piperacillin/kg/d, divided into doses administered every 6 hours; 2–9 months of age, 240 mg piperacillin/kg/d, divided into doses administered every 8 hours; ≥ 9 months of age, 300 mg piperacillin/kg/d, divided into doses administered every 8 hours; maximum, 16 g piperacillin/d)
- IV cefepime (150 mg/kg/d, divided into doses administered every 8 hours; maximum, 2 g per dose)
- IV meropenem (60 mg/kg/d, divided into doses administered every 8 hours; maximum, 1 g per dose)

Add a secondary agent, depending on the probable source of infection. For example, add vancomycin if the patient has a central line infection. Also expand coverage if the likelihood of resistant organisms is high or if the patient becomes hemodynamically unstable. Add fungal coverage if the patient is at high risk of developing invasive fungal disease, fever persists for more than 4 days despite broad-spectrum antibacterial administration, and no source has been identified.

The organism and site of infection determine the antibiotic duration. Transition to oral antibiotics once the patient is clinically well and showing signs of marrow recovery. If no source is identified, continue treatment until culture results are negative for at least 48 hours, the patient is afebrile for at least 24 hours, and there is evidence of marrow recovery.

Disposition

- **Intensive care unit transfer:** Hemodynamic instability, septic shock
- **Discharge criteria:** Evidence of bone marrow recovery, no fever for 24 hours or more, culture results negative for 48 hours or more, and antibiotics (if indicated) transitioned to an oral regimen

Follow-up

- **Primary care:** 1 week if benign or if transient cause suspected; check the CBC with differential twice weekly for 6 to 8 weeks to evaluate the patient for resolution and/or patterns of recurrence
- **Hematology/oncology:** 1 to 2 weeks, depending on the final diagnosis

Pearls and Pitfalls

- A normal ANC in an infant between the ages of 1 month and 1 year can be as low as 1,000 cells/mcL.
- Standard precautions including hand hygiene and infection-specific precautions/isolation are sufficient for hospitalized neutropenic patients. Neither reverse isolation nor strict neutropenic diets are of any benefit.

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CHAPTER 48

Sickle Cell Disease

Introduction

Sickle cell disease (SCD) is an inherited hematologic disorder characterized by having genes for 2 abnormal hemoglobins that result in the sickling of red cells. The clinical features of the disease result from chronic hemolysis and end-organ insult secondary to vasoocclusion and vascular injury. Homozygous hemoglobin SS is the most common and severe form of SCD, but similar manifestations may occur when heterozygous hemoglobin S is combined with an alternative hemoglobin abnormality, such as in the conditions of hemoglobin SC (also known as sickle hemoglobin C disease) and hemoglobin S β-thalassemia (which can be as severe as homozygous SS disease).

The most common complications of SCD that lead to hospitalization are infection, including a serious bacterial infection such as sepsis and osteomyelitis, vasoocclusive episode (VOE), acute chest syndrome (ACS), stroke, splenic sequestration crisis, aplastic crisis, acute cholecystitis, and, rarely, priapism. A patient with SCD has splenic dysfunction and is therefore at high risk of invasive infection from encapsulated organisms, particularly *Streptococcus pneumoniae*. In addition, there is an increased risk of osteomyelitis from *Staphylococcus aureus* and *Salmonella* species. A patient with SCD is also at increased risk of VOE and ACS after receiving general anesthesia.

Other serious but rare complications include hyperhemolysis, hepatic sequestration, multiorgan failure, orbital compartment syndrome, and subarachnoid hemorrhage.

Clinical Presentation

The presentations of the most common complications of SCD are summarized in Table 48–1, and the serious rare complications are presented in Table 48–2.

History

Ask about the patient's usual blood count levels (hemoglobin, white blood cell [WBC] count, reticulocyte count), daily medications (penicillin, folate, hydroxyurea), history of ACS, recent surgeries (especially splenectomy), history of asthma, prior transfusions (and the indications), transcranial Doppler ultrasonography (US) results, and the name of the physician (usually a hematologist) managing the SCD. Risk factors for ACS include history of asthma, prior history of ACS, and recent surgeries, especially abdominal, which can be associated with poor respiratory effort.

Table 48–1. Common Complications of Sickle Cell Disease

Diagnosis	Clinical Features
ACS	Fever, cough, tachypnea, chest pain Hypoxia New lobar or segmental infiltrate on chest radiographs
Acute cholecystitis Choledocholithiasis	Fever in acute cholecystitis Right upper quadrant abdominal pain (+) Murphy sign
Aplastic crisis	Pallor, fatigue, tachypnea, tachycardia with or without hypotension No increase in spleen size ↓ Hemoglobin level (from baseline) with ↓ reticulocyte level (< 1%–2%)
Bacteremia/sepsis	Fever Toxicity/patient ill appearing ↑ or ↓ White blood cell count (compared to baseline)
Hepatic sequestration	Pallor Enlarging liver, right upper quadrant tenderness, ↑ alanine aminotransferase and aspartate transaminase levels ↓ Hemoglobin level (from baseline), normal or ↑ reticulocyte level
Osteomyelitis	Fever Bone pain localized or located at an atypical site
Priapism	Painful erection lasting > 4 h
Splenic sequestration	Pallor, fatigue, tachypnea Tachycardia with or without hypotension Left upper quadrant tenderness Increasing palpable splenomegaly from baseline ↓ Hemoglobin level > 2 g/dL (> 20 g/L) (from baseline), normal or ↑ reticulocyte level May also have thrombocytopenia
Stroke	Unilateral weakness or hemiparesis Altered mental status, seizures Slurred speech, aphasia Facial droop
VOE	Acute pain at typical or multiple sites (extremities, chest, back) Occurs with or without fever (usually < 38.6°C [< 101.5°F])

Abbreviation: ACS, acute chest syndrome.
+ indicates positive finding; ↑, elevated level; ↓, decreased level.

The patient with an established diagnosis of SCD is often admitted for pain and/or fever. Determine the characteristics of the pain, such as location, quality, intensity, radiation, and alleviating and exacerbating factors, and compare these to the patient's typical pattern of sickle cell pain. Common locations for VOE pain are the extremities, abdomen, and back, but specifically note the presence of chest pain or any respiratory complaints. In addition, ask about the response to current and previous pain management strategies, in both the inpatient and outpatient settings. Determine if there have been any

Table 48–2. Rare Serious Complications of Sickle Cell Disease

Diagnosis	Clinical Features
Hyperhemolysis	Causes: RBC transfusion, drugs, infections, glucose-6-phosphate dehydrogenase deficiency Pallor with worsening scleral icterus and jaundice Pain that may mimic a vasoocclusive episode ↓ Hemoglobin level (from baseline), normal or reticulocyte level Dark, heme (+) urine without RBCs
Multiorgan failure	Confusion (nonfocal encephalopathy) Fever Rapid decrease in hemoglobin level and platelet count ↑ Aspartate transaminase, alanine transaminase, lactate dehydrogenase, bilirubin, and creatinine levels Failure of lungs, liver, or kidneys
Orbital compartment syndrome (orbital bone infarct)	Eye pain Proptosis
Subarachnoid hemorrhage	"Worst headache of my life" Altered mental status

Abbreviation: RBC, red blood cell.
+ indicates positive finding; ↑, elevated level; ↓, decreased level.

recent stressors, exposure to cold, or viral illness symptoms, because these are common triggers for a VOE. Note the duration and height of the fever and any measures taken to manage it.

Physical Examination

Priorities at examination are the vital signs, because sepsis is the primary consideration when there is fever higher than 38.5 °C (> 101.3 °F). Tachycardia and tachypnea can occur in ACS, aplastic crisis, and splenic sequestration. Look for other signs of ACS (accessory muscle use, wheezing or focal rales on auscultation), aplastic crisis (pallor, heart failure), and splenic sequestration (splenomegaly, tenderness to palpation over left upper quadrant, hypovolemic shock). In addition, tachycardia may be secondary to pain, so recheck the vital signs after appropriate analgesia has been administered and reassess the pain level frequently.

Compare the degree of scleral icterus, jaundice, splenomegaly, and location(s) of bone pain to the patient's baseline or typical findings. Palpate areas of pain by paying close attention to the long bones, looking for areas of point tenderness that may suggest a focal inflammatory process, such as osteomyelitis. Examine the abdomen for tenderness, distention, organomegaly (spleen and liver), and tenderness over the right upper quadrant (gallbladder) or left upper quadrant (spleen). Check the genitourinary area in males if there

is a concern for priapism. Perform a complete neurologic examination if there are any neurologic symptoms or a change in mental status.

Laboratory Workup and Radiology Examinations

Obtain a complete blood cell count and reticulocyte count and compare the results to the patient's baseline values to assess for leukocytosis or leukopenia, worsening anemia, thrombocytopenia, or bone marrow suppression. A patient on hydroxyurea will have a lower WBC count and higher mean corpuscular volume than those not taking the drug, and an elevated WBC count may indicate noncompliance with the hydroxyurea. Evaluate electrolyte levels, creatinine level, liver function test results (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels), and C-reactive protein (CRP) level, if indicated by clinical findings.

If the patient has a temperature higher than 38.5 °C (> 101.3 °F), also order a blood culture, urinalysis, and urine culture (all females and males < 12 months of age). Obtain a chest radiograph and blood culture if the patient has lower respiratory symptoms and/or chest pain that could be consistent with ACS. When osteomyelitis is a diagnostic consideration, obtain a blood culture, CRP level and/or erythrocyte sedimentation rate, and magnetic resonance (MR) imaging of the bone, although it may be difficult to differentiate between a bony infarct and osteomyelitis.

If there is concern for a stroke, order emergent MR imaging/MR angiography (MRA) if the patient is stable enough to tolerate the examination. Computed tomography of the head is an alternative if MR imaging/MRA is not available. However, do not delay treatment if a stroke is suspected clinically. There is no role for transcranial Doppler in the acute management of a possible stroke.

If hepatobiliary disease is possible (acute cholecystitis, choledocholithiasis), perform US of the right upper abdominal quadrant, as well as MR cholangiopancreatography (if available) or endoscopic retrograde cholangiopancreatography. Also perform abdominal US to visualize the spleen when splenic sequestration is suspected but the spleen is not palpable.

When transfusion might be needed (aplastic crisis, splenic sequestration, ACS, stroke), perform blood typing that includes minor antigens C, D, E, and Kell. Confirm that the blood used for transfusions is sickle negative, leukocyte reduced, and matched for the selected minor antigens.

Differential Diagnosis

Always maintain a broad differential diagnosis and do not assume that the patient's complaints are secondary to SCD. For example, a patient may present with an acute disease that is unrelated to the SCD, such as appendicitis or asthma.

The most common diagnostic challenge involves the combination of pain and fever. Depending on location of the pain, the differential diagnosis includes infection, VOE, ACS, and osteomyelitis. Although both VOE and osteomyelitis appear with pain and swelling in the affected bone(s) at presentation, the pain of osteomyelitis tends to localize to a single site that may represent an atypical location for the patient.

Chest pain associated with fever, cough, wheezing, and tachypnea suggests ACS. Radiographic confirmation of a new lobar or segmental infiltrate is required to assign the diagnosis, although the initial study early in the course may be normal.

Rule out other potentially life-threatening complications, such as aplastic crisis, hyperhemolysis, and splenic or hepatic sequestration. Pallor, fatigue, tachycardia, and tachypnea occur with aplastic crisis and splenic sequestration. Left upper quadrant abdominal pain can occur with splenic sequestration, whereas right upper quadrant pain is seen with cholelithiasis, choledocholithiasis, pancreatitis (from gallstones), or hepatic sequestration.

Neurologic signs, such as change in mental status, facial droop, lateralized weakness, aphasia, or slurred speech, may occur with a stroke. Emergent treatment is needed.

Treatment

Acute Chest Syndrome

Manage pain aggressively (see the Vasoocclusive Episode section in this chapter), add orally administered azithromycin (10 mg/kg/d, 1,500-mg maximum; 5 mg/kg/d for 4 more days, 250-mg maximum) to the antibiotic regimen described for fever (see the Fever/Presumed Sepsis section in this chapter), and provide oxygen to maintain the oxygen saturation at 92% or higher, while encouraging the use of hourly incentive spirometry. If the patient has a history of asthma, or wheezing or rales, add nebulized albuterol (2.5 mg if the patient weighs $<$ 30 kg and 5 mg if the patient weighs $>$ 30 kg, every 4–6 hours) and intravenous (IV) methylprednisolone 1–2 mg/kg every 12 hours (60-mg/d maximum) or intramuscular (IM), IV, or oral dexamethasone 0.15–0.3 mg/kg once (12-mg maximum).

However, consult with a hematologist before initiating the systemic steroids, as they have been associated with rebound VOEs and hemorrhagic stroke. Assess the hemoglobin level every 12 hours until it is stable.

If the patient has worsening respiratory symptoms, such as decreased air movement, inspiratory and expiratory wheezing, increasing use of accessory muscles, increasing oxygen requirements, and a hemoglobin concentration

more than 1 g/dL (> 10 g/L) below baseline, consult with a hematologist to consider a simple transfusion (10 mL/kg packed red blood cells [RBCs]) to a goal hemoglobin level of 9 to 10 g/dL (90–100 g/L) and transfer the patient to an intensive care unit (ICU). Avoid transfusing to a target hemoglobin level higher than 10 g/dL (> 100 g/L) to prevent hyperviscosity. Arrange for an exchange transfusion or erythrocytapheresis if there is increasing respiratory distress, persistent oxygen saturation below 90% with supplemental oxygen, worsening pulmonary infiltrates, and continued decrease in hemoglobin concentration after simple transfusion.

Acute Cholecystitis/Cholelithiasis/Hepatic Sequestration

The treatment for biliary disease is the same as for a patient without SCD (see Chapter 37, Gallbladder Disease). Arrange a surgery consult, give the patient nothing by mouth, provide analgesia, and administer antibiotic coverage for gram-negative bacilli and anaerobes. Although urgent surgery may be necessary for worsening pain and fever, arrange for elective cholecystectomy (preferably laparoscopic) after resolution of the acute episode. For hepatic sequestration, perform a simple or exchange transfusion after consultation with a hematologist.

Aplastic Crisis

The goal of therapy is to prevent cardiovascular compromise secondary to the worsening anemia. If stable, monitor the patient closely and provide IV and oral hydration at maintenance levels until blood is available. If the hemoglobin level is less than 5 g/dL (< 50 g/L) or the patient is symptomatic, transfuse 10 mL/kg of packed RBCs over 4 hours with an expected increase of 2 g/dL (20 g/L) in the hemoglobin level and a goal of achieving a near-baseline hemoglobin level. If the patient is not stable, admit to an ICU and initiate fluid resuscitation while awaiting transfusion. Assume that the patient has a parvoviral infection (pending serologic examination findings) and institute appropriate isolation policies.

Fever/Presumed Sepsis

For the febrile (> 38.5 °C [> 101.3 °F]) patient, administer parenteral antibiotics that cover *S pneumoniae* and gram-negative organisms, immediately after blood cultures are performed. Do not delay initiating therapy while awaiting laboratory results. Treat with IV cefotaxime (150 mg/kg/d, divided into doses administered every 8 hours; 6-g/d maximum) *or* ceftriaxone (50–100 mg/kg/d, divided into doses administered every 12 hours; 4-g/d maximum) *or* ampicillin/sulbactam (100 mg/kg/d of ampicillin divided into doses administered every 6 hours; 8-g/d maximum) per local antibiotic

susceptibilities. If the patient has a known allergy to cephalosporin or penicillin, use IV clindamycin (40 mg/kg/d, divided into doses administered every 6 hours; 4.8-g/d maximum). If the patient is ill appearing or a central nervous system infection is suspected, add IV vancomycin (10–15 mg/kg every 6 hours, 4-g/d maximum).

The treatment of osteomyelitis in a patient with SCD is the same as for a normal host (see Chapter 94, Osteomyelitis and Septic Arthritis). Administer antimicrobial coverage for both *S aureus* and group A *Streptococcus* with vancomycin and/or clindamycin or linezolid, depending on the local prevalence of methicillin-resistant, as well as clindamycin-resistant, *Staphylococcus* bacteria. Whichever is prescribed, add ceftriaxone to treat possible *Salmonella* infection.

Priapism

The goals of care in priapism are to control the pain (see the Vasoocclusive Episode section in this chapter) and prevent ischemic damage. This requires close consultation with both a urologist and a hematologist. Initiate aggressive oral or IV fluid hydration immediately, along with oral and/or IV analgesia. Corporal aspiration, with or without irrigation, is indicated for persistent priapism that lasts more than 4 hours that is not responsive to fluid hydration and analgesia. If surgical correction is indicated, arrange for a preoperative transfusion.

Splenic Sequestration

The goal of treatment is to prevent the progression of hypovolemic shock while awaiting the release of the blood trapped in the spleen. Transfer the patient to an ICU, consult with a hematologist, initiate IV fluid resuscitation if needed, and order a packed RBC transfusion of 5 to 10 mL/kg, generally over 4 hours, but deliver it more rapidly if the patient is in hypovolemic shock. Aim for a posttransfusion hemoglobin level of less than 9 g/dL (< 90 g/L) to prevent hyperviscosity, because once the sequestered blood is returned from the spleen, the hemoglobin level may increase by another 1 to 2 g/dL (10–20 g/L). Obtain a surgical consult to arrange for an elective splenectomy if the patient has had recurrent splenic sequestration episodes or symptomatic hypersplenism.

Stroke

Admit the patient to an ICU and consult with a hematologist to arrange emergent exchange transfusion or erythrocytapheresis. The goal is to increase the hemoglobin level to about 10 g/dL (100 g/L) and decrease the hemoglobin S level to less than 30%. Do not delay transfusion therapy while performing

imaging studies, and administer oxygen while awaiting the procedure. See Chapter 76, Acute Hemiparesis, for the general management of a stroke.

Vasoocclusive Episode

Because a patient admitted for VOE has not responded to home and/or outpatient pain management, use IV opioids via patient-controlled analgesia (PCA), continuous infusion, or scheduled interval dosing, with rescue doses available for breakthrough pain. Titrate the dose to an adequate therapeutic response, which is ideally a minimum of a 50% reduction in pain on the visual scale. Never initiate as-needed dosing alone for a patient with a VOE. Be aware that a patient with previous opioid exposure may require higher than usual doses of opiates or an alternative drug. Morphine is more often used for PCA, but some patients may have a better response to a different opiate, such as hydromorphone.

The preferred method of pain management is PCA, once a child is able to understand that pushing the button decreases pain. For most patients, this occurs by 6 years of age. A typical morphine PCA regimen starts with a total dose of 0.05 to 0.20 mg/kg/h. The usual basal (continuous) rate is one-third to one-half of this total hourly dose. Calculate the PCA dose (demand) by using the remainder of the total hourly dose and dividing it by the number of total potential doses (6–10) available over an hour. For example, using 0.1 mg/kg/h as the hourly dose, start with a basal rate of 0.033 mg/kg/h, with a 0.0067-mg/kg PCA dose permitted every 6 minutes. Therefore, for a 25-kg patient, the continuous rate is 0.8 mg/h with 0.17-mg PCA doses (up to 10 doses in 1 hour). Note that the PCA dose refers to the patient-controlled dose and has many synonyms, including *intermittent dose, interval dose, interval bolus,* and *demand dose.*

Reevaluate the patient frequently. Additional physician-ordered rescue doses (0.05 mg/kg every 30 minutes) may be needed until the pain is adequately controlled. Readjust the basal and PCA doses every 12 to 24 hours, basing any changes on the total amount of morphine given to control the pain over that period. Increase the basal rate if the patient demands more than 3 PCA doses per hour and decrease the basal rate if the patient appears oversedated. When the pain is well controlled for 24 hours and the patient is using fewer than 3 PCA doses per hour, begin weaning the patient off of the medication by decreasing the basal dose by 10% to 20%, as tolerated.

For a patient unable to use PCA, order scheduled interval dosing of morphine (0.05–0.15 mg/kg every 2–4 hours), although a continuous infusion (0.05–0.10 mg/kg/h) is an acceptable alternative. Treat breakthrough pain with 25% to 50% of the interval dose every 20 to 30 minutes, as needed.

Readjust the dose based on the total amount of medication needed to control the pain over time. In some cases, a morphine administration rate greater than 0.1 mg/kg/h may be needed, but this requires careful monitoring for respiratory depression by assessing the respiratory rate, level of sedation, and pulse oximetry. If possible, manage opioid-associated respiratory failure with ventilatory support (bag-valve mask). The use of naloxone (0.1 mg/kg) may be lifesaving in treating respiratory failure, but it will also reverse pain control. When the pain is well controlled for 24 hours, begin weaning the patient off of the medication by decreasing the infusion or scheduled dosing by 10% to 20%.

Aggressively treat the side effects of opioids. Manage nausea with IV/oral ondansetron (0.05–0.10 mg/kg every 6 hours as needed; maximum, 4 mg per dose) or IV/oral metoclopramide (0.1–0.2 mg/kg every 6–8 hours; maximum, 10 mg per dose). Treat pruritus with either oral diphenhydramine (5 mg/kg/d, divided into doses administered every 6 hours, or 0.5 mg/kg every 2 hours; 300-mg/d maximum) or oral hydroxyzine (2 mg/kg/d, divided into doses administered every 8 hours; 50-mg/d maximum if patient aged $<$ 6 years, 100-mg/d maximum if patient aged $>$ 6 years, 600-mg/d maximum for adults) or change to IV hydromorphone (0.015–0.020 mg/kg every 3–4 hours). Start a bowel regimen (stool softeners, docusate, polyethylene glycol) if multiple opiate doses are anticipated (see Chapter 35, Constipation).

Intravenous ketorolac (0.5 mg/kg every 6 hours; maximum, 30 mg per dose) is a useful adjunct if there are no contraindications (dehydration, gastritis, ulcer, coagulopathy, renal impairment). Do not use for more than 5 days. Oral or IV acetaminophen (15 mg/kg/dose given every 6 hours) may also be helpful, if there are no contraindications (liver failure, transaminitis, acute liver injury).

Begin the transition to oral opioids at an equianalgesic dosing level (see Chapter 103, Pain Management) when the pain is well controlled, the IV morphine dose has been tapered to 0.25 mg/kg/h or less, and the patient has normal gastrointestinal functioning (able to eat and drink without being nauseated). One approach is to first convert the basal rate to the equivalent dose of a long-acting oral opioid, then 24 hours later convert the PCA dose to an equivalent short-acting oral opioid.

To prevent withdrawal symptoms for a patient whose pain has resolved but who has been receiving opioids for 10 days or more, first taper the opioid dose by 10% to 20% per day, as tolerated, with close monitoring, over 5 to 7 days. Then, over the next 3 to 5 days, increase the interval from every 6 hours to every 12 hours to every day.

Supportive therapy includes the correction of any fluid-deficit dehydration, as well as providing IV and/or oral maintenance isotonic fluid. There is no evidence that increased hydration is helpful, and overhydration can lead to

fluid overload; therefore, provide no more than maintenance IV hydration to a euvolemic patient. Provide oxygen as needed to maintain oxygen saturation at 92% or higher. Also order incentive spirometry (10 breaths every 1 hour when awake) and encourage early ambulation to prevent ACS. Other comfort measures include the use of heating pads and relaxation techniques.

Rare Complications

Immediately consult with a hematologist if the patient has one of the rare complications listed in Table 48–2. The critical challenge for the hospitalist is to recognize these rare problems as they develop in a patient with SCD who is admitted for another reason.

Patient Requiring General Anesthesia

Order incentive spirometry and perioperative oxygen. Also perform a preoperative transfusion to raise the hemoglobin level to at least 10 g/dL ($\geq$ 100 g/L) to minimize the risk of VOE or ACS. However, do not over transfuse due to the risk of hyperviscosity.

Indications for Consultation

- **Hematology:** ACS, splenic sequestration, acute aplastic crisis, hyperhemolysis, priapism, possible cerebral vascular accident, pain difficult to manage
- **Neurology:** Possible cerebral vascular accident
- **Ophthalmology:** Orbital compartment syndrome
- **Pain management specialist:** Standard pain management modalities are ineffective for VOE
- **Surgery:** Consideration of cholecystectomy for gall bladder disease or splenectomy for splenic sequestration
- **Urology:** Priapism lasting more than 4 hours

Disposition

- **ICU transfer:** Septic shock, ACS requiring respiratory support, acute cerebral vascular accident, need for exchange transfusion
- **Discharge criteria:** Septicemia excluded (patient afebrile with negative blood culture results), pain adequately managed with oral medications, no ongoing complications (ACS, cerebral vascular accident, etc), patient stable and no longer requiring inpatient interventions

Follow-up

- **Primary care:** 1 to 2 weeks
- **Sickle cell center/pain specialist:** 1 week

Pearls and Pitfalls

- Care coordination between the inpatient and outpatient setting in conjunction with a sickle cell center and pain specialist is essential.
- Be judicious with fluid administration in a patient with known cardiac or pulmonary or renal insufficiency, because the chronic high output state secondary to anemia is a risk factor for fluid overload and pulmonary edema. This can be difficult to differentiate from ACS.
- As with any immunosuppressed patient, the child's appearance may belie the serious clinical situation.
- If possible, transfuse with minor antigen–matched (C, D, E, Kell), sickle-negative, and leukocyte-depleted, packed RBCs.
- A packed RBC transfusion of 10 mL/kg typically increases the hemoglobin level by 2 g/dL.
- When administering a packed RBC transfusion, always monitor for clinical signs of an acute or delayed transfusion reaction (fever, chills, tachycardia, hypotension, urticaria, hemoglobinuria), as the patient may be at heightened risk for a transfusion reaction, given previous exposure to multiple blood products.
- Delayed hemolytic transfusion reactions occur 7 to 21 days after transfusion and may mimic an acute VOE.
- Except for a patient going to the operating room, do not transfuse to a hemoglobin level greater than 10 g/dL, which may then result in hyperviscosity.
- Establish a multimodal, individualized approach to pain management.
- Opioid-induced sedation precedes respiratory depression.

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CHAPTER 49

Thrombocytopenia

Introduction

Platelets, also known as thrombocytes, are essential for primary hemostasis. The normal number of platelets in a child is 150,000–450,000/mcL, while thrombocytopenia is defined as platelet count less than 150,000/mcL. Bleeding signs and symptoms become apparent when the platelet count is less than 50,000/mcL, and severe thrombocytopenia is less than 20,000/mcL.

Thrombocytopenia can be secondary to either increased destruction or decreased production. There is a greater likelihood of a serious disorder if the thrombocytopenia is associated with neutropenia and anemia.

In the acute inpatient setting, thrombocytopenia may present with evidence of a bleeding disorder, or it may be a secondary finding when evaluating the patient for other medical conditions, such as bacterial or viral infections or systemic disease processes.

Clinical Presentation

History

Determine the time of onset, the clinical course of the illness, and the site of bleeding (if any). Ask about a history of easy bruising, nosebleeds, gingival bleeding, blood in stool, hematuria, recent illness, trauma, and prescription (sulfonamides, quinine, vancomycin, valproic acid, phenytoin, carbamazepine, and heparin) medication use.

Ask about a personal and/or family history of bleeding disorders, splenectomy, and increased bleeding with prior surgery or dental procedures. In a postpubertal female patient, get a complete menstrual history, including cycle length and frequency, and heaviness of bleeding.

History that raises a concern of more serious conditions includes unexplained or persistent fevers, weight loss, fatigue, night sweats, bone or joint pain, severe headaches, and lymphadenopathy.

Physical Examination

Perform a thorough physical examination, looking for signs of bleeding (petechiae, purpura, ecchymoses, hematomas, hemarthrosis), including on the mucous membranes (wet purpura). Also evaluate for any bruising and petechiae in pressure areas, such as bra strap, waistbands, backpack straps, and blood pressure cuffs. Check for hepatosplenomegaly and lymphadenopathy, which suggest a systemic disorder.

Underlying congenital causes of thrombocytopenia can be associated with dysmorphic features, including skeletal abnormalities (abnormal thumbs or forearms) and hearing deficits.

Laboratory Workup

If the patient is actively bleeding, or has a positive bleeding history, obtain a complete blood count, prothrombin time (PT) and partial thromboplastin time (PTT) to screen for a clotting or bone marrow disorder. Tests to exclude other etiologies of thrombocytopenia include a complete metabolic panel to evaluate liver and kidney disease, inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), and a workup for bacterial sepsis.

Further evaluation is warranted when 1 or 2 of the other cell lines are abnormal. Possibilities include malignancy, infection, autoimmune disorders, drug-induced thrombocytopenia, and bone marrow failure.

After confirmation of isolated thrombocytopenia (low platelets with normal PT and PTT), check the mean platelet volume (MPV, normal 7–9 fL). Review the peripheral smear to evaluate the platelet granularity and clumping. The MPV and peripheral smear will help differentiate between small and large platelets, to better understand if the problem is platelet production (small) or destruction (large).

Immature platelet fraction (IPF) measures young platelets in peripheral blood. It is similar to a reticulocyte count in anemia. An increased IPF is consistent with peripheral platelet destruction, while a decreased IPF is correlated with bone marrow failure. Immature platelet fraction will help determine bleeding risk in immune thrombocytopenic purpura (ITP) (lower IPF correlates with higher bleeding risk) and whether a prophylactic platelet transfusion is needed or if watchful waiting for recovery is warranted.

In most cases of isolated thrombocytopenia, bone marrow examination is not required unless there is concern for bone marrow infiltration or failure. Consult a hematologist for consideration of bone marrow aspiration or if other features of the illness are not consistent with ITP.

Differential Diagnosis

When a low platelet count is inconsistent with clinical presentation, obtain a repeat platelet count to rule out laboratory error or an artifact. Pseudothrombocytopenia, or a spurious platelet count, occurs when platelet clumping occurs in the standard ethylenediaminetetraacetic acid (EDTA; anticoagulant) tube. To double-check, review the blood smear, which will have clumps along with a normal number of platelets. If further confirmation is needed, repeat the platelet count in a citrated or heparinized tube.

Bruising without petechiae on the chest, abdomen, back, or buttock is unusual with a normal platelet count and suggests possible inflicted trauma. Fever, lymphadenopathy, and hepatosplenomegaly are concerning for underlying systemic disease process, such as a malignancy, liver disease, and systemic lupus erythematosus.

Thrombocytopenia with large platelets (MPV > 10 fL) is consistent with increased production due to consumptive process, as seen in ITP, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and drug-induced thrombotic microangiopathy. A low MPV (< 7 fL) suggests decreased platelet production, as seen in malignancies, aplastic anemias, and congenital thrombocytopenia disorders. Giant platelets the size of red blood cells occur in hereditary macrothrombocytopenia. In DIC and end-stage liver failure, the platelet count will be low and the PT and PTT are prolonged.

The classic presentation of ITP is a previously healthy 1- to 4-year-old with a history of a viral illness in the past 1 to 4 weeks. There is the acute onset of generalized petechiae and purpura with otherwise normal physical examination findings. The diagnosis is virtually always ITP if there is a profound isolated thrombocytopenia of less than 10,000/mcL.

The differential diagnosis of thrombocytopenia in children is summarized in Table 49–1.

Treatment

The management of thrombocytopenia is determined by the underlying cause. The goal of therapy is to maintain a safe platelet count, which prevents significant hemorrhaging, and not to achieve a normal level. For a given patient, a safe platelet level can be variable and dependent on the etiology and other aspects of hemostasis.

Immune Thrombocytopenic Purpura

In most instances, ITP is a self-limited disease. However, treatment is indicated if the platelet count is less than 10,000/mcL or if the patient has uncontrolled bleeding or wet purpura. First-line management varies among institutions and includes steroids, intravenous immunoglobulin, and anti-D immunoglobulin (Table 49–2). If the ITP is refractory to these therapies, consult a hematologist for consideration of rituximab, immunosuppressive agents, chemotherapy, thrombopoietin agonists, and splenectomy. Platelet transfusions are rarely indicated because they are rapidly destroyed by circulating antibodies but are necessary when there is life-threatening hemorrhage.

Table 49–1. Differential Diagnosis of Thrombocytopenia in Children

Diagnosis	Clinical Features
Pseudothrombocytopenia	Falsely low platelet count, secondary to EDTA-induced clumping Obtain blood sample in citrate or heparinized tube
Increased Platelet Destruction	
Idiopathic thrombocytopenia purpura	Most common cause of thrombocytopenia Peak at 1–4 years of age Occurs 1–4 weeks after an innocuous viral illness Generalized petechiae and purpura Normal white blood cells, hemoglobin, PT/PTT Large platelets (MPV > 10 fL)
Drug-induced thrombocytopenia	Occurs 1–2 weeks after starting new medication or acutely after a single dose Recovery begins within 1–2 days of stopping drug May be associated with sulfonamides, vancomycin, valproic acid, phenytoin, carbamazepine, heparin
Systemic lupus erythematosus	Thrombocytopenia can be the initial manifestation Occurs in 20%–40% of patients Can be associated with antiphospholipid antibody syndrome
Hemolytic uremic syndrome	Associated with Shiga toxin–producing *Escherichia coli* colitis Bloody diarrhea, renal failure, oliguria, hypertension Involves platelet activation and consumption
Thrombotic thrombocytopenic purpura	Fever, microangiopathic hemolytic anemia, abnormal renal function, central nervous system changes Large platelets (MPV > 10 fL)
Hypersplenism	Palpable spleen secondary to sickle cell splenic sequestration, chronic liver disease, malaria Other cell lines may be affected
Von Willebrand disease	Heavy menstrual bleeding
Decreased Platelet Production	
Infection	Signs of the primary infection: viruses (Epstein-Barr virus, cytomegalovirus, parvovirus, varicella, HIV), rickettsia, toxic shock syndrome, histoplasmosis, toxoplasmosis
Acquired bone marrow failure Infiltrative bone marrow disease	Other cell lines may be affected May have lymphadenopathy and/or hepatosplenomegaly Small platelets (MPV < 7 fL)
Genetic Causes	
Wiskott-Aldrich syndrome	History of eczema and recurrent illness, small platelets
Thrombocytopenia with absent radius	Bilateral absent radii, but thumbs are normal Other skeletal, genitourinary, heart anomalies

Abbreviations: EDTA, ethylenediaminetetraacetic acid; ITP, idiopathic thrombocytopenia purpura; MPV, mean platelet volume; PT, prothrombin time; PTT, partial thromboplastin time.

Table 49–2. First-Line Management Options for Immune Thrombocytopenic Purpura		
Treatment Type	**Dose**	**Acute Side Effects**
Glucocorticosteroids	*Oral prednisone* 1–2 mg/kg/d divided into doses administered every 12 h, 60-mg/d maximum Treat for at least 2–4 wk, followed by taper *IV methylprednisolone (high dose)* 30 mg/kg/d, for 3–7 d, 1-g maximum	Gastritis/gastrointestinal hemorrhage Hyperglycemia Hypertension Increased appetite Mood disturbances
IV immunoglobulin	One dose, 1 g/kg IV over 4–6 h *Premedicate:* Diphenhydramine: 1–2 mg/kg/dose Acetaminophen: 10–15 mg/kg/dose	Anaphylaxis (immunoglobulin A–deficient patients) Fever Headache
Anti-Rho (D) immune globulin (Rh–positive patient only)	Single dose 50–75 mcg/kg IV	Fever, chills, nausea, vomiting Headache Hemolysis, renal failure

Abbreviation: IV, intravenous.

If a patient with ITP has a severe headache, altered mental status, or neurologic changes, arrange for emergent head computed tomography. Platelet transfusions, intensive drug therapy, and neurosurgical consultation are necessary if an intracranial hemorrhage is found.

Platelet Transfusion in the Inpatient Setting

Table 49–3 shows the relationship between platelet count and bleeding. In children and adolescents with active bleeding, transfuse if the platelet count is less than 50,000/mcL. For major invasive surgical procedures, the goal is to keep the platelet count greater than 50,000/mcL. For minor procedures such as lumbar punctures and central lines, a platelet count between 30,000 and 50,000/mcL is satisfactory.

Table 49–3. Relationship Between Platelet Count and Bleeding	
Platelet Count (×1000/mcL)	**Signs and Symptoms**
> 100	None
50 to 100	Mild (can occur after major trauma and surgery)
30 to 50	Moderate (cutaneous and mucosal)
10 to 30	Severe (high risk of excessive bleeding with trauma)
< 10	Severe, spontaneous bruising and bleeding (cutaneous, mucosal, and central nervous system)

Indications for Consultation

- **Hematology/oncology:** Diagnosis unclear, ITP unresponsive to first-line therapies, concern for bone marrow failure, bone marrow aspirate required, need for long-term management, suspicion of malignancy
- **Rheumatology:** Patient has multisystem complaints; systemic lupus erythematosus or antiphospholipid syndrome are suspected

Disposition

- **Intensive care unit transfer:** Hemodynamic instability, concern for intracranial bleeding, need for plasmapheresis or dialysis
- **Discharge criteria:** Acute bleeding resolved, platelet count stable in a safe range
- **Discharge instructions:** Avoid aspirin and nonsteroidal anti-inflammatory drugs and refrain from contact/collision sports. Notify the dentist or other providers prior to any surgical procedure.

Follow-up

- **Primary care:** 1 to 2 weeks
- **Hematology:** 1 to 2 weeks, depending on the diagnosis and condition at discharge

Pearls and Pitfalls

- Always rule out pseudothrombocytopenia to avoid unnecessary additional workup. Review the peripheral smear for clumping or repeat blood in citrated or heparinized tube.
- Immune thrombocytopenic purpura is the most common acquired bleeding disorder of childhood. Typically, a well-appearing child will have a low platelet count but normal white blood cell count and differential, hemoglobin, PT, and PTT.
- Intracranial hemorrhage is life-threatening but exceedingly rare in ITP.
- Avoid chest physiotherapy and lumbar punctures when platelets are less than 50,000/mcL.

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Hospitalist Practice

Billing

Introduction

There are 2 types of billing for all hospitalized patients: professional and facility/hospital. Professional billing covers the medical expertise of the physician/clinician for that day's patient care. The facility bill represents everything except the physician/clinician's bill, including the room charges, nursing, medications, radiographic studies, laboratory studies, and ancillary staff (eg nutritionists, case workers) who are employed by the facility and cannot report separately.

Professional Billing

Professional bills are submitted each day the patient is seen by a physician/clinician. Every clinical service that sees the patient submits a daily bill. However, multiple providers from the same specialty (eg, day and night hospitalist) usually cannot submit separate bills, except for unusual circumstances such as worsening clinical status requiring an increased level of care. So, on a given day, multiple physicians, such as the attending physician and consultants, may provide care and submit a bill for their services. Professional billing is based on either medical decision-making (MDM) or documented time spent in the care of the patient for that day.

Evaluation and Management

The selection of the evaluation and management (E/M) level is based on the complexity of the visit and the condition of the patient. Choose the code set from which you obtain your level, based on the service provided. For example, as the attending physician seeing the patient for their initial hospital care, you choose a code from that code set. If you are a specialist performing an inpatient consultation, you report a code from that code set. The level of the code selected is based on the MDM or documented time. Note the following guidelines exclude the daily intensive care and all critical care codes.

History and Physical Examination

Starting January 1, 2023, E/M services only require documenting a medically appropriate history and/or physical examination, when performed. The nature and extent of the history and/or physical examination are determined by the treating physician or other qualified health care professional reporting the service. However, the extent of history and physical examination is not an element in selection of the level of code for the service provided (eg, initial hospital care).

Medical Decision-Making

Medical decision-making is defined by the complexity of the problem, the data the clinician reviews, and the risk of the problems. There are 4 levels of MDM: straightforward, low complexity, moderate complexity, and high complexity. Table 50–1 illustrates how MDM is determined. Those levels are reached based on the 3 elements of MDM.

- Number and complexity of problems addressed at the encounter
- Amount and/or complexity of data to be reviewed and analyzed
- Risk of complications and/or morbidity or mortality of patient management

The level of MDM is based on meeting or exceeding 2 of the 3 sections. For example, if the patient has moderate problems, moderate risk, but high data, report the code for moderate MDM.

When using MDM or time for code selection, a continuous service that spans the transition of two calendar dates is a single service and is reported on one date. If the service is continuous before and through midnight, all the time may be applied to the reported date of the service.

Time-Based Billing

If billing is based on time, document clearly the amount of time, in minutes, that was spent in the care of the patient. Use the time when reporting services, such as inpatient/observation daily care, or as the sole determinant for discharge care. This includes documenting both direct (face-to-face) and nondirect (non–face-to-face) care.

Inpatient and Observation Discharge

All inpatient and observation discharges are based on time. Report one code for either 30 minutes or less or another for greater than 30 minutes.

Split/Shared Services

Many hospitals employ split/shared billing for patients in the hospital. A split/shared bill occurs when a patient is managed by both a physician and

Table 50–1. Medical Decision-Making

MDM Level	Number and Complexity of Problems Addressed	Amount /Complexity of Data Review/ Analyzed	Risk of Complications
Straightforward	Minimal	Minimal or None	Minimal
Low	Low	Limited	Low
Moderate	Moderate	Moderate	Moderate
High	High	Extensive	High

Abbreviation: MDM, medical decision-making.

a nonphysician provider (NPP) within the same group. For hospitalized patients, if a physician provides face-to-face care, the bill may be submitted under the physician or the NPP. If the bill is submitted under the physician, documentation is required of the physician's face-to-face time, and the physician and NPP notes are linked. If the physician provides only non–face-to-face care, the bill is submitted under NPP.

Facility Billing

The facility/hospital charges may be paid in a variety of ways. For inpatients, the fee for service, per diem, and percent of charges payment models have been the primary models for most hospitals in the United States.

Fee for Service

Payment for services is rendered each day the patient is in the hospital. The hospital submits bills to the insurance plan with a line-item list of charges for each hospital day (eg, room/board, pharmacy, radiology, laboratory).

Per Diem

The hospital is paid a flat fee for each day the patient is in the hospital. For most admissions, the bulk of charges occur in the first few days and the cost of care may closely match the payment. However, over time, payments may likely outweigh charges.

Percent of Charges

The hospital receives a prenegotiated percentage of all charges submitted to the insurance plan. These payment models provide little incentive for hospitals to do less or reduce the length of stay (LOS). To encourage hospitals to be more mindful of spending and bring awareness to LOS costs, some insurance plans have moved to diagnostic-related group (DRG) or "bundled payments" models.

Diagnostic Related Group/Bundled Payments

These are also referred to as "episode of care" payments. The hospital is paid for the entire episode of care (hospital stay) in one bundled payment based on DRG assignments. There are 2 DRG systems: the Medicare System DRG (MS-DRG) and the All Patient Refined DRG (APR-DRG). MS-DRG was created by Medicare and is primarily used by Medicare and many commercial insurance companies who often have a larger adult member population. APR-DRG was created by 3M and is considered more specific to pediatrics, so that most Medicaid plans use APR-DRG. In addition, some commercial insurance companies may use APR-DRG for their pediatric members.

Regardless of the DRG system, the concept of payment is the same. The DRG bundle is assigned by the principal diagnosis, which is the condition responsible for the patient's admission to the hospital. For example, if a patient is admitted to the hospital for community-acquired pneumonia, the patient will be assigned to the pneumonia DRG. Within each DRG, there are "tiers," defined by the secondary diagnoses. Secondary diagnoses may be chronic conditions that the patient had prior to admission (eg, spastic quadriplegia), but they can also be conditions that developed over the course of an admission (eg, acute respiratory failure). Within the MS-DRG system, each bundle is divided into 3 tiers: base DRG (with no co-morbidities), DRG with a CC (comorbid condition), and DRG with an MCC (major comorbid condition). Medicare releases a yearly list of nearly 150 pages of CCs and MCCs. In the APR-DRG system, the bundle is divided into 4 tiers based on severity of illness (SOI) scores, which range from 1 to 4 (4 being the highest). Unlike the MS-DRG system, there is not a published list of which diagnoses impact the SOI in the APR-DRG system.

All of the diagnoses used to define the DRG and its tier are based on physician/clinician documentation. Therefore, documentation must be explicit (hyponatremia instead of low sodium) and specific (profound intellectual impairment instead of developmental delay). This is in contrast to the fee for service model, where a line-item bill is sent to the payer for hospital billing. As a result, there has been a shift to much greater emphasis on accurate diagnosis documentation by clinicians in this newer DRG reimbursement model.

Observation Care Facility Fees

While inpatient stays are paid by the above payment models, observation cases are generally paid by time and/or services rendered. The payments for observation care are generally significantly lower than inpatient, as it is believed that observation patients have a lower acuity and severity. This may be true in many cases, but in pediatrics, observation care and inpatient may be similar for many conditions.

Hospitals have clinical documentation improvement (CDI) teams, which can assist hospitalists and other physicians/clinicians to ensure accurate documentation. These teams comprise nursing and coding specialists who review inpatient charts to ensure that the documentation is clear for the assignment of the DRG to the patients. If there is need for clarity, a CDI query can be sent to the physician/clinician to capture the necessary documentation for that particular case.

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CHAPTER 51

Cultural Effectiveness

Introduction

As pediatric hospitalists care for an increasingly diverse population of children, they are challenged with efficiently gathering essential information and quickly establishing rapport with patients and their families. Shared decision-making and respecting each family's unique values and culture are key to establishing this rapport.

Key Concepts in Culturally Effective Care

Culturally effective care is defined by the American Academy of Pediatrics (AAP) as "the delivery of care within the context of appropriate physician knowledge, understanding, and appreciation of all cultural distinctions leading to optimal health outcomes." Practicing culturally effective care is an essential component for the development of patient–physician and parent–physician relationships, reduction of health care disparities, and promotion of the patients' health beyond hospital discharge.

Culture goes beyond race and ethnicity. Among other factors, religion, sex, age, politics, sexual orientation, gender identity, socioeconomic status, education, geographic location/country of origin, age generation, and disability can all shape culture. Differences within races, ethnicities, and cultures can be more significant than differences across them. Making inferences about an individual from a certain background, based on previous experiences with the group to which that individual belongs, contributes to bias and is a barrier to culturally effective care.

The dynamic complexity of culture renders it impossible to fully achieve cultural competency. Rather, cultural humility is the goal. That is, providers seek to be open to and respectful of differences in each family's beliefs and values, deliver optimal care, demonstrate receptiveness to different cultures, communicate with families to understand their unique perspectives, adapt clinical practices (if possible) to acknowledge each family's values, and recognize the impact of one's implicit bias in each patient encounter.

Culturally Effective Care in Practice

Provider Education

In addition to practicing the key concepts listed above, commit to acquiring cross-cultural training and providing a role model for learners and staff. Learn about the variability in health beliefs, practices, and literacy that may

be encountered in practice in order to communicate and problem-solve effectively. Examples of variability in health beliefs include when to use the emergency department, expression of pain, use of traditional medicinal practices, traditions surrounding birth and death, the role of women and men in medical decision-making, feeding practices, views on bed sharing, obesity, and mental health.

Addressing Provider Implicit Bias

Implicit bias refers to associations and/or stereotypes that all providers subconsciously make that may lead to an inaccurate or negative evaluation of a patient. The use of reflective tools and exercises can help one become more aware of implicit biases. One such tool is the Implicit Association Test (https://implicit.harvard.edu/implicit/takeatest.html). Another tool is the 5 *R*'s of Cultural Humility, which can be used to reflect on and address implicit bias in the clinical setting (Table 51–1).

Patient Interviews

To identify cultural influences, incorporate specific questions and techniques into the medical history. Do this for all patients, not just specific ones based on implicit biases. Ask the patient or parent what they believe is causing the illness and what therapies or treatments were used at home. Allow them to fully describe their concerns without interruption. Use a model, such as RESPECT (Table 51–2), to facilitate open dialogue between patients, parents, and health care providers.

Table 51–1. The 5 *R*'s of Cultural Humility

Reflection	Aim: One will approach every encounter with humility and understanding that there is always something to learn from everyone. Ask: What did I learn from each person in that encounter?
Respect	Aim: One will treat every person with the utmost respect and strive to preserve dignity and respect. Ask: Did I treat everyone involved in that encounter respectfully?
Regard	Aim: One will hold every person in their highest regard while being aware of and not allowing unconscious biases to interfere in any interactions. Ask: Did unconscious biases drive this interaction?
Relevance	Aim: One will expect cultural humility to be relevant and apply this practice to every encounter. Ask: How was cultural humility relevant in this interaction?
Resiliency	Aim: One will embody the practice of cultural humility to enhance personal resilience and global compassion. Ask: How was my personal resiliency affected by this interaction?

Adapted by permission from Springer Nature: Masters C, Robinson D, Faulkner S, Patterson E, McIlraith T, Ansari A. Addressing biases in patient care with the 5Rs of Cultural Humility, a clinician coaching tool. *J Gen Intern Med*. 2019;34(4):627–630. © 2019. https://www.springer.com/journal/11606.

Table 51–2. RESPECT Model	
Respect	Convey respect for the patient and family.
Explain	Use an explanatory model of the illness, where the patient/parents explain their ideas of what is causing the condition and what treatment may entail.
Social context	Understand the patient's social context, including strengths, support networks, stressors, and spirituality.
Power	Equalize the power in the relationship, including seeking the patient's and parents' input in decision-making.
Empathy	Convey empathy in the patient encounter.
Concerns	Elicit underlying concerns and fears.
Trust	Determine and enhance the trust level and come to an agreement on shared goals.

Derived from Mostow C, Crosson J, Gordon S, et al. Treating and precepting with RESPECT: a relational model addressing race, ethnicity, and culture in medical training. *J Gen Intern Med.* 2010;25(Suppl 2):S146–S154.

Interpreter Services for Families With Limited English Proficiency

Ask all patients and families to identify their preferred spoken and written language. If the patient's choice is not English, always provide a trained professional medical interpreter or bilingual provider and document their use in the medical record. Allow additional time for the use of interpretive services, preferably with live personnel. However, in many cases, video remote interpretation services or telephone interpreters may be the only option, depending on the language needed and hospital resources. Note that it is a Joint Commission standard that pediatric inpatient services have one of these linguistic services available to support effective communication. This includes deaf and hard of hearing and any other communication needs. In addition, have prescriptions and discharge instructions professionally translated.

Prior to the encounter, introduce the interpreter to the patient and discuss what you expect to cover during the visit. Address the patient directly, rather than talking to the interpreter. Speak slowly, avoid medical jargon, and provide pauses throughout the conversation so the interpreter can translate. When the interpreter is speaking, try not to interrupt them.

Children in Immigrant Families

Children in immigrant families refers to patients who are either foreign-born or have one or more foreign-born parent(s). Children in immigrant families are a rapidly growing population, currently accounting for a quarter of all children in the United States. Compared to patients born in the United States, these children are more likely to live below the federal poverty level, be uninsured, and face barriers to seeking care. Additionally, some immigrant families come to the United States to flee persecution and seek safe haven.

It is therefore important to apply a trauma-informed lens when caring for children in immigrant families. For more information on this population and state-specific resources, please refer to the AAP *Immigrant Child Health Toolkit* (see Bibliography).

Staff/Health Care Provider/Learner Diversity

Staff, providers, and learners whose cultural backgrounds are comparable to those of the local patient population can serve as cultural brokers, linking patients and providers with dissimilar backgrounds. There is an increase in trust-building when patients are able to engage with medical team members from similar backgrounds. However, this is not always possible, and cultural humility is essential in all patient interactions.

Hospital/Community-Based Partnerships

It is incumbent upon hospitals to develop relationships with local community-based organizations. These partnerships may have specific resources needed to provide culturally effective care, such as hiring an interpreter for a particular language or building rapport with certain cultural groups.

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CHAPTER 52

Patient Safety

Introduction

Hospitalists are expected to engage in and lead local hospital-based patient safety initiatives and accreditation activities. This requires competence in areas such as causal analysis and sentinel event management, among others. Importantly, hospitalists should adhere to the guiding principle of *primum non nocere* (first do no harm): patients' well-being is the primary factor that drives intervention decisions. This means that testing and treatments may result in harm from purposeful "not doing" as much as "doing."

Systems improvements and personal accountability are central to developing programs to prevent or respond to medical error or patient harm. The single greatest impediment to error prevention is fear of punishment for making mistakes. It is important to recognize that not all errors may result in harm (eg, administering a double dose of intravenous ampicillin) and that not all harms are preventable (eg, vancomycin flushing syndrome caused by vancomycin). This is best balanced in a system that fosters a "just culture of safety," which encourages the reporting of errors without fear of retribution, supports learning, and focuses on proactive management of system design and behavior choices. A "just culture" distinguishes reckless human actions from at-risk behaviors or human error. Events are addressed in a compassionate, collegial manner, where "second victims"—the team members involved—are supported. This approach augments wellness and resilience for all health care professionals.

The errors reported most frequently involve medications. The most common contributing factors to these and other errors are communication failure, stress, fatigue, and distraction. Errors in patient identification, left/right confusion, and others also occur, but the reporting of these errors is limited. Diagnostic errors caused by cognitive mistakes can be addressed through group and individual interventions to improve skills and behaviors. This may include continuing medical education activities, simulation training, case discussion, self-reflection, and creation of real-time clinical decision-making and clinical algorithms. To date, health care systems have not been ranked on the basis of rates of correct treatment or diagnosis, but this is an area of intense interest.

Basic Terms and Tools

Adverse event: Any medical error, regardless of severity or cause.

At-risk behavior: A behavior choice that increases risk, such as not consistently using 2 patient identifiers when indicated. Either the risk is not recognized, or it is mistakenly believed to be justified.

Error: An inadvertent action; a slip, lapse, or mistake. Slips (incorrect action) and lapses (action forgotten) are failures due to inattention. Mistakes are errors due to failure to choose correctly (inexperience).

Failure mode and effects analysis: Error analysis conducted prospectively to determine or predict failures and the relative effects of each failure. It allows for prioritization of targets for improvement based on a number (criticality index).

Hard stop: A step in a process that must be completed to continue, such as scanning a patient identification bar code for a medication to be dispensed from a locked cabinet.

Harm: An unintended injury resulting from or exacerbated by medical care.

High-reliability organization (HRO): Any organization that operates under hazardous conditions yet has few adverse events. HROs are focused on failure, resilient when failure occurs, and attentive to operations, while they prioritize a culture of safety.

Just culture: A commitment to safety at all levels in the organization that acknowledges the high-risk, error-prone nature of an organization's activities. This is a blame-free environment that still expects personal accountability. There is an expectation of collaboration across ranks and a willingness to direct resources to address safety concerns.

Root/apparent cause analysis (RCA/ACA): A structured method used to identify and evaluate contributing or causal factors associated with adverse events or near misses, implement solutions, and monitor effects of solutions.

Sentinel event: An unexpected occurrence that involves death or serious physical or psychological injury or risk thereof. "Sentinel" means the event requires immediate investigation and response.

Trigger tool: The use of "triggers," or clues, retrospectively (eg, identification of a preceding adverse event by means of the rescue medication given) or prospectively (eg, abrupt discontinuation of a chronically used medication may lead to instability). This is an effective method for measuring the overall level of harm from medical care in a health care organization.

Selected Best Practices

Choosing Wisely: A national campaign initiated by the American Board of Internal Medicine that includes multiple statements from national societies, all focused on preventing harm and overuse by judicious and purposeful avoidance of testing and treatments. Available at https://www.choosingwisely.org/societies/society-of-hospital-medicine-pediatric.

Fatigue recognition training: Education about the effects of fatigue on cognition and motor performance, usually paired with sleep education. The training encourages self-awareness and includes prevention tips.

Peer review: A clinical review of a case with unintended or complicated outcome and/or unexpected variability compared to similar cases. The review serves to address best practices, diagnostic errors, and systems failures (eg, communication, products, environment); classify the error; and list actions to address these failures.

Postevent debrief (PED): A structured method with a checklist tool used in cases of unexpected complications, unanticipated death or harm, potential sentinel event, or staff request because of potential emotional effects on the staff. Often a first step in a formal RCA, the PED is held within 24 to 48 hours and includes front-line staff.

Safety huddles/daily safety call: Quick team briefings (often 15 minutes long) that focus on key patient safety issues with brainstorming of solutions. In a hospital ward, huddle team members may include nursing and physician leaders and other front-line staff. For a hospital system, participants may include many others from diverse clinical and nonclinical areas. Safety huddles may also be performed remotely.

Safety walk rounds: Typically, weekly rounds performed by senior leadership (eg, board members, patient safety officers, chief nursing officers) to connect with front-line staff. Common questions asked are, "Is there anything that might harm your patient today?" and "How can I help?" Focus is on immediately remediable safety issues, employing a nonpunitive, positively engaging manner.

Second victim rapid-response team: A dedicated team with knowledge and experience in supporting practitioners during the acute stages of emotional trauma in the immediate wake of a harmful error. Use of such teams can significantly aid in the recovery, wellness, and resilience of second victims.

SBAR model: A communication tool that describes the situation, background, assessment, and recommendation related to an acute event.

Stop the line: A policy and procedure that gives all staff, parents, trainees, and visitors the responsibility and authority to immediately intervene to protect the safety of a patient. All staff are expected to immediately stop and respond to the request by reassessing the patient's safety.

Time-out: Per the Joint Commission Universal Protocol, perform a time-out prior to starting a procedure. Time-outs ensure that all team members agree on the patient's identity, the anatomic site of the procedure, and the procedure

to be performed. Other elements, such as anticipated specimens, may be added by the institution.

External Reporting

Insurers may not pay for care that is necessary because of preventable harms. In addition, payment may be affected by proof of adherence to best practices and documenting better outcome. "Pay for performance" is the act of paying a provider for performing at or above a certain standard of quality for a given indicator. Some examples of external reporting include sentinel events (reported to the state), infections (reported to the state public health department), and negligent care delivery (reported to the state medical board). Each can result in mandatory action plans, on-site audits, fines, or other disciplinary or legal actions.

Pearls and Pitfalls

- Lead: Be involved in safety walk rounds or a local initiative. Support just culture and HRO attributes. Integrate safety practices and a 5-minute "safety story" into clinical rounds, conferences, and journal clubs.
- Communicate clearly: Ask clarifying questions, use tools such as SBAR when acute events occur, and use a standardized handoff tool when coming on and off service or transferring patients to other services.
- Seek patient and family input: Anticipate problems by assessing how processes will be completed by patients and families. Whenever possible, integrate patients and families into patient safety initiatives.
- Work with interprofessional teams: Engage on hospital committees and with hospital and community staff and leaders from all services and specialties.
- *Do not* use education and reminders as sole methods to address a problem. These are the least effective methods of error avoidance. Use system-embedded hard stops whenever possible.
- *Do not* fail to report "near misses" or "good catches" in your safety reporting system. These offer great insight into how to do processes well.
- *Do not* fail to perform a thorough RCA/ACA when investigating errors, using just culture. Situational, behavioral, and patient-specific issues are often lost if an RCA/ACA is not complete. Include "second victim" support.

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CHAPTER 53

Surge Planning

Introduction

Surge capacity is the ability of the health care system to expand quickly beyond normal service to meet an increased demand for medical care. Constant preparation is required for these low-frequency, high-risk events. All hospitals, even those that are non-pediatric and non-trauma, may be faced with a surge in pediatric patients due to a disaster, pandemic, or other unexpected event. Children will be brought to a local, convenient hospital and not necessarily transported to a pediatric center further away. This is especially true for community hospitals, where over 80 percent of all pediatric emergency department (ED) visits occur each day. Thus, preparing for a surge in pediatric patients is reliant on day-to-day readiness.

Structure and Leadership

A pediatric emergency care coordinator can help ensure the hospital is prepared for a surge in pediatric patients. A pediatric hospitalist can fill this role and/or work in conjunction with ED providers. It is vital that pediatric needs are integrated into the hospital's emergency operations plan, and that the plan accounts for low-capacity times (ie, nights and weekends).

During a surge, the hospital may establish a hospital incident command center—a multi-disciplinary, central information hub with the purpose of efficiently addressing issues and delegating responsibility. Under the leadership of the incident commander, the staff will provide logistical and administrative support through effective communication with the operational leaders in the hospital. This includes the mobilization and coordination of personnel, equipment, and supplies to fulfill incident objectives and needs throughout the hospital.

Whether pediatrics is a small part of a larger community hospital or the entire hospital population at a children's hospital, every pediatric hospitalist medicine group needs a disaster champion who can interact with the incident command center and be the point person for questions and issues as they arise in each area.

Capacity

Rural community hospitals often face a more significant burden during a surge event due to the limited number of hospitals in the community to share the influx of patients. Prior to the COVID-19 pandemic, hospitals were encouraged to plan for surge capacity, but there was no consensus on the

amount of capacity required. During the COVID-19 pandemic, the actual surge reached 50% or more of normal capacity in many hospitals, both rural and urban.

Hospital capacity is more than just the number of hospital beds. Rather, it is often referred to as the 4 *S*'s: Staff, Stuff, Structure, and Systems (Table 53–1).

- **Staff:** The hospital leadership needs to think beyond bedside providers when planning for capacity. Essential staff members include environmental services, food service, security, and medical records, among many others.
- **Stuff:** Stuff is all the supplies, medications, beds, and equipment needed to care for the patients. This can vary, depending on the cause of the surge.
- **Structure:** The space needed to care for patients is the structure. This is more than an open space. Is oxygen or suctioning required? How are rapid responses, codes, and other alerts called?
- **Systems:** Lastly, systems are essential to provide ongoing communication, safety, security, and support for staff working in a stressful environment. The Health and Human Services Office of the Assistant Secretary for Preparedness and Response (ASPR) has many resources available for detailed assessment and planning (https://asprtracie.hhs.gov/).

Communication

Expect that hospital-wide communications will be sent from the incident command center, in multiple modes (eg, electronic notification systems, radio, overhead paging, text, email), as communication redundancy is

Table 53–1. The 4 *S*'s of Hospital Capacity

Internal	External
Staff: Clinical and Ancillary	
Reduce demand: elective procedures and early discharges Adapted skill set: reassign providers to fill need	Retired staff Community providers/volunteers
Stuff	
Equipment: beds, cribs, ventilators, IV pumps, etc. Medications	Supplies: linen, patient supplies, personal protective equipment Food and water
Structure	
Clinical space: adapt acute care as ICU bed Nonclinical or clinic space	Other medical facility or non–acute care hospital Nonmedical facility: convention center, gym
Systems	
Electronic health record Process (medical staff, training)	Communication: information, phones, pagers Safety culture: checklists, protocols, huddles

critical during a disaster, when some of the typical means of communication have likely failed. The command center will also share information with the media, families, and community stakeholders. Effective communication is clear, concise, and provided at regularly scheduled intervals to keep staff informed of ongoing changes. In addition, group-specific communication can be coordinated through the disaster champion to keep everyone informed and provide an avenue for reporting concerns and clarifying any uncertainties.

Planning and Protocols

To function optimally during a disaster, hospitals and larger communities need to drill for disaster scenarios at least annually, with pediatric patient simulations included. During these drills, incorporate community pediatricians, emergency medical services, and other outside resources since they will perform key roles during an actual disaster. The drills need to be thoughtfully designed to match the goals of the hospital and community. They can be tabletop, discussion-based drills versus operational, real-time exercises. It is critical to consider children with medically complex and/or technology-dependent conditions, unaccompanied children, and children with mental and behavioral health issues. These exercises must include a focus on skills specific to pediatric patients.

Since many community hospitals do not have pediatric intensive care services, it is vitally important to preemptively establish transfer agreements with children's/tertiary care hospitals. Telehealth (see Chapter 54, Transport) can bring pediatric specialists virtually into the community, serving as extensions of the children's hospital when resources for transport to a higher level of care are unavailable.

Scope of Practice and Just-in-Time Training

Disasters often require staff to work outside their normal roles, routines, and comfort zones. It is necessary to consider the training and safety tools needed to support the health care team in providing safe patient care. Consider what roles a provider can be trained to do in a short period of time, but be mindful of the limitations within each group to avoid unintended adverse patient events. Develop and use protocols, pathways, and/or checklists to promote standardized, equitable, and safe care during high volume and stress. Information sharing among hospitals can provide just-in-time training, as demonstrated by the POPCoRNetwork, which rapidly established a multiinstitutional collaborative during the COVID-19 pandemic and provided education, resources, and protocols from multiple institutions.

Maintaining Safety

During a surge there is an increased risk of serious safety events due to the high volume, severity of conditions, adaptation to new roles, and fatigue. Highly resilient organizations maintain safety and minimize error through deliberate practice of key behaviors and culture. Rigorous analysis of failure and a commitment to act on even small errors is needed to avoid serious safety events. Avoid anchoring biases and explore what was missing or errant in a provider's care during the crisis. This requires a reliable and supportive communication pathway from the front line to the supervisors. Resilient leaders understand that the individuals with the necessary expertise for the current crisis may not be the ones with titles or administrative roles. Once the surge subsides, strive to understand and learn from the event, asking, "How can we continue to improve and prepare for the future?"

Wellness and Burnout

During a disaster, be aware of caregiver fatigue, as provider wellness and resiliency will be critical to the community's response and recovery. Physician wellness and burnout have a direct correlation with patient safety and quality. In addition to patient safety, the COVID-19 pandemic highlighted the effect of a crisis on health care provider burnout. Resilience studies have shown that burnout does not affect all workers equally, with women and younger health care workers most affected. To enhance wellness and reduce burnout, both during and after a crisis, focus on reducing unnecessary administrative burdens, modify work schedules to allow flexibility, use technology to limit burdens, and encourage self-care, including access to mental health services.

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CHAPTER 54

Transport

Introduction

Hospitalist involvement in pediatric interfacility transport is evolving. Pediatric hospitalists may find themselves as either the referring physician looking for a higher level of care or the physician accepting the patient at the higher-level institution.

Communication

Securing the correct care team and appropriate transport vehicle depends on complete, accurate, and timely communication. Transport programs differ in the method of access for referring physicians. Some have communication centers, whereas others have hospital-based personnel who answer the calls and organize all aspects of the transport. Either way, the safest and most efficient means to coordinate transfers is to have one telephone number with 24-hour coverage, so referring personnel can easily make contact.

On both ends, log and save all communications in the medical record. Triage decisions depend on the patient's diagnosis and whether the proposed receiving hospital has the higher-level capabilities desired. Personnel answering the telephone must know to whom to route the call (hospitalist, emergency department [ED], or intensive care unit [ICU] attending physician). See the Criteria for Critical Care of Infants and Children (Hsu and colleagues in the Bibliography) for decisions regarding when to refer a child to a pediatric ICU. The fourth edition of the AAP *Guidelines for Air and Ground Transport of Neonatal and Pediatric Patients* (see Bibliography) has a sample intake form (in Figure 5.3).

Transport Team Composition

Transport teams vary among institutions, with several possible combinations that include physicians, nurse practitioners (NPs), registered nurses (RNs), physician assistants, respiratory therapists, emergency medical technicians (EMTs), and paramedics. The medical control physician (MCP), along with the accepting and referring physicians, assesses the patient's needs and determines the team composition accordingly.

There are 3 levels of transport: basic life support (BLS), advanced life support (ALS), and critical care transport. Individual state pediatric guidelines vary, with some more stringent than others. BLS transports involve only EMTs, usually no medications or intravenous (IV) fluids, and minimal oxygen

administration. EMTs are trained in basic cardiopulmonary resuscitation, and just a small part of their training and encounters involves children. ALS transport teams involve paramedics and/or RNs and can administer various medications, infuse IV fluids, provide oxygen, and maintain temperature control. Critical care transport teams include specialized RNs, NPs, and/or physicians and can address higher-level, critical care needs, often for patients with one or more failing organ systems. Critical care transport teams can be hospital based or a service provided by an ambulance or air transport company, which may have limited pediatric experience. Therefore, it is important to know their skill set before summoning them.

Using a specialized hospital-based team improves patient outcomes, although this does not necessarily mean that a physician must be present. However, if response time is crucial (ie, the patient requires an emergent procedure that can only be performed at the accepting institution), then it may be more effective to send a BLS team, which can be mobilized in much less time than an entire critical care team. In addition, sending a critical care team for a patient with simple medical needs can be an inefficient use of resources. It is always helpful to speak with the referring physicians and understand their preferences.

When accepting a patient from a private practitioner's office or clinic, consider whether there is a risk of inadvertently exposing the child to a lower level of care during transit to the hospital. The referring and accepting providers may decide that the safest approach would be using local emergency medical services to transport the patient to a nearby ED, as this is often the faster approach.

It is imperative to choose the correct transport team composition, as patient deterioration occurs in approximately 10% of transports. This can be a challenging process, often influenced by varying levels of experience, insufficient communication, and inaccurate assessment of a child's clinical status. Applying an objective scoring system, such as the Pediatric Transport Triage Tool, can help decrease resource utilization, with fewer transport nurses and physicians needed on calls, and less frequent use of rotor-wing transports.

Referral hospitals must abide by the federal Emergency Medical Treatment and Labor Act, which requires hospital personnel to evaluate all patients who arrive with emergent conditions and to stabilize them before transfer. The MCP must review the case with the referring physician when deciding about the proper composition of the transport team, personnel, and mode. Once the receiving hospital accepts a patient, the medicolegal responsibility becomes shared. Therefore, the MCP must work in conjunction with the referring physician to help make these decisions.

Role of the MCP

Once the transport team arrives at the bedside, the MCP can begin to care for the patient and provide advice to the referring physician about the continuing evaluation and management of the child. However, the referring provider retains authority and ultimate responsibility for the care of the patient until the transport team leaves their facility. At this point, the MCP may also need to consult with subspecialists. It is important for the MCP to have easy communication with the transport team (via radio or cell phone), especially when difficult situations or questions arise. It is also vital that the MCP has knowledge of the transport environment and equipment.

Of note, state regulations may dictate who can act in the role of MCP. In many cases, it can be any pediatrician, but in some states, it needs to be a critical care or ED physician. The role of an MCP is evolving, though, and with the increased presence of pediatric hospitalists who are familiar with transport program protocols and the transport environment, a program can rely on the hospitalist to act as the primary MCP.

Telemedicine

Telemedicine can be particularly useful when caring for sick children, given the regionalization of care, with many hospitals being distant from pediatric inpatient and intensive care units. Compared to telephone consultations, activating telemedicine can improve the quality of care in the ED, especially when the patient is critically ill and/or in a rural or underserved setting. Telemedicine can play a key role in helping to stabilize critically ill children at referring sites, enhancing the concept of a "mobile ICU." Telemedicine can also assist with disposition and resource utilization and potentially lead to cost savings, if it is determined that transfer to a specialty site is not necessary.

One significant barrier when using the internet for telemedicine is the Health Insurance Portability and Accountability Act (HIPAA). Use encryption software or a virtual private network and consult with the hospital's legal department to ensure the best way to achieve HIPAA compliance.

Equipment

Do not assume that the referring hospital can provide any of the equipment required for transport. Rather, develop and maintain a supply of dedicated specialized storage packs designed to cover pediatric critical care needs for all age and weight ranges. The fourth edition of the AAP *Guidelines for Air and Ground Transport of Neonatal and Pediatric Patients* has sample supply lists (in Tables 6.1, 6.2, and 6.3). Know what supplies accompany every transport and

which additional supplies you may need to request for a given service. Check the equipment daily to ensure that oxygen and battery supplies are sufficient for the expected duration of any potential transport.

Vehicle Selection

The 3 different types of vehicles are ambulance, fixed-wing plane, and helicopter. The MCP makes the decision about which vehicle to use, in coordination with the referring hospital. Selection criteria include severity of the illness or injury, distance to the referring hospital, travel time required, weather conditions, vehicle and staff availability, equipment needs, and expense. Factors to keep in mind when considering whether or not to fly are that fixed-wing planes require several ambulance transfers, flying at certain altitudes can affect partial pressure in body cavities and increase the volume of entrapped air, and space is a constraint in air transport, so equipment and personnel may be limited.

Safety

Safety is a priority with each transport. Air transport may be faster but carries inherent risks, including weather, mechanical failure, and collisions. Weather plays a significant role in all modes of transport. The Commission on Accreditation of Medical Transport Systems offers guidelines for minimal safe weather conditions. If a transport is delayed because of weather, the MCP must continue to guide the management of the patient until a transport can take place. In addition, advise ambulances not to use lights and sirens, because the data indicate that this has no positive effect on patient outcome.

Quality Improvement

As in other areas of medicine, quality improvement is an essential part of a pediatric transport program, to ensure that the team is providing high level, safe, timely, and quality care for all patients. The goals are to identify and review quality metrics, evaluate concerns, review serious adverse events, and plan strategies for improvement.

Until 2014, each transport program was expected to create its own set of quality metrics to track, and there was no standard against which to compare those metrics. In 2014, the Ground and Air Medical Quality Transport (GAMUT) database was created to overcome this obstacle (http://gamutqi.org/index.html). It is a free resource for transport teams to track, report, analyze, and compare their performance on 27 specific quality metrics.

COVID-19 and Transport

The COVID-19 pandemic presents transport teams with unique challenges. Communication and the intake process become even more critical, as the personnel taking the initial calls need to thoroughly assess the patient for signs, symptoms, and risk factors of acute COVID-19 disease. They then need to share those facts with the transport and receiving hospital providers. Personal protective equipment is essential and must be provided to the entire transport team. Bag valve masks and other ventilatory equipment must be equipped with high-efficiency particulate-absorbing (HEPA) or other viral filters. Essential safety protocols include masking the patient (even over masks/tubing); keeping the driver and patient compartment separated, if possible, with doors and windows shut or all air vents and ventilation fans on; and decontaminating the vehicle and equipment after every use.

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CHAPTER 55

Utilization Management

Introduction

Utilization management, or utilization review, refers to the process of ensuring high-quality, evidence-based care through case-by-case assessments of medical necessity. This process occurs within hospital systems and with payors (insurance companies). For hospitalized patients, utilization review occurs at the time of admission. Admission status (inpatient or observation) is determined by the admitting physician and communicated to the payor along with supporting clinical documentation.

Denials may occur during, or even after, the admission if the payor deems that the care provided did not meet the qualifications of medical necessity, which is determined by severity of illness, risk of mortality, and intensity of services provided, as well as standard clinical guidelines. Peer-to-peer conversations and the appeals process are often available to rebut these denials. In pediatrics, the patient's admission status rarely affects the location or quality of care provided, and therefore many physicians are not formally educated on the principles of utilization management.

Admission Status

According to the Centers for Medicare and Medicaid Services (CMS), the admitting provider is responsible for determining the patient's admission status. The 4 most common hospital statuses are inpatient, observation, extended recovery/same day surgery care, and outpatient in a bed. As many providers are not familiar with the differences among these, utilization review/management or case management departments within hospitals often help guide these decisions. Milliman Care Guidelines (MCG) and InterQual are the 2 national guidelines most often used by hospital systems and payors. These evidence-based guidelines serve as screening tools to determine patient status based on medical necessity. A basic knowledge regarding common diagnosis and applicable MCG and InterQual criteria can be helpful in improving appropriate status assignment at the time of admission. These criteria are typically updated annually and may change.

Inpatient Admission

An inpatient admission is appropriate when the intensity of services, patient's risk of mortality, and severity of illness can only be safely provided or cared for in the inpatient hospital setting. Unlike adults, Medicare's "two midnight rule" often does not apply to pediatric patients. The length of stay for a hospitalized

child does not always correlate with the acuity of the illness, so a patient may be admitted as an inpatient and have a hospital stay of less than 48 hours or "two midnights." Patient status is determined at the time of admission. Therefore, if a patient has an unexpected recovery but was acutely ill at the time of admission, inpatient status is still appropriate. Within inpatient status, there are subcategories of level of care. These can be defined as *acute* or *med/surge, intermediate,* or *intensive care*. Higher levels of care are applied if a patient's condition requires more than *routine* inpatient care, such as intermediate or intensive levels of care. These classifications and typical applicable services provided are defined in both the MCG and InterQual criteria.

Generally, inpatient hospital care is reimbursed at a higher rate than observation hospital care. Depending on their insurance benefits, the patient and family may have more financial liability in observation care. As institutional and state regulations vary on observation and inpatient status assignments, refer to your individual state Medicaid provider manual for specific regulations.

Observation Care

Observation care is defined by CMS as "a well-defined set of specific, clinically appropriate services, which include ongoing short-term treatment, assessment, and reassessment, that are furnished while a decision is being made regarding whether clients will require further treatment as hospital inpatients or if they are able to be discharged from the hospital." Generally, observation care is appropriate when further monitoring for either progression or rapid improvement in patient symptoms is required. Observation care is considered an outpatient service and can occur in a variety of locations, including on dedicated observation units or intermingled among inpatient beds. Physicians often use the term "observation" as synonym for "monitoring," while payors interpret this as a determination of patient status. To avoid confusion, do not use the word "observation" in your documentation.

Extended Recovery or Same Day Care/Surgery

This is used for a patient recovering from a planned surgical procedure. If the procedure was completed with no complications and the patient is recovering as expected, the patient can be placed in a hospital bed to complete recovery under the status of *extended recovery*. If the procedure was complicated, or the patient is experiencing symptoms that were not expected following surgery, the patient may qualify for either observation or inpatient status depending on the specific details of the case. Extended recovery payment is bundled into the procedure reimbursement, and no additional reimbursement is provided to the hospital for extended recovery time.

Outpatient in a Bed

This is used for a procedure or evaluation that is routinely performed in a clinic but in some circumstances must be completed in a hospital. An example is a patient who has a regularly scheduled blood transfusion on Mondays. When there is a holiday on a Monday and the clinic is closed, the patient may be placed in a hospital bed to receive that service. Despite higher resource utilization of the hospital for this service, the reimbursement is provided at a rate similar to the ambulatory reimbursement for that service. This status is the least commonly used and may not be available at every hospital.

Fortunately, it is not necessary for physicians to explicitly memorize MCG or InterQual criteria. It is the responsibility of the hospital's utilization management department to assist in the process of assigning appropriate status. At the same time, clinicians must focus on documenting clearly, and in detail, the severity of the patient's illness (eg, desaturations, presence of retractions, intravenous [IV] pain medications), the hospital services required (eg, frequent laboratory or vital sign monitoring, supplemental oxygen), and the reason for continued hospitalization each day. With accurate, timely, and detailed documentation, the most appropriate status can be correctly assigned to the patient at admission. However, be careful when completing templated admission and progress notes, as they may not accurately reflect the patient's status.

Denials

There are a number of types of denials that the caring physician may receive when the care provided is questioned by the payor's medical director. Payors may deny inpatient admission as not medically necessary but may approve observation services. Occasionally, payors deny certain days of an inpatient admission if there is no documentation to support continued medical necessity. A "delay in care" denial occurs if it is perceived by the payor that care should have been coordinated more expeditiously.

Physicians are often asked by the hospital to assist in justifying the admission or treatment plan to the payor. This typically occurs in a peer-to-peer discussion between the payor's medical director and the treating provider. To prepare for a successful peer-to-peer discussion, review the documentation, services provided (IV fluids or pain medications, oxygen), patient's severity of illness (tachypnea, retractions, altered mental status, hypoxia), and underlying comorbidities. The hospital's utilization management or case management department may be able to provide applicable MCG or InterQual guidelines for the patient's specific diagnosis, which can then support your clinical judgment on medical necessity. Present a detailed summary of events

to the payor's medical director to accurately justify the indications for admission or continued hospitalization.

Occasionally, the medical director may not have received the necessary documentation or does not have the pediatric expertise to fully understand the complexities of care. This is the time to share those additional details of the patient's specific case and/or pediatric evidence-based criteria or standards of care. If the peer-to-peer conversation is unsuccessful, it may be necessary to a write an appeal letter that summarizes the hospitalization in detail. It can be submitted on the patient's behalf by the hospital or the treating physician.

This additional work is often completed by the hospital's physician advisor, who can assist providers and hospital systems in understanding the complexities of the denials process and interactions with the payors. In pediatrics, this role is relatively new. Given the unique characteristics of pediatric illnesses, pediatric-trained physician advisors combine MCG and InterQual criteria along with their broad medical knowledge to justify medical necessity to payors and relieve this administrative burden on the practicing physicians. Many payors allow a physician advisor to complete peer-to-peer conversations on behalf of the treating physician. For certain payors who do not allow this, the physician advisor can familiarize the treating physician with the appropriate criteria to reference during a peer-to-peer conversation. Additionally, physician advisors support documentation improvement through physician education and improve hospital operations.

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Immunology and Rheumatology

CHAPTER 56

Arthritis Associated With Systemic Disease

Introduction

Arthritis is inflammation of a joint, characterized by swelling, erythema, tenderness, and warmth. A number of etiologies of arthritis are associated with systemic illness that may necessitate hospitalization. These include systemic juvenile idiopathic arthritis (sJIA), acute rheumatic fever (ARF), poststreptococcal arthritis (PSA), reactive arthritis, disseminated gonococcal infection (DGI), and serum sickness (SS) or serum sickness–like reactions (SSLRs). The differential diagnosis for arthritis syndromes appears in Table 56–1.

Septic arthritis, Lyme disease, and gonococcal arthritis are discussed in more depth in Chapter 94, Osteomyelitis and Septic Arthritis.

Acute Rheumatic Fever

Clinical Presentation

Acute rheumatic fever is a diffuse inflammatory process triggered by group A streptococcal (GAS) pharyngitis. Children aged 5 to 15 years are most commonly affected, typically 10 to 28 days after the acute GAS infection. The arthritis is typically migratory and predominantly affects the large joints. In three-quarters of cases, ARF is an acute febrile illness with arthritis/arthralgia and carditis. Less commonly, ARF presents with chorea and carditis without fever or arthritis/arthralgia.

History

Arthritis is often the earliest sign of ARF, beginning 2 to 4 weeks following pharyngitis. Inquire about the location(s), migration, and time line of arthritis, especially of the large joints. Typically, symptoms start in one joint and progress to involve other joints every few days, as the previously affected joints start to improve. Ask about response to treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), which is prompt, with some degree of improvement within hours of the first dose. Inquire about fever and rash, which may suggest erythema marginatum—pink, evanescent, serpiginous lesions that enlarge centrifugally. Ask about skin lumps that may indicate subcutaneous nodules, which are firm, painless, and symmetrically present on the extensor surfaces without overlying skin changes. Inquire about involuntary

Table 56–1. Arthritis Syndromes in Children

Sign/Symptom	Clinical Features
Acute Rheumatic Fever	
Arthritis	Migratory, asymmetric polyarthritis, severely painful, 2–4 weeks postinfection Dramatic response to NSAIDs/ASA
Fever	Common
Rash	Erythema marginatum (evanescent)
Trigger	Recent GAS pharyngitis
Carditis	Valvulitis, pancarditis, prolonged PR interval
Other	Meets Jones criteria (Table 56–2)
Disseminated Gonococcal Infection	
Arthritis	Tenosynovitis, polyarthralgias
Fever	Common
Rash	Petechial, pustular
Etiology	*Neisseria gonorrhea* infection
Synovial fluid	WBC 2,000–50,000/mL ($2–50 \times 10^9$/L) with neutrophil predominance
Henoch-Schönlein Purpura	
Arthritis	Arthritis or arthralgias of knees/ankles
Fever	Uncommon
Rash	Lower extremity petechiae, palpable purpura
Vasculitis	Abdominal pain, immunoglobulin A nephropathy, hematuria
Complications	Intussusception, gastrointestinal bleeding
Inflammatory Bowel Disease	
Arthritis	Spondylitis, sacroiliitis, enthesitis, peripheral arthritis
Fever	Variable
Rash	Erythema nodosum
Other	Failure to thrive, weight loss, anemia, iritis, uveitis Abdominal pain, diarrhea, bloody stools, rectal fissure
Kawasaki Disease	
Arthritis	Arthralgia is more common than small joint arthritis, progressing to large joint arthritis
Fever	Minimum 5 days with marked irritability
Rash	Polymorphous, palmar/plantar erythroderma
Cardiac	Coronary artery dilation or aneurysms
Other	Nonpurulent conjunctivitis, inflamed oropharynx, hand/foot dorsal edema Unilateral cervical lymphadenopathy
Complications	Coronary artery aneurysms
Langerhans Cell Histiocytosis	
Fever	Common
Rash	Chronic seborrhea-like rash, otorrhea

Table 56–1. Arthritis Syndromes in Children, continued	
Sign/Symptom	**Clinical Features**
Arthritis	Lytic bone lesions are more common
Other	Failure to thrive, weight loss, hepatosplenomegaly, lymphadenopathy
Leukemia, Lymphoma	
Arthritis	Bone pain is more common
Fever	Common
Rash	Variable
Other	Weight loss, fatigue, hepatosplenomegaly, lymphadenopathy, pancytopenia
Lyme Arthritis	
Arthritis	Mono- or oligoarticular weeks to months following infection Knee without erythema; no joint destruction
Fever	Uncommon
Rash	Erythema migrans
Etiology	Bite of tick infected with *Borrelia burgdorferi*
Other	Headache, photophobia, cranial nerve VII palsy, myalgias
Synovial fluid	WBC 20,000–30,000/mL ($20–30 \times 10^9$/L) with neutrophil predominance
Poststreptococcal Arthritis	
Arthritis	Persistent, additive, nonmigratory, 1–2 wk postinfection
Fever	Variable
Trigger	Recent GAS pharyngitis
Carditis	If present, consider ARF
Other	Does not meet Jones criteria Poor response to NSAIDs/ASA
Reactive Arthritis	
Arthritis	Arthritis: mono- or oligoarthritis of lower extremities or sacroiliac joint 1–4 wk postinfection
Fever	Uncommon; presence may relate to precipitating infection
Rash	Balanitis circinata, keratoderma blennorrhagica
Trigger	Recent enteric infection (*Salmonella, Campylobacter, Shigella, Yersinia*) Recent genitourinary infection (*Chlamydia*)
Other	Conjunctivitis, uveitis, urethritis, enthesitis, dactylitis
Septic (Pyogenic) Arthritis	
Arthritis	Monoarticular, large joints
Fever	Common, high
Rash	Rare
Etiology	*Staphylococcus aureus,* GAS
Other	Ill appearance with severe and persistent pain
Synovial fluid	WBC > 50,000/mL (> 50×10^9/L) with neutrophil predominance

Continued

Table 56–1. Arthritis Syndromes in Children, continued	
Sign/Symptom	**Clinical Features**
Serum Sickness/Serum Sickness-Like Reaction	
Arthritis	Elbows, knees, ankles are most commonly affected
Fever	High fever
Rash	Urticarial, targetoid, or morbilliform Persistent, urticaria-like, may develop central clearing or purpura
Trigger	Exposure to new medication during previous 5–14 d
Other	Improvement within 48 h of removing offending agent
Systemic Juvenile Idiopathic Arthritis	
Arthritis	Polyarthritis, large effusions, relatively less painful, worse with disuse
Fever	High-spiking quotidian, in evenings
Rash	Evanescent salmon-colored macular
Other	Hepatosplenomegaly, lymphadenopathy, serositis, elevated ESR
Complications	MAS including persistent fever, consumptive coagulopathy Paradoxical decline in ESR, ferritinemia, liver dysfunction, hypertriglyceridemia
Systemic Lupus Erythematosus	
Arthritis	Painful, symmetric, polyarthritis; small and large joints
Fever	Common
Rash	Malar, photosensitive, alopecia, oral ulcers
Serositis	Pericarditis, endocarditis, pleuritis
Other	Hepatosplenomegaly, lymphadenopathy, nephritis, hemolytic anemia, thrombocytopenia, immune deficiency
Complications	Renal failure, cerebritis, pleural/pericardial effusion, heart failure
Toxic Synovitis	
Arthritis	Arthralgia, most common in hip
Fever	Common, low grade
Rash	None
Trigger	Viral infection or idiopathic
Other	Rhinorrhea, pharyngitis, mild increase in CRP/ESR
Viral Infection	
Fever	Common
Rash	Common, maculopapular
Arthritis	Symmetric polyarthritis or polyarthralgia
Other	Prodrome of fever, fatigue, pharyngitis, headache
Triggers	Parvovirus B19, rubella (or rubella vaccine), hepatitis B, arboviruses

Abbreviations: ARF, acute rheumatic fever; ASA, acetylsalicylic acid; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GAS, group A *Streptococcus;* MAS, macrophage activation syndrome, NSAID, nonsteroidal anti-inflammatory drug; WBC, white blood cell.

jerking movements, which suggest Sydenham chorea. Chorea typically presents 1 to 6 months after GAS infection and is often an isolated finding. Review a history of recent infections, especially pharyngitis, and antibiotic use.

Physical Examination

Fever is variably present. Inspect the large appendicular joints (knees, ankles, elbows, wrists) and perform inspection, palpation, and passive/active range-of-motion testing to identify effusions, warmth, mobility, and tenderness. Inspect the skin for erythema marginatum, and auscultate for the characteristic murmurs of mitral regurgitation (holosystolic, loudest at apex) or aortic regurgitation (early diastolic murmur at base of heart). Palpate for subcutaneous nodules on extensor surfaces of the elbows (olecranon), wrists, knees, occipital region, and spinal processes.

Laboratory Workup

Assess the patient for evidence of recent streptococcal infection using a rapid antigen test, throat culture, or elevated or rising streptococcal antibody titers such as ASO and anti-deoxyribonuclease-B (upper limit of normal varies by age, so refer to the specific laboratory reference ranges). Obtain an erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), which are markedly elevated. Order an electrocardiogram to evaluate the PR interval and echocardiogram with Doppler to evaluate for carditis.

Differential Diagnosis

The modified Jones criteria establish the diagnosis: evidence of a recent GAS infection and 2 major criteria or 1 major and 2 minor criteria (Table 56–2). The differential diagnosis of ARF is summarized in Table 56–1.

Treatment

Nonsteroidal anti-inflammatory drugs are highly effective, with dramatic relief of ARF-associated arthritis. Prescribe oral ibuprofen 30 mg/kg/d administered in 3 daily doses (maximum single dose, 800 mg; maximum daily dose, 2,400 mg) or naproxen 10 to 15 mg/kg/d administered in 2 daily doses (maximum daily dose, 1,000 mg) until the arthritis symptoms completely resolve (typically 2–6 weeks). Administer intramuscular (IM) penicillin G benzathine (600,000 U IM for patients < 27 kg; 1.2 million U IM for patients > 27 kg). Arrange for long-term IM penicillin, at the same weight-based dose every 3 to 4 weeks, as prophylaxis of GAS infection, which may exacerbate existing carditis. Rheumatology and cardiology consultations are indicated for ongoing monitoring of arthritis and carditis, respectively.

Table 56–2. Revised Jones Criteria for Rheumatic Fever	
For All Patient Populations With Evidence of Preceding GAS Infection	
Diagnosis: Initial ARF	2 major manifestations or 1 major plus 2 minor manifestations
Diagnosis: Recurrent ARF	2 major manifestations or 1 major and 2 minor manifestations or 3 minor manifestations
Major Criteria	
Low-Risk Populations[a]	**Moderate and High-Risk Populations**
Carditis[b]—clinical and/or subclinical	Carditis—clinical and/or subclinical
Arthritis—polyarthritis only	Arthritis—monoarthritis or polyarthritis; polyarthralgia[c]
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
Minor Criteria	
Low-Risk Populations[a]	**Moderate and High-Risk Populations**
Polyarthralgia	Monoarthralgia
Fever (≥ 38.5 °C [≥ 101.3 °F])	Fever (≥ 38 °C [≥ 100.4 °F])
ESR ≥ 60 mm in the first hour and/or CRP level ≥ 3.0 mg/L (≥ 28.58 nmol/L)[d]	ESR ≥ 30 mm in the first hour and/or CRP level ≥ 3.0 mg/L (≥ 28.58 nmol/L)
Prolonged PR interval	Prolonged PR interval

Abbreviations: ARF, acute rheumatic fever; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GAS, group A *Streptococcus*.

[a] Low-risk populations are those with ARF incidence ≤ 2 per 100,000 school-aged children or all-age rheumatic heart disease prevalence of ≤ 1 per 1,000 population per year.

[b] Subclinical carditis indicates echocardiographic valvulitis.

[c] Should only be considered as a major manifestation in moderate- to high-risk populations after exclusion of other causes. Additionally, joint manifestations can only be considered in either the major or minor categories, but not both in the same patient.

[d] The CRP value must be greater than the upper limit of normal. Also, because ESR may evolve during the course of ARF, peak ESR values should be used.

From Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography. A scientific statement from the American Heart Association. *Circulation.* 2015;131(20):1806–1818.

Disseminated Gonococcal Infection

Clinical Presentation

Disseminated gonococcal infection occurs in up to 3% of patients with a urogenital infection with *Neisseria gonorrhoeae,* particularly in a patient with an asymptomatic mucosal infection. Disseminated gonococcal infection presents with tenosynovitis, rash, and polyarthralgia. Less common features of DGI include endocarditis, hepatitis, meningitis, and, rarely, osteomyelitis.

History

Inquire about fever, myalgias, and joint, genitourinary, and dermatologic complaints. Ask specifically about distal joints and tendon pain. The rash may be pustular, vesicular, bullae (sometimes hemorrhagic), or it may present as tender purpuric papules. Inquire about recent sexual activity, sexually

transmitted infections (STIs), and unprotected sexual intercourse of any type within the past few weeks. Ask about dysuria and penile or vaginal discharge.

Physical Examination

Fever and myalgias are common, and polyarthralgia is more frequent than arthritis. Examine for enthesitis (inflammation at tendon insertions) with special attention to the Achilles tendon. Perform a complete skin examination, looking for erythematous pustules or tender papules on the fingers, arms, legs, trunk, or scalp. Auscultate for cardiac murmurs, examine the right upper quadrant for hepatomegaly or tenderness, and check for meningismus. Perform a genitourinary examination, looking for urethral, penile, or vaginal discharge. In a sexually active female, evaluate for cervical discharge or cervicitis.

Laboratory Workup

Obtain a nucleic acid amplification test (NAAT) for *N gonorrhoeae* of urine, vaginal swab, pharyngeal swab, or rectal swab, which are likely to be diagnostic. If gonococcal arthritis is suspected, aspirate the joint fluid. It will have 2,000 to 50,000 WBCs/mL ($2–50 \times 10^9$/L), with subsequent brisk growth of gram-negative diplococci in culture. If *N gonorrhoeae* infection is confirmed, perform testing for other STIs, including *Chlamydia trachomatis.*

Differential Diagnosis

See Table 56–1.

Treatment

Treat with intravenous ceftriaxone (< 45 kg, 50 mg/kg/dose once daily; > 45 kg, 1,000 mg once daily). After clinical improvement, transition to oral cefixime 8 mg/kg/d (maximum dose, 400 mg) or cefpodoxime 5 mg/kg/dose administered every 12 hours (maximum dose, 200 mg) for 1 to 2 weeks of total therapy. Treat any additional identified STIs, and refer sexual partners for treatment.

Poststreptococcal Arthritis

Clinical Presentation

Poststreptococcal arthritis develops about 7 to 10 days after a nonarticular GAS infection. Children aged 8 to 14 years are most likely to be affected, and they notably do not meet the modified Jones criteria for ARF. In contrast to ARF-associated arthritis, PSA is commonly nonmigratory, persistent, and additive. It may affect any joint (small or large) and is minimally responsive to acetylsalicylic acid (ASA) or NSAIDs. The arthritis symptoms may persist for months.

History

Ask specifically about large, small, and axial joints. Review any recent infections, especially pharyngitis. Note the time interval between pharyngitis and the onset of arthritis and the response to NSAIDs, which will be only partial.

Physical Examination

Fever and rash are typically absent. Examine all joints for tenderness, erythema, and warmth. Examine the heart for any signs of carditis, and, if present, consider the diagnosis of ARF rather than PSA.

Laboratory Workup

Evaluate for evidence of recent streptococcal infection, including a rapid antigen test, throat culture, anti-streptolysin O (ASO), deoxyribonuclease-B, (DNase-B) or other streptococcal antibodies. The ESR and CRP are relatively less elevated than in ARF.

Differential Diagnosis

See Table 56–1.

Treatment

In contrast to ARF, PSA does not respond as well to ASA or NSAIDs. Consult a rheumatologist and cardiologist for ongoing outpatient monitoring, as there is some risk for development of carditis and valvular heart disease, which may need antibiotic prophylaxis.

Reactive Arthritis

Clinical Presentation

Reactive arthritis results from an immune reaction to an extra-articular infection, most often urethral, genital, or enteric. Common predisposing pathogens include *C trachomatis, Salmonella, Campylobacter, Yersinia,* and *Shigella* species. Reactive arthritis occurs more commonly in males (3:1) and is more severe among HLA-B27–positive patients. Arthritis begins 1 to 4 weeks after the predisposing infection, so that the patient may or may not still have signs of acute infection, such as gastroenteritis or pelvic inflammatory disease. Symptoms last for weeks to months.

History

Inquire about joint, ophthalmologic, genitourinary, and dermatologic complaints. Note any low back pain, which may suggest sacroiliitis. Ask about dysuria, urinary frequency, and urethral discharge, which suggest urethritis. Inquire about conjunctivitis and eye discharge, the most frequent ocular

manifestations of reactive arthritis. Inquire about skin changes, especially on the genitals, palms, and soles. Note any signs of autoimmune disease, including fatigue, weight loss, and fever. Ask about a family history of autoimmune disease, which may indicate HLA-B27 positivity. Inquire about recent infections, especially gastrointestinal infections, as well as recent sexual activity, signs of STI, and, in an adolescent female, rubella vaccination.

Physical Examination

Monoarthritis or asymmetric oligoarthritis most commonly affects the knees, ankles, feet, and sacroiliac joints. Examine for enthesitis, with special attention to the Achilles tendon and plantar aponeuroses. Examine the digits for dactylitis, and perform an eye examination for conjunctivitis and photophobia, which indicates uveitis. Inspect the palms and soles for keratoderma blennorrhagica (vesiculopustular waxy lesions with yellow-brown color, which coalesce into plaques). In a sexually active male, perform a genital examination, looking for balanitis circinata (shallow serpiginous penile ulcerations of the glans penis) and urethral discharge. In a sexually active female, perform a pelvic examination, looking for cervical discharge, cervicitis, and urethral discharge (see Chapter 3, Sexually Transmitted Infections).

Laboratory Workup

Reactive arthritis is a clinical diagnosis that may be suspected by a thorough evaluation for the typical predisposing infections. Send a NAAT of urine or cervical swab for *C trachomatis* in a sexually active patient. Obtain a stool culture or gastrointestinal pathogen panel in a child with enteritis.

Differential Diagnosis

See Table 56–1.

Treatment

Provide supportive care with rest and oral NSAIDs (ibuprofen 30 mg/kg/d administered in 3 daily doses [maximum single dose, 800 mg; maximum daily dose, 2,400 mg] or naproxen 10 to 15 mg/kg/d administered in 2 daily doses [maximum daily dose, 1,000 mg]). Consult a rheumatologist for symptom monitoring, as a substantial proportion of patients develop chronic disease. Treat identified STIs and ensure partner treatment.

Serum Sickness/Serum Sickness–Like Reaction

Clinical Presentation

Serum sickness is a type III hypersensitivity reaction that occurs after repeated exposure to a medication, pathogen, or autoantigen. Well-described triggers

include rituximab, bee stings, antisera for rabies and tetanus, and antivenom for snake bites. Serum sickness is characterized by complement activation with immune complex formation and subsequent tissue injury and small vessel vasculitis. Symptom onset is 1 to 2 weeks after exposure.

Serum sickness–like reaction describes a similar but less severe illness that is more common in children. There is no hypocomplementemia, immune-complex formation, or vasculitis. This reaction occurs after repeated exposure to a medication such as antibiotics, antiepileptic drugs, chemotherapeutic agents, antidepressants, antihypertensives, and/or NSAIDs. Symptom onset is 5 to 10 days after exposure, which is slightly more rapid than SS.

History

A suggestive history includes some combination of fever, polyarthritis, polyarthralgia, rash (often pruritic), peripheral and facial edema, and localized lymphadenopathy. More severe symptoms are consistent with SS rather than SSLR. Urticarial-like rash and low-grade fevers suggest SSLR. Inquire about recent drug exposures, especially those occurring 1 to 3 weeks prior to symptom onset.

Physical Examination

Examine all joints for evidence of inflammation, with the elbows, knees, and ankles being the ones most commonly affected. Facial and periorbital edema may be present, but there is no enanthem. Perform a careful skin inspection for a macular, urticarial, morbilliform, or targetoid rash. Urticarial-type lesions often begin in flexural areas and then generalize. Unlike true urticaria, individual lesions may persist for days. They evolve centrifugally and may develop central clearing or slight purpura. Palpate for lymphadenopathy. Mucous membrane involvement is notably absent.

Laboratory Workup

Obtain a CRP, ESR, complete blood cell count (CBC), serum electrolytes, blood urea nitrogen, creatinine, and liver panel for a patient with suspected SS and SSLR. Also send complement levels if SS is possible.

Differential Diagnosis

See Table 56–1.

Treatment

Immediately discontinue the inciting medication. The arthralgias and fever will remit within 48 hours, and no new rash will appear. Give oral NSAIDs (ibuprofen 10 mg/kg/dose administered every 6 hours; maximum dose, 600 mg; maximum daily dose, 2,400 mg) and antihistamines (diphenhydramine

1 mg/kg/dose every 6 hours; maximum dose, 50 mg) for symptomatic relief. For severe or persistent symptoms, administer intravenous glucocorticoids, with transition to oral steroids after improvement. If the diagnosis is uncertain, obtain dermatologic and/or rheumatologic consultation.

Systemic Juvenile Idiopathic Arthritis

Clinical Presentation

Juvenile idiopathic arthritis (JIA) is the most common rheumatologic disease in children, whereas sJIA is the most likely JIA subtype to be encountered by the hospitalist. The peak onset is at 2 years of age, with a range between 1 and 5 years of age. Whereas the diagnosis of most JIA subtypes does not require fever, sJIA is the exception. It can be suspected after 2 weeks of fever and confirmed after 6 weeks of arthritis. Importantly, sJIA is a diagnosis of exclusion that is typically identified after a thorough evaluation for infectious and neoplastic etiologies of fever.

The presentation typically begins with daily fevers, often prior to the onset of arthritis. Some children will also have hepatomegaly, splenomegaly, lymphadenopathy, and serositis, which may raise the suspicion of a malignancy. Of utmost importance is recognizing the most severe acute complication of sJIA, macrophage activation syndrome (MAS), which may be the initial presentation and carries a mortality rate of 20% to 30%. Macrophage activation syndrome affects 5% of children with sJIA and is characterized by persistent fever, pancytopenia, consumptive coagulopathy, ferritinemia, and liver dysfunction.

History

Determine the timing, onset, duration, and intensity of symptoms. The fever of sJIA typically is 2 or more weeks of daily (quotidian) or twice-daily high-spiking fevers, usually during the evening, which then spontaneously regress. The patient may develop an evanescent, salmon-colored macular rash in the presence of fever or with exposure to warm water (eg, a bath), and the rash may be pruritic. The arthritis of sJIA may be rapidly progressive and destructive. It affects at least 2 peripheral joints concurrently, most commonly the knees, ankles, and wrists. Other involved joints include the hands, cervical spine, temporomandibular joint, and hips. Morning stiffness or "gelling" with inactivity is suggestive of sJIA. The stiffness improves slowly with use.

Ask about symptoms of autoinflammatory disease, including weight loss, fatigue, and hair and nail changes. Inquire about a family history of autoimmune diseases.

Physical Examination

Complete a thorough physical examination, including all peripheral joints, as well as the temporomandibular joint, sacroiliac joint, and vertebral articulations. Perform inspection, palpation, and passive/active range-of-motion testing to identify effusions, warmth, mobility, and tenderness, and compare with the contralateral side. Examine all tendons for enthesitis, including warmth, tenderness, and swelling. Check the fingers for rheumatoid nodules and contractures. Clubbing or fingertip erythema suggest pulmonary disease and a poor prognosis. A patient with sJIA tends to look ill only during febrile episodes and may develop an associated salmon-colored macular rash at the trunk, waist, or axillae. Scratching unaffected skin may elicit an identical rash (Koebner phenomenon).

In addition, evaluate for lymphadenopathy, splenomegaly, and hepatomegaly, which are characteristic of sJIA. Lymphadenopathy is typically bilateral and symmetric and affects the cervical, axillary, and/or inguinal nodes. Signs of serositis may also be present. Auscultate for a pericardial friction rub, which indicates pericarditis, or decreased breath sounds, which may suggest pleuritis. Obtain ophthalmologic consultation to assess for uveitis.

Laboratory Workup

The International League of Associations for Rheumatology criteria for the diagnosis of sJIA do not include laboratory values, as no test is diagnostic for sJIA. However, ESR, CRP level, and ferritin level ($>$ 1,000 mcg/L) are typically elevated, whereas the rheumatoid factor and antinuclear antibody tests are usually negative. Other associated laboratory abnormalities include thrombocytosis, leukocytosis, transaminitis, and anemia.

In MAS, pancytopenia, triglyceridemia, hepatitis, and disseminated intravascular coagulation are common. Progression of MAS leads to ferritinemia, up to 10,000 mcg/L. Consumptive coagulopathy depletes fibrinogen, causing a paradoxical decrease in ESR. Obtain a CBC, liver panel, prothrombin time, partial thromboplastin time, D-dimer, fibrinogen, lactate dehydrogenase, triglyceride, and ferritin. If MAS is suspected, arrange for a bone marrow biopsy to exclude hemophagocytic lymphohistiocytosis (HLH), lymphoma, and leukemia.

Differential Diagnosis

See Table 56–1.

Treatment

Therapy for sJIA depends on the disease severity. For mild disease, start an oral NSAID, such as ibuprofen 30 mg/kg/d administered in 3 daily doses (maximum dose, 800 mg; maximum daily dose, 2,400 mg), or naproxen

10 to 15 mg/kg/d administered in 2 daily doses (maximum daily dose, 1,000 mg). The patient will show rapid improvement if they are going to respond to NSAIDs. Consult with a rheumatologist for consideration of disease-modifying anti-rheumatic drugs, including interleukin-1 and interleukin-6 inhibitors if the patient has not improved with NSAIDs in 1 to 2 weeks, or if the patient has moderate to severe disease (serositis, moderate to severe polyarthritis, concern for early MAS). Because of the adverse effects of systemic corticosteroids and immunomodulators, prompt consultation with a pediatric rheumatologist is essential. Early and aggressive therapy most effectively treats chronic arthritis, the long-term sequela of sJIA.

The treatment of MAS must be directed by a pediatric rheumatologist. Initial treatment consists of high-dose methylprednisolone, cyclosporine, and anakinra. Transfer the patient to an intensive care unit (ICU) or a facility where rheumatology consultation is available.

Indications for Consultation

- **Cardiology:** For carditis associated with ARF; for monitoring of carditis development in PSA
- **Infectious diseases:** Fever of unknown origin (FUO) and suspected infectious arthritis with systemic illness
- **Oncology:** As needed for bone marrow biopsy to exclude neoplastic processes and HLH
- **Rheumatology:** Suspected noninfectious or systemic arthritic syndrome

Disposition

- **Transfer to a center with rheumatology consultation available:** Any patient with suspected MAS or new-onset sJIA
- **ICU transfer:** Progressive MAS, sepsis, worsening cardiac function
- **Discharge criteria:** Improvement of clinical symptoms, decreasing systemic inflammation, and appropriate follow-up

Follow-up

- **Primary care:** 1 to 7 days
- **Rheumatology:** 1 to 4 weeks
- **Cardiology:** 1 to 4 weeks as needed
- **Infectious diseases/oncology:** As needed

Pearls and Pitfalls

- The arthritis of sJIA may not manifest during the initial febrile illness, which often presents as an FUO with daily high-spiking fevers.

- In MAS there is a paradoxical decrease in the ESR due to fibrinogen consumption, whereas the CRP rises.
- Consider ARF and PSA if the patient develops arthritis 1 to 4 weeks after GAS pharyngitis. Early identification and treatment can help prevent long-term morbidity.

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Henoch-Schönlein Purpura (Immunoglobulin A Vasculitis)

Introduction

Henoch-Schönlein purpura (HSP), now known as *immunoglobulin A vasculitis*, is a systemic, predominantly immunoglobulin A (IgA)–mediated vasculitis. It is characterized by nonthrombocytopenic palpable purpura and the presence of any 1 of the following 4 criteria: (1) diffuse acute-onset abdominal pain, (2) histopathological findings of typical leukocytoclastic vasculitis with predominant IgA deposits or proliferative glomerulonephritis with predominant IgA deposits, (3) arthritis/arthralgia, and (4) renal manifestations in the form of hematuria or proteinuria. HSP is the most common vasculitis of childhood, with 75% of cases occurring between 2 and 11 years of age and a peak incidence at 5 years of age. There is a seasonal predilection in the fall and winter. Although the precise etiology is unknown, most cases are preceded by upper respiratory tract infections (URTIs) caused by organisms such as group A *Streptococcus,* parainfluenza, Epstein-Barr virus, *Mycoplasma,* respiratory syncytial virus, influenza, and parvovirus B19.

Generally, HSP is a benign illness, and in most cases the symptoms resolve completely, but in 1% to 2% of patients, it can progress to renal failure.

Acute hemorrhagic edema of infancy (AHEI) is another small-vessel vasculitis that has clinical features similar to HSP. At presentation, AHEI appears with a classic triad of sudden development of large, palpable purpuric lesions that are distributed on the face, ears, and limbs; edema; and fever in a non–toxic-appearing child younger than 24 months. There is often a history of recent URTI, immunization, or medication use. AHEI has a benign long-term prognosis.

Clinical Presentation

History

As noted earlier, there is usually a history of a preceding URTI, often associated with malaise and low-grade fever. The classic symptoms then begin to appear simultaneously or sequentially, over a period of days to weeks. About three-quarters of patients complain of colicky, episodic, abdominal pain that can be associated with vomiting, hematemesis, and/or grossly bloody stools. About two-thirds of the time, the patient reports pain and swelling of the large joints,

such as the knees and ankles. Rarely, gross hematuria is noted. The classic purpuric rash may not be evident at presentation, and the initial eruption may be urticarial. Eventually all patients or parents report a purpuric or urticarial rash on the buttocks and lower extremities.

Physical Examination

The order of presentation of physical examination findings can vary, but typically there is an erythematous, blanching, lacy, macular or urticarial rash that quickly evolves into palpable purpura on the buttocks, lower extremities, upper extremities, and, less commonly, the trunk. The patient may also have a toxic appearance. There may be abdominal tenderness and, if intussusception is present, rebound and abdominal guarding. The patient can also present with warmth, tenderness, and swelling, with or without erythema, of the knees and ankles. Hypertension may be noted, but it is more common in a patient with renal involvement.

Laboratory Workup

There are no definitive or diagnostic tests for HSP. The remainder of the laboratory evaluation depends on the differential diagnosis.

Afebrile Patient With Classic Rash and No Signs of Sepsis

Perform a complete blood cell count (platelet count is normal), stool guaiac test, and urinalysis, but coagulation studies are unnecessary. Approximately 50% of patients develop microscopic hematuria, whereas a minority have gross blood, white blood cells, and protein in the urine. If hematuria and/or proteinuria is found, obtain electrolyte, blood urea nitrogen, creatinine, and albumin levels. To quantify the degree of proteinuria (if present), calculate the spot urine protein/creatinine ratio to determine whether the patient has nephrotic range proteinuria (ratio > 2).

Well-Appearing Patient Younger Than 2 Years With Rapid Onset of Large, Tender Purpuric Lesions and Edema of the Face, Ears, and Limbs

Perform the same tests as for an afebrile patient with the classic rash and no signs of sepsis.

Ill-Appearing Patient With Classic Rash

In addition to the tests mentioned for an afebrile infant with the classic rash, obtain blood and urine cultures. If the patient has meningeal signs or an altered mental status, perform a lumbar puncture.

Arthritis Without Classic Rash

Obtain an erythrocyte sedimentation rate and/or C-reactive protein level and perform a rheumatologic workup (see Chapter 56, Arthritis Associated With Systemic Disease), including rheumatoid factor, antinuclear antibody, and complement levels.

Possible Intussusception (Crampy Abdominal Pain, Drawing Up of the Legs)

See Chapter 106, Acute Abdomen.

Differential Diagnosis

See Table 57–1 for the differential diagnosis of purpura. If diagnostic uncertainty persists, consult with a dermatologist to arrange a skin biopsy, looking for IgA deposition in the smaller blood vessel walls. In both HSP and acute hemorrhagic edema of infancy, leukocytoclastic vasculitis will be found.

Treatment

If the patient has widespread palpable purpura, along with fever and a toxic appearance, immediately perform a blood culture and treat with intravenous (IV) antibiotics, either ceftriaxone (100 mg/kg/d, divided into doses administered every 12 hours) or cefotaxime (200 mg/kg/d, divided into doses administered every 12 hours; 6-g/d maximum). Add doxycycline (2.2 mg/kg per dose; maximum, 100 mg per dose, every 12 hours) if a rickettsial infection is suspected.

There is no specific treatment for HSP. In most cases the illness is benign and self-limiting, and symptoms usually resolve in 4 to 6 weeks. If the patient

Table 57–1. Differential Diagnosis of Purpura

Diagnosis	Clinical Features
Coagulopathy	Ecchymoses Abnormal prothrombin time and/or partial thromboplastin time
Drug reaction	History of taking an offending agent (penicillin, sulfonamide, oral contraceptives)
Idiopathic thrombocytopenic purpura	Petechiae without purpura Mucosal bleeding Thrombocytopenia
Septicemia (eg, bacterial, rickettsial infection)	Fever, toxicity Purpura not limited to lower extremities
Subacute bacterial endocarditis	Heart murmur or history of heart disease Osler nodes, Janeway lesions, splinter hemorrhages

has joint swelling and pain, administer a nonsteroidal anti-inflammatory drug (NSAID) such as naproxen (10–20 mg/kg/d, divided into doses administered every 12 hours; 1,000-mg/d maximum) or ibuprofen (10 mg/kg per dose every 6 hours; 40-mg/kg/d maximum), although NSAIDs may be contraindicated with renal impairment or gastrointestinal bleeding.

Treat a patient with severe abdominal pain and normal ultrasonographic and/or radiologic findings or joint swelling and pain unresponsive to NSAIDs with methylprednisolone (1 mg/kg/d for 2 weeks, 80-mg/d maximum) and slowly taper over 1 to 2 weeks or longer, depending on the response. Use the IV route to start because oral absorption is poor secondary to the gastrointestinal vasculitis. However, systemic corticosteroids do not prevent the onset of immunoglobulin A vasculitis nephritis.

Consult surgery if small bowel intussusception is found. However, it often self-resolves and is not amenable to reduction by enema.

Indications for Consultation

- **Nephrology:** Hypertension, decreased renal function, nephrotic syndrome, or proteinuria for more than 1 week
- **Surgery:** Intussusception, intestinal hemorrhage, obstruction, or perforation

Disposition

- **Intensive care unit transfer:** Severe hypertension that requires continuous antihypertensive therapy
- **Discharge criteria:** Tolerating oral diet, symptoms (abdominal pain, arthritis) are no longer incapacitating, and renal function is normal or improving

Follow-up

- **Primary care:** Blood pressure check and urinalysis in 1 week for an uncomplicated case (no hematuria or proteinuria and normal renal function); continue weekly for 3 weeks, then monthly until 6 months after presentation
- **Nephrology:** 1 week if the patient has significant proteinuria for more than 1 week; immediate consultation if the patient has renal failure or nephrotic syndrome

Pearls and Pitfalls

- In as many as 30% to 50% of patients, the classic rash will develop up to 2 weeks after other clinical manifestations.

- Renal disease can develop over the subsequent 6 months, despite normal initial urinalysis results.
- Most patients with AHEI require symptomatic treatment only.

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CHAPTER 58

Immunodeficiency

Introduction

Primary immunodeficiencies (PIs) are inherited disorders of the immune system that predispose patients to recurrent infections, malignancies, and autoimmune diseases. Unusually severe, long-lasting, atypical, or repeated infections are indications for an immune system evaluation. Warning signs also include the need for intravenous (IV) antibiotics, recurrent deep-seated infections, and chronic oral or cutaneous candidiasis. Other clues for immunodeficiency include chronic diarrhea, atypical infections, complications from live vaccines, autoimmune disease (eg, idiopathic thrombocytopenic purpura), and malignancies (eg, lymphoma).

There are some typical patterns of age of onset, infectious organism(s), and site(s) of infection for each type of PI (Table 58–1). In addition to the classic categories of humoral, cellular, combined, phagocytic, and complement-mediated PI, the classification is now revised to include diseases of immune dysregulation, innate immunity, autoinflammation, and bone marrow failure.

Clinical Presentation

History

Obtain a thorough history, including age of onset and locations of infections, types of organisms, previous antimicrobial use, duration of treatment, and need for IV antibiotic therapy. Defects in antibody production typically present after 6 months of age, with sinopulmonary infections in a patient who is otherwise thriving. Combined T- and B-cell defects appear early in infancy, with failure to thrive (FTT), diarrhea, rash, opportunistic or life-threatening infections, severe candidiasis, and pneumonia. Predominantly antibody defects tend to present with sinopulmonary infections once maternal antibody levels wane after 3 to 4 months of age. Phagocytic defects typically present in infancy to early adulthood as skin, lymph node, and visceral organ abscesses and pneumonia. Complement component 3, or C3, deficiency may appear early in life with severe recurrent pyogenic infections, while late component deficiencies (C5–C9) predispose older children and young adults to recurrent *Neisseria* infections.

Assess the patient's growth pattern and document the vaccine status, as well as whether there have been any severe or unusual adverse reactions to live vaccines. Check the family history for any recurrent infections or known

Table 58–1. Primary Immunodeficiencies

Presentation	Defects	Examples	Organisms	Onset	Initial Laboratory Workup
Recurrent sinopulmonary infections (sinusitis, otitis media, pneumonia), diarrhea, chronic meningoencephalitis	Antibody	X-linked agammaglobulinemia, IgA deficiency, CVID	Encapsulated bacteria, *Giardia duodinales,* enterovirus meningoencephalitis	After 6–9 mo of age	Ig levels (IgA, IgG, IgM)
FTT, rash, thrush, pneumonia, opportunistic infections	Combined	SCID, DiGeorge syndrome, Wiskott-Aldrich syndrome, hyper-IgM	Adenovirus, *Candida,* CMV, Epstein-Barr virus, *Pneumocystis jirovecii,* varicella	Infancy	Ig levels T, B, natural killer cells Chest radiography Flow cytometry or mitogen stimulation
Skin or solid organ abscesses, pneumonia, osteomyelitis, dental infections	Phagocytic	CGD, leukocyte adhesion defect, hyper-IgE syndrome	*Burkholderia cepacia, Aspergillus, Nocardia, Serratia, Staphylococcus aureus*	Infancy to young adult	Complete blood cell count, IgE, flow cytometry
Sinopulmonary infections, glomerulonephritis, meningitis	Complement	Complement component 3, membrane attack complex, regulatory components	Encapsulated bacteria, especially *Streptococcus pneumoniae* and *Neisseria* spp	Infancy to young adult	CH50
Mucocutaneous fungal infections, mycobacterial multifocal osteomyelitis, *Mycobacterium avium* complex, herpes simplex virus encephalitis	Cellular	Chronic mucocutaneous candidiasis, IFN-g/interleukin-12 receptor deficiency	*Candida* spp, *Mycobacterium* spp, *Salmonella* spp	Young child to adolescent	IFN-g level, delayed type hypersensitivity or lymphocyte proliferation for *Candida*

Abbreviations: CGD, chronic granulomatous disease; CH50, total complement activity; CMV, cytomegalovirus; CVID, common variable immune deficiency; FTT, failure to thrive; IFN, interferon; Ig, immunoglobulin; SCID, severe combined immune deficiency.

immunodeficiency, consanguinity, and deaths in infancy or childhood. The most common forms of severe combined immune deficiency (SCID), agammaglobulinemia, and chronic granulomatous disease (CGD) are all X-linked, so note the sex of affected individuals. Assess the child for developmental delays, which may be seen in some syndromic PIs, such as DiGeorge syndrome, ataxia-telangiectasia, hyperimmunoglobulin E syndrome, Kabuki syndrome, and Chediak-Higashi syndrome. Conduct a full review of systems for conditions associated with PI, such as autoimmune endocrinopathies, inflammatory bowel disease, periodic fevers, cold urticaria, atopic dermatitis, and chronic pulmonary disease. Finally, document all previous culture and serologic results.

Rather than presenting with a severe infection, a PI can also present with an autoimmune disease or a malignancy. Some patients with common variable immune deficiency (CVID) develop immune thrombocytopenic purpura prior to any infections. Some PIs, such as autoimmune lymphoproliferative syndrome and X-linked lymphoproliferative syndrome, are predominantly immune dysregulation that present with fever, adenopathy, and hepatosplenomegaly.

Physical Examination

Perform a complete physical examination (Table 58–2), paying special attention to any rash (including in the diaper area), evidence of previous or current skin infections or abscesses, thrush, the lack of tonsils or palpable lymph nodes (especially in the neck and groin), and signs of otitis media, sinusitis, or pneumonia. Digital clubbing can be seen with recurrent pneumonias with subsequent bronchiectasis and respiratory failure. A right-sided apical pulse may indicate situs inversus and possible Kartagener syndrome. Plot the child's growth curves and review them for signs of FTT. Assess for any dysmorphisms that can be associated with syndromic PIs.

Laboratory Workup

The types of infection(s) guide the initial laboratory testing (Table 58–1). For any patient with suspected PI, perform a complete blood cell count (CBC) with differential, peripheral blood smear, comprehensive metabolic panel, HIV screen, and quantitative immunoglobulin (Ig) levels (IgA, IgG, IgM, and IgE) *prior to* consulting an immunologist. Order a sweat chloride test if the patient has had frequent sinopulmonary infections, especially if the newborn cystic fibrosis screening results are not available. Lymphopenia can be a clue for SCID, so an absolute lymphocyte count less than 2,500/ mm^3 [$< 2.5 \times 10^9$/L] in a newborn must be investigated urgently. All 50 states now perform

Table 58–2. Physical Examination Findings and Associated Immune Deficiencies

Physical Examination Findings	Associated Immune Deficiency
Aphthous ulcers	CGD
Ataxia or telangiectasia	Ataxia-telangiectasia
Digital clubbing	Any immune deficiency leading to recurrent pneumonia or bronchiectasis
Delayed umbilical cord separation Severe gingivitis	Leukocyte adhesion defect
FTT	T-cell defects (SCID)
Granuloma formation Lymphoid hyperplasia	CGD CVID Hyper-IgM
Hypertelorism, heart murmur, low-set ears, microcephaly, cleft lip and/or palate	DiGeorge syndrome
Hypopigmentation of skin and hair	Chediak-Higashi, Griscelli, and Hermansky-Pudlak syndromes
Lack of tonsils and palpable lymph nodes (especially in the neck and groin)	XLA SCID
Nonspecific rash	SCID
Otitis media/sinusitis findings (perforated or scarred tympanic membranes, purulent nasal discharge)	B-cell defects (XLA, IgA deficiency, CVID)
Petechiae	Wiskott-Aldrich syndrome
Severe diaper dermatitis Persistent or recurrent thrush	T-cell defects (SCID, chronic mucocutaneous candidiasis)
Severe eczema	Hyper-IgE syndrome Wiskott-Aldrich syndrome
Skeletal abnormalities	Cartilage-hair hypoplasia Hyper-IgE syndrome
Skin abscess or adenitis (unusual organisms or severe/recurrent infection with *Staphylococcus aureus*)	Phagocytic defect (CGD)

Abbreviations: CGD, chronic granulomatous disease; CVID, common variable immune deficiency; FTT, failure to thrive; Ig, immunoglobulin; SCID, severe combined immune deficiency; XLA, X-linked agammaglobulinemia.

newborn screening for SCIDs, but this will not identify PIs with normal lymphocyte counts. In addition, a low neutrophil count and thrombocytopenia may be seen in certain PIs. A low globulin fraction on a metabolic panel suggests decreased Ig levels.

Obtain an immunology consult if there is a high index of suspicion or abnormal initial laboratory values. However, if immunology services are not available, pursue further workup based on the pattern of infection and initial laboratory results, as described below.

For recurrent sinopulmonary infections with encapsulated organisms consistent with a B cell defect, obtain IgA, IgM, and IgG levels, although IgG subclasses are typically not helpful. If the Ig levels are less than 2 SDs below normal or if a humoral defect is a concern, order antibody titers (tetanus, diphtheria, pneumococcus). After infancy, an IgG level less than 200 mg/dL (< 2 g/L) or a total Ig level (IgG, IgA, and IgM) less than 400 mg/dL (< 4 g/L) suggests a severe humoral defect and warrants urgent consult with an immunologist. Most laboratories can determine Ig levels, but confirm that appropriate age-based normal levels are used when interpreting the results. In a patient older than 12 months, order isohemagglutinin levels, as the absence of isohemagglutinin titers in a patient who is blood type A, B, or O suggests a defect in antibody production.

Suspect a phagocyte deficiency if there are skin, lymph node, or solid organ abscesses, especially with unusual organisms such as *Klebsiella* or *Serratia;* delayed wound healing; cavitary pneumonias; or infections with *Staphylococcus aureus, Burkholderia cepacia, Serratia, Nocardia,* or *Aspergillus.* Obtain a CBC, peripheral smear for neutrophils, total IgE level, and CGD assay. The dihydrorhodamine low cytometric assay is preferred over the classic nitro blue tetrazolium test.

If a child has low lymphocyte count for age (< 2,500/ mm^3 [< 2.5×10^9/L] in an infant; < 1,500/ mm^3 [< 1.5×10^9/L] in a child 1–6 years of age; < 1,000/ mm^3 [< 1.0×10^9/L] for a child older than 6 years), an abnormal SCID newborn screening result, or a history of opportunistic infections, contact immunology urgently for recommendations on testing and management. A low lymphocyte count, conotruncal cardiac defects, and craniofacial anomalies suggest 22q11 deletion syndromes, including DiGeorge syndrome.

In a patient with recurrent pyogenic infections (especially if associated with glomerulonephritis) or recurrent *Neisseria* infections, order a total complement activity (CH50) test. A normal CH50 result excludes most serious complement deficiencies. If the CH50 finding is low or if complement deficiency is still suspected, an immunologist can assist with testing specific complement components, such as an alternate pathway AH50 assay.

Order a sweat chloride test for a patient with recurrent sinopulmonary infections.

Obtain a chest radiograph if the patient has respiratory symptoms. Findings may include pneumonia, absence of a thymic shadow (SCID, DiGeorge syndrome), or pneumatoceles (hyper-IgE syndrome). Also, obtain blood and urine cultures if the patient is febrile, as well as wound and abscess cultures when indicated. Obtain stool samples for culture or gastrointestinal pathogens if a patient with a suspected PI has diarrhea.

Differential Diagnosis

Over 50% of recurrent infections occur in normal, healthy children, who may experience 4 to 10 minor infections per year, each lasting up to 7 to 14 days. For preschool children, this is particularly true if they attend day care or have older school-aged siblings. Recurrent benign viral infections are rarely a manifestation of an immune deficiency and do not warrant specialized testing. Failure to thrive without associated infections (especially opportunistic infections or pneumonia) is rarely the result of a PI. Recurrent infections at a single site are more likely to represent anatomic abnormalities, while PIs generally cause recurrent infections at more than 1 anatomical location.

About 10% of children with recurrent serious infections will end up having a PI. Secondary, or acquired, immune deficiencies (Table 58–3) are more common than primary disorders and must also be considered in a patient with frequent infections. Atopic diseases (eg, eczema and asthma), underlying

Table 58–3. Secondary Causes of Immune Deficiency

Cause	Examples
Autoimmune diseases	Juvenile idiopathic arthritis Systemic lupus erythematosus
Infections	CMV Epstein-Barr virus HIV
Immune suppressants	Corticosteroids Chemotherapy Monoclonal antibodies
Malignancies	Leukemia Lymphoma
Immunoglobulin or leukocyte loss	Nephrotic syndrome Lymphatic malformations or injury (chylothorax) Protein-losing enteropathy
Asplenia	Sickle cell disease Postsurgical disease
Malnutrition	Protein deficiency Vitamin deficiencies (A, B_6, B_{12}, C, D, E) Zinc deficiency
Other	Cirrhosis Cystic fibrosis Diabetes mellitus Inborn errors of metabolism Primary ciliary dyskinesia Radiation therapy Stress Uremia

Abbreviation: CMV, cytomegalovirus.

anatomic defects, and chronic diseases (eg, cystic fibrosis and diabetes) all predispose children to frequent infections. Exposure to tobacco smoke is a risk factor for recurrent respiratory infections. Although protocols to prevent vertical transmission of HIV have been extremely successful, perinatal HIV can still occur, especially in children born in resource-limited countries. Order an HIV screening prior to initiating a complex workup. HIV can present in a manner similar to SCID, although it will generally manifest later in life, because it may take several years for CD4 counts to decrease to levels associated with AIDS.

Numerous medications, especially chemotherapy and immune suppressants, are common causes of secondary immunodeficiency. Long-term or frequent short-term courses of systemic corticosteroids, anti-epileptics, cyclosporine, and rituximab are iatrogenic causes of reduced Ig levels.

Treatment

The management of a PI is dependent on the condition, but focus the immediate treatment on active infections. A patient with a phagocytic defect, combined T/B cell immunodeficiency, or severe hypogammaglobulinemia (X-linked agammaglobulinemia, hyper-IgM syndrome, CVID) will typically require aggressive IV antibiotic therapy at higher than typical doses and for a prolonged course (eg, 2–4 weeks or more). The choice of antimicrobials is based on location of suspected infection, the most common organisms for the specific condition, and local susceptibilities (Table 58–4). If possible, try

Table 58–4. Empiric Antibiotic Therapy for Immunodeficient Patients[a]

Defects	Organisms	Typical Antibiotics[b]
Antibody deficiencies	Encapsulated bacteria	Ceftriaxone or levofloxacin
Cellular deficiencies	*Candida* spp, *Mycobacterium* spp, *Salmonella* spp	Ceftriaxone Fluconazole Triple therapy for *Mycobacterium*
Combined defects	Adenovirus, *Candida* spp, Epstein-Barr virus, CMV, parainfluenza virus, *Pneumocystis jirovecii*, varicella	TMP/SMX *plus* extended β-lactam (eg, meropenem, piperacillin/tazobactam, cefepime) Add vancomycin if the patient appears septic or MRSA is suspected Add fluconazole if a fungal infection is suspected or there is no response to initial antibiotics Interstitial pneumonia: add macrolide
Complement defects	Encapsulated bacteria, *Neisseria* spp	Same as antibody defects
Phagocytic defects	*Aspergillus* spp, *Burkholderia* spp, *Nocardia* spp, *Serratia marcencens*, *Staphylococcus aureus*	Voriconazole *plus* meropenem Add vancomycin if the patient appears septic or MRSA is suspected

Abbreviations: CMV, cytomegalovirus; MRSA, methicillin-resistant *Staphylococcus aureus*; TMP/SMX, trimethoprim-sulfamethoxazole.

[a] See specific chapters on infectious diseases for dosing guidelines.

[b] See *Nelson's Pediatric Antimicrobial Therapy* (www.aap.org/nelsonsabx) for dosing guidelines.

Table 58–5. Antimicrobial Prophylaxis Regimens for an Immunodeficient Patient	
Antibiotic	**Organisms Targeted**
TMP/SMX	*Pneumocystis jirovecii, Nocardia* spp, *Staphylococcus aureus*
Fluconazole	*Candida* spp
Itraconazole	*Aspergillus* spp
Azithromycin	*Mycoplasma pneumoniae,* nontuberculous *Mycobacteria* spp
Acyclovir	Herpes simplex virus, varicella zoster virus
Valganciclovir	CMV

Abbreviations: CMV, cytomegalovirus; TMP/SMX, trimethoprim sulfamethoxazole.

to get a definitive diagnosis (eg, via cultures, bronchoscopy) to guide therapy. The patient will often need a central line catheter for several weeks, but avoid permanent indwelling access devices because they significantly increase the long-term infection risk.

Discuss antimicrobial prophylaxis for suspected or confirmed PI with immunology and infectious disease specialists. Give trimethoprim sulfamethoxazole (TMP/SMX), palivizumab, fluconazole, and acyclovir to a patient with SCID. In a patient with CGD, use TMP/SMX and itraconazole, which has better activity against *Aspergillus* (Table 58–5).

Suspected SCID is an emergency. Immediately consult with an immunologist if lymphocyte studies are low. A patient with SCID is at risk for graft versus host disease and must be given irradiated, cytomegalovirus (CMV)–negative blood products.

A patient with PI is at increased risk for malignancies and autoimmune diseases. Autoimmune hemolytic anemia, thrombocytopenia, and neutropenia are frequently seen with CVID, hyper-IgM syndrome, and other PIs. Consult both an immunologist and a hematologist because the patient may need corticosteroids, high-dose intravenous immunoglobulin (IVIG), or rituximab.

A patient with complete IgA deficiency may have anti-IgA antibodies, which can rarely lead to anaphylactic reactions to IVIG and other blood products. Order washed red blood cells and consider IVIG preparations with low IgA levels, although testing for anti-IgA antibodies is not helpful.

Indications for Consultation

- **Genetics:** Presence of syndromic features
- **Hematology-oncology:** Cytopenias
- **Immunology:** Abnormal immune laboratory test results or opportunistic infection
- **Infectious diseases:** Complex or opportunistic infection
- **Pulmonologist:** Chronic pulmonary infections, bronchiectasis

Disposition

- **Intensive care unit transfer:** Septic shock, respiratory failure
- **Discharge criteria:** Afebrile for 24 to 48 hours or longer with appropriate treatment of acute infection underway

Follow-up

- **Primary care:** 1 week
- **Immunology or infectious diseases (if involved):** 2 to 4 weeks

Pearls and Pitfalls

- Promptly initiate IV antibiotics for a patient with severe immune deficiency and a temperature of 38.3 °C (101 °F) or obvious infection.
- Obtain appropriate cultures as quickly as possible, preferably prior to antimicrobial therapy. However, do not delay treatment pending cultures for an ill-appearing patient.
- Complete the laboratory evaluation (Ig levels, vaccine and isohemagglutinin titers) prior to treatment with Ig.
- Initiate proper isolation precautions, especially for a patient with suspected SCID.
- While rare, if a patient with complete IgA deficiency is given Ig, monitor closely for anaphylaxis.
- Suspect SCID in an infant with a lymphocyte count less than 2,500/ mm^3 [$< 2.5 \times 10^9$/L].
- Transfuse only irradiated CMV-negative blood products for a patient with suspected SCID.
- If a PI is suspected, defer administering live vaccines until after the patient is evaluated by immunology.

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CHAPTER 59

Kawasaki Disease

Introduction

Kawasaki disease (KD) is an acute, multiorgan vasculitis of small and medium-sized arteries. Eighty percent of patients are younger than 5 years, with a peak incidence at 13 to 24 months, although it can occur in infants younger than 6 months. The etiology of KD is unknown, although it occurs most commonly in the winter and spring.

The most significant complication of KD is vasculitis of the coronary arteries, leading to coronary artery aneurysm (CAA) formation. This occurs in about 20% of untreated patients but is seen in just 4% if they are treated appropriately with intravenous immunoglobulin (IVIG) in the first 10 days of the acute illness. Risk factors for the development of CAA include age younger than 12 months or older than 8 years, male sex, duration of fever more than 10 days prior to treatment, and lack of response to initial IVIG dose. Certain laboratory value abnormalities also predict a higher risk of CAA, including low hematocrit level, low albumin level, hyponatremia, and increased alanine transaminase level.

A patient with Kawasaki disease shock syndrome (KDSS) presents with, or develops, hypotension with a systolic blood pressure more than 20% lower than baseline and/or signs of poor perfusion.

Clinical Presentation

History

There are 3 distinct stages of illness in KD. Most patients will present during the acute stage (first 1–2 weeks), which is characterized by the abrupt onset of high fever (38.9–40.0 °C [102–104 °F]) for at least 5 days that is associated with irritability and without any obvious source for fever. Within 2 to 5 days of the onset of fever, 90% of patients develop a polymorphous erythematous rash (often in the diaper area; may involve the palms and soles), nonpurulent limbic-sparing conjunctivitis (80%–90% of patients), erythema and cracking of the lips or strawberry tongue (75%–90% of patients), cervical lymphadenopathy with a single lymph node larger than 1.5 cm in diameter, and erythema and swelling of the dorsum of the hands and feet. However, some of the classic features, such as conjunctivitis or rash, may have already resolved by the time the patient presents to the hospital. Less common complaints are abdominal pain, vomiting, and arthralgia.

The subacute phase of KD (approximately 2–6 weeks) is characterized by resolution of the classic symptoms. Periungual desquamation may occur during the second to third week of the illness. If not already present, cardiac complications, including CAAs, coronary obstruction, and myocardial and endocardial inflammation, can develop, along with a marked thrombocytosis (platelet count > 1,000,000/mcL [> $1{,}000 \times 10^9$/L]). The risk of sudden death, although rare, is greatest during this phase.

In the final stage, usually 6 to 8 weeks from the beginning of the illness, the physical findings are no longer apparent, and the inflammatory markers normalize. Coronary artery ectasia (if present) may resolve, progress to myocardial ischemia or infarction, or remain unchanged.

Physical Examination

Perform a thorough examination of the head, eyes, ears, nose, and throat. As noted above, typical findings in the acute stage include conjunctival injection, with perilimbic sparing and no exudate; erythema of the mouth and pharynx; strawberry tongue; dry, cracked lips; and a unilateral cervical lymph node larger than 1.5 cm in diameter. Other findings include erythema and swelling of the dorsum of the hands and feet and a polymorphic, erythematous rash that may involve the palms and soles. Irritability is a cardinal feature in younger children. In many cases, within a few days of the appearance of the rash, desquamation of the perineal/diaper region (but not periungual areas) occurs.

Cardiac involvement can manifest with tachycardia, a flow murmur, muffled heart sounds, or a gallop rhythm.

A less common feature is arthritis that involves the small joints during the acute phase and later, the large, weight-bearing joints. Myringitis, urethritis with sterile pyuria, aseptic meningitis (nuchal rigidity), acalculous cholecystitis, and hydrops of the gallbladder (rare; right upper quadrant abdominal mass) may also occur.

During the subacute phase, there can be desquamation of the hands and feet and in the diaper area. Cardiac manifestations during this stage, if present, are more severe and may reveal signs and symptoms of congestive heart failure, valvular regurgitation, ventricular arrhythmias (premature ventricular contractions, ventricular tachycardia), or myocardial ischemia.

Laboratory Workup

If KD is suspected, obtain a complete blood cell count with differential; erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level; serum chemistry values with liver function tests, including alanine transaminase,

aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels; and a urinalysis. Leukocytosis with neutrophil predominance, normocytic normochromic anemia, increased liver enzyme levels and alkaline phosphatase level (seen in hydrops of the gallbladder), decreased albumin and serum sodium levels, and sterile pyuria are suggestive of KD. The ESR and CRP level are increased early in the clinical course, whereas thrombocytosis (platelet count $> 1{,}000{,}000/mm^3$ [$> 1{,}000 \times 10^9/L$]) may not occur until the second or third week of illness. Thrombocytosis and increased ESR may persist for 6 to 8 weeks, and normalization of these values coincides with resolution of the disease, although a steady decline in the CRP level occurs promptly after successful treatment with IVIG.

If KD is strongly suspected, obtain an echocardiogram, although a normal study does not rule out KD. Also, do not delay initiating treatment if an echocardiogram is not immediately available. Obtain an electrocardiogram, which may demonstrate changes such as tachycardia, prolongation of the PR interval, abnormal Q waves, and nonspecific ST wave changes.

Blood, throat, and viral cultures may be helpful in differentiating KD from other infectious causes with prolonged fever (see Chapter 64, Fever of Unknown Origin). An increased brain natriuretic peptide level may aid in the diagnosis of KD, particularly when the etiology of the febrile illness is unclear.

Differential Diagnosis

Strongly suspect KD if a patient between 6 weeks and 12 years of age has a fever for more than 3 to 5 days in association with 4 of the following 5 major manifestations:

- Bilateral bulbar conjunctival injection without exudate
- Erythema of the mouth and pharynx; strawberry tongue; and cracked, red lips
- Erythematous rash of almost any pattern (except vesicular)
- Edema and induration of the hands and feet with erythematous palms and soles
- Isolated, cervical lymphadenopathy (most often unilateral), larger than 1.5 cm in diameter

An atypical presentation, often termed *incomplete KD,* is increasingly common, especially among infants younger than 12 months. The patient has prolonged fever and fewer than 4 of the principal diagnostic features. However, while the physical examination may not be clearly diagnostic, the laboratory value abnormalities follow a pattern similar to what is seen in classic disease. Given that infants and patients with delayed diagnosis of KD are at increased risk for cardiac disease, it is critical to diagnose KD when the clinical picture is "incomplete" but the abnormal laboratory values and echocardiogram findings are consistent with the diagnosis.

In KDSS, the patient tends to have higher CRP and/or ESR levels and a greater percentage of immature neutrophils, with a lower hemoglobin concentration and platelet count. The patient is likely to be resistant to immunoglobulin therapy and may require additional anti-inflammatory treatments.

There is a broad differential diagnosis for KD, including a wide variety of infectious diseases (toxic shock syndrome, rheumatic fever, scarlet fever, staphylococcal scalded skin syndrome, Rocky Mountain spotted fever, leptospirosis, adenovirus, Epstein-Barr virus, influenza, measles) and noninfectious etiologies (Stevens-Johnson syndrome, drug reaction, juvenile idiopathic arthritis, mercury toxicity) that may have similar symptoms at presentation (Table 59–1).

A systemic inflammatory disease (see Chapter 65, Multisystem Inflammatory Syndrome in Children [MIS-C]) can occur several weeks after SARS-CoV-2 infection. It has a similar presentation as KD, and often the patient will meet the criteria of complete or incomplete KD. However, a patient with MIS-C tends to be older and have either a positive antibody to SARS-CoV-2 or a history of COVID-19 disease. They may have multisystem involvement with a shock-like presentation, which is uncommon in KD.

Table 59–1. Differential Diagnosis of Kawasaki Disease

Diagnosis	Clinical Features
Acute rheumatic fever	History of strep infection No conjunctivitis Migratory polyarthritis and/or carditis (regurgitation)
Adenovirus	Exudative pharyngitis Purulent conjunctivitis Mild increase of inflammatory markers
Juvenile idiopathic arthritis	Joint pain and/or swelling Lack of conjunctival and oral findings Lymphadenopathy more generalized
Measles	Exanthem progresses in a cephalocaudad pattern Conjunctivitis Lack of swelling of the hands and feet
MIS-C	Two-thirds of patients > 4 years of age Multisystemic disease, may present in shock
Stevens-Johnson syndrome	Erythema multiforme with involvement of 2 or more mucous membranes May have conjunctivitis, oral ulcers, or diarrhea Sudden onset with progression to shock if secondary infection
Toxic shock syndrome	Presence of inciting bacterial agent—*Streptococcus* or *Staphylococcus* Signs of shock, including hypotension May have end organ damage with renal involvement with ↑ blood urea nitrogen/creatinine level or increased liver function tests

Abbreviation: MIS-C, multisystem inflammatory syndrome in children.
↑ indicates increased level.

Treatment

Management in the acute phase is aimed at reducing inflammation in the myocardium and coronary artery wall, as well as preventing thrombosis. The mainstay of inpatient therapy is high-dose IVIG (2 g/kg IVIG administered over 10–12 hours). During the IVIG infusion, many patients will become afebrile, with dramatic improvement in the signs and symptoms. However, fever can persist after IVIG administration, so do not consider a patient to be IVIG nonresponsive until there is a documented fever more than 36 hours after the end of the infusion.

Approximately 10% to 20% of patients with KD will ultimately be IVIG nonresponsive and remain febrile beyond 36 hours. These patients are at increased risk for coronary artery abnormalities. Options include a second course of IVIG (2 g/kg) alone, or in conjunction with pulse methylprednisolone therapy (30 mg/kg/d) for 3 days or infliximab (5 mg/kg). Cyclosporine and methotrexate are additional treatment options, but reserve them for a patient who fails to respond to multiple treatment courses.

During the first 7 to 10 days of the illness, also administer high-dose aspirin (80–100 mg/kg/d, divided into doses administered every 6 hours), then switch to low-dose aspirin (3–5 mg/kg/d as a single daily dose) after the patient has been afebrile for 48 hours. Continue the low-dose aspirin until the inflammatory markers (CRP level, ESR) normalize and the patient has completed a follow-up appointment with a cardiologist to confirm that no coronary artery abnormalities have developed. If CAAs are identified, long-term antiplatelet therapy is indicated.

Indications for Consultation

- **Cardiology:** All patients
- **Infectious diseases:** The diagnosis of KD is unclear or there is concern for other infectious etiologies
- **KD expert, if available (may be a pediatric hospitalist, cardiologist, rheumatologist, or infectious diseases specialist):** Fever persists for more than 36 hours after first immunoglobulin dose

Disposition

- **Intensive care unit transfer:** Cardiac involvement with compromised cardiac function, KDSS
- **Discharge criteria:** Patient afebrile with improvement of clinical symptoms and decreased inflammatory markers ($\geq$ 36 hours after completion of IVIG treatment)

Follow-up

- **Primary care:** 1 to 3 days
- **Cardiology:** 1 to 2 weeks

Pearls and Pitfalls

- Incomplete KD may be more common and difficult to diagnose than a classic presentation, especially at the extremes of the age spectrum.
- KD can present as an acute abdomen, leading to admission to a surgical service, or with a cervical lymphadenitis-like picture, resulting in admission to the ear, nose, and throat service.
- Cough, congestion, and petechial, purpuric, and vesicular rashes are not features of KD.
- Defer live virus vaccines for 11 months after administration of IVIG for KD.

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CHAPTER 60

Systemic Lupus Erythematosus

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune disease characterized by episodic periods of increased systemic inflammation known as "flares." Up to 20% of SLE cases are diagnosed before 18 years of age (ie, childhood SLE [cSLE]). The mean age of onset of cSLE is 11 to 12 years, with few cases in children under 5 years of age. There is a female predominance in childhood (3:1), which triples during puberty (9:1). Due to a higher prevalence of complications within the first 2 years of illness, cSLE has higher morbidity and mortality than adult-onset SLE (aSLE).

The most common cSLE complications are disease flares and systemic infections. Within individuals, disease flares may resemble the initial disease presentation. Patients are at risk for systemic infections because of features of the disease (cytopenias, immune system dysregulation, and complement deficiencies) and the adverse effects of treatments (systemic steroids and immunosuppressives). Other serious complications include progressive nephritis, renal failure, thrombotic events, and neuropsychiatric (NP) complications.

Clinical Presentation

The American College of Rheumatology and the European League Against Rheumatism developed criteria for the classification of SLE. To diagnose SLE, the patient must have an antinuclear antibody (ANA) titer of at least 1:80 on HEp-2 cells or an equivalent positive test result at least once. In addition, there are classification criteria assigned various point values. The diagnosis of SLE can be made if the patient has at least 1 clinical criterion and 10 or more points (Table 60–1).

The common clinical presentations of cSLE complications are summarized in Table 60–2. Renal and NP complications within 1 to 2 years of diagnosis are more frequent in cSLE, whereas pulmonary complications, Raynaud phenomenon, and photosensitivity are more common among affected adults.

History

Each patient with cSLE presents with a different profile of symptoms, the most common ones being fever, malaise, fatigue, anorexia, weight loss, lymphadenopathy, joint involvement, and rash (malar and/or photosensitive). Given the episodic nature of the illness, an incomplete review of systems may delay diagnosis. Symptoms of cSLE emerge over time and need not be present simultaneously. In a patient with known cSLE, key questions to ask include the

Table 60–1. Criteria for the Diagnosis of Systemic Lupus Erythematosus

Organ System	Clinical Signs and Symptoms	Points
Constitutional	Fever	2
Hematologic	Leukopenia	3
	Thrombocytopenia	4
	Autoimmune hemolysis	2
NP	Delirium	2
	Psychosis	3
	Seizure	5
Mucocutaneous	Nonscarring alopecia	2
	Oral ulcers	2
	Subacute cutaneous *or* discoid lupus	4
	Acute cutaneous lupus (malar rash or photosensitivity)	6
Serosal	Pleuritic *or* pericardial effusion	5
	Acute pericarditis	6
Musculoskeletal	Joint involvement	6
Renal	Proteinuria > 0.5 g/24 h	4
	Renal biopsy class II or V lupus nephritis	8
	Renal biopsy class III or IV lupus nephritis	10
Immunologic	Anticardiolipin Ab or anti–β2 glycoprotein 1 Ab or lupus anticoagulant	2
	Low C3 or low C4	3
	Low C3 and low C4	4
	Anti–double stranded DNA Ab or anti-Smith Ab	6

Abbreviations: Ab, antibodies; C3, complement component C3; C4, complement component C4; NP, neuropsychiatric.
Adapted from Aringer M, Costenbader K, Daikh D, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol.* 2019;71(9):1400–1412.

similarities between the present and previous flares and current medication usage (including adherence and adverse effects).

Physical Examination

Perform a complete physical examination focusing on the patient's vital signs, growth, and general appearance. Check for fever (infection or disease flare), hypertension (nephritis), pulsus paradoxus (pericardial effusion), and hypoxemia (pneumonia, alveolar hemorrhage, or pulmonary embolism). Pallor (autoimmune hemolytic anemia) or jaundice (autoimmune hemolysis and/or autoimmune hepatitis) may be present. Abnormalities are possible in every organ system.

Mucocutaneous findings include malar rash, photosensitive rash, alopecia (frontal or temporal), and/or painless oral ulcers. The malar rash appears raised or flat, spares the nasolabial folds, is sometimes photosensitive, and is nonpruritic and nonscarring. Discoid rash is less common in cSLE. Inspect the

Table 60–2. Clinical Presentation of Complications of Childhood Systemic Lupus Erythematosus

Complications	Clinical Findings/Laboratory Studies
Disease flares	Worsening or return of initial SLE symptoms ↑ ESR, anti–double stranded DNA ↓ Complement components C3 and C4
Systemic infections	Worsening of SLE symptoms, fever ↑ CRP
Neuropsychiatric	Headaches, seizures, cognitive dysfunction, mood disorders, psychosis
Progressive nephritis Renal failure	↑ Creatinine level and protein/creatinine ratio Hypoalbuminemia Severe hypertension, dependent edema Oliguria, anuria, or high urine output
Thrombotic events	Severe headache (cerebral vein thrombosis) Thrombosis of any-sized vessel (deep venous thrombosis, pulmonary embolism) Thrombotic thrombocytopenic purpura (thrombotic microangiopathy) ↑ Risk with (+) antiphospholipid Ab

Abbreviations: Ab, antibodies; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SLE, systemic lupus erythematosus.
+ indicates positive finding; ↑, elevated level; ↓, decreased level.

nail beds (splinter hemorrhages), and perform funduscopic examination of the retinas (vasculitis). Edema may be seen with nephritis or malnutrition.

Arthritis (see Chapter 56, Arthritis Associated With Systemic Disease) is painful, polyarticular, and frequently symmetric. Both small (hands, feet) and large joints may be involved. Myositis and myalgias may also occur.

Pleuritic chest pain and/or decreased or abnormal breath sounds suggest pleuritis. Hemoptysis suggests alveolar hemorrhage, and dyspnea is concerning for pulmonary embolism, pericarditis, pericardial effusion, pleuritis, pleural effusion, and severe anemia. A cardiac rub suggests pericarditis.

Generalized lymphadenopathy and/or hepatosplenomegaly are common. Abnormal mental status (delirium, psychosis) and/or neurologic (seizure) findings may be present.

Laboratory Workup

Laboratory studies serve a dual purpose in SLE: to aid in diagnosis and to monitor disease activity during and between flares. Immunologic, hematologic, and renal criteria play key roles in diagnosing SLE (Table 60–1).

Absence of ANA makes the diagnosis of aSLE unlikely, but ANA is more variable in cSLE. The most diagnostic immunologic tests for SLE-specific antibodies (Ab) include

- Antinuclear Ab (ANA) (most sensitive)
- Anti–double-stranded DNA (most specific)
- Anti-Smith Ab (correlates with disease severity)

Other Ab that may be present include anti–ribonuclear protein, anti-Ro (neonatal lupus), anti-La (anti–Sjögren syndrome type B), and antihistone (both cSLE and drug-induced lupus). Antiphospholipid Ab levels assess for hypercoagulability and support the diagnosis of cSLE, but the turnaround time can be long. Hypocomplementemia (low C3 and C4) also supports the diagnosis and disease activity of cSLE.

Hematologic and coagulation evaluations are useful for initial diagnosis. Obtain a complete blood cell count to evaluate for the presence of cytopenias (hemolytic anemia [most common], leukopenia, thrombocytopenia). Screen patients for antiphospholipid Ab (lupus anticoagulant, anticardiolipin, or anti–β2 glycoprotein 1).

Renal biopsy findings (classes II, III, IV, V lupus nephritis) are diagnostic for SLE. Prior to biopsy, the most helpful diagnostic renal test is proteinuria greater than 0.5 g/24 h. Prior to 24-hour urinary collection, urinalysis may identify proteinuria, hematuria, urinary casts, and/or hemoglobinuria. Nephritis severity is a key predictor of mortality in cSLE.

The erythrocyte sedimentation rate (ESR) is typically increased during both initial presentation and flares, whereas C-reactive protein (CRP) levels remain normal to minimally increased in SLE flares (except in systemic infection, serositis, or macrophage activation syndrome [MAS]). A liver panel often reveals transaminitis, which occurs with SLE flares, adverse effects of therapeutics, and MAS.

Maintain a high index of suspicion for opportunistic infections, especially for a patient receiving systemic steroids or immunosuppressive agents. If MAS is a concern, check for hyperferritinemia, cytopenias, transaminitis, and rising CRP level with falling ESR (due to fibrinogen consumption).

Diagnosis

As noted previously, the 2019 diagnostic criteria for SLE are summarized in Table 60–1. To diagnose SLE, the patient must have an ANA titer of at least 1:80, along with a total score of 10 of the weighted criteria. Initial validation studies in children indicate that a total score of 13 may be more appropriate for diagnosing cSLE.

Differential Diagnosis

The differential diagnosis of cSLE (Table 60–3) includes considerations for both the initial presentation and disease flares, which are often similar. Given the wide array of presenting symptoms, there is often a delay in diagnosis. The differential diagnosis of cSLE includes other systemic rheumatologic diseases, infectious or postinfectious diseases, malignancies, and Crohn disease.

Table 60–3. Differential Diagnosis of Systemic Lupus Erythematosus

Diagnosis	Clinical Features
Crohn disease	Abdominal pain, diarrhea, weight loss, anemia Erythema nodosum, oral/anal ulcers Arthritis, arthralgias
FUO	(See Table 64–1 for the differential diagnosis)
Hemolytic uremic syndrome	Oliguria, hypertension, uremia Anemia, thrombocytopenia
Hemophagocytic lymphohistiocytosis	Fever, jaundice, hepatosplenomegaly, lymphadenopathy Pancytopenia, hyperferritinemia
Juvenile dermatomyositis	Heliotrope (pinkish-purple) rash of face and eyelids Gottron papules on hands Calcinosis, muscle weakness/contractures, arthritis
Kawasaki disease	Fever, rash, conjunctivitis, extremity changes, mucous membrane changes, lymphadenopathy ↑ ESR/CRP, leukocytosis, anemia, thrombocytosis, sterile pyuria, anemia, elevated alanine aminotransferase, echocardiogram changes
Langerhans cell histiocytosis	Fever, weight loss, bone lesions, rash Enlarged liver, spleen, and/or lymph nodes
Leukemia or lymphoma	Fever, weight loss, bleeding, bruising, pallor, lymphadenopathy Anemia, ↑ or ↓ white blood cell count, thrombocytopenia Arthralgias, bone pain
Multisystem inflammatory syndrome in children due to prior acute COVID-19 disease	(See Tables 65–1 and 65–2) Recent COVID-19 illness or exposure Fever, rash, fatigue, conjunctivitis, extremity changes, red cracked lips, lymphadenopathy, shock, thrombosis ↑ ESR/CRP, ↑ ferritin, ↑ lactate dehydrogenase, ↑ brain natriuretic peptide/troponin, ↑ D-dimer, hyponatremia Lymphopenia < 1000/mcL (< 1×10^9/L), thrombocytopenia < 150,000/mcL (< 150×10^9/L), neutrophilia
Systemic juvenile idiopathic arthritis	(See Table 56–1) Fever, arthritis, and a salmon-pink rash
Vasculitis	Headache, weight loss, myalgia Rash, ulcers, aneurysms FUO

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FUO, fever of unknown origin.
↑ indicates elevated level; ↓, decreased level.

Treatment

The multidisciplinary, inpatient treatment of cSLE typically includes a rheumatologist, hospitalist, and nephrologist who tailor treatments to disease severity. Other specialists (adolescent medicine, cardiology, dermatology, gastroenterology, gynecology, hematology, immunology, neurology, palliative care, physiatry, psychiatry, and psychology) are included, depending on disease manifestations. The goals of care include controlling

target organ damage, minimizing adverse effects of treatment, and maximizing quality of life.

The Childhood Lupus Improvement Index establishes cutoffs that define whether the response to therapy (ie, improvement in disease) is classified as minor, moderate, or major. This then guides the indication labeling by the US Food and Drug Administration (FDA).

Many medications used in the treatment of cSLE have serious side effect profiles. Treatment decisions must be made judiciously, weighing the risk–benefit ratio, in close consultation with a pediatric rheumatologist. Close monitoring for adverse effects is indicated with initiation and titration of therapies. Many medications are *not* approved for use in cSLE by the FDA. However, various classes of medications may be used for the management of cSLE including nonsteroidal anti-inflammatory drugs (NSAIDs), antimalarials, steroids, disease-modifying antirheumatic drugs (DMARDs), and biologic agents. In addition, plasma exchange and/or intravenous (IV) immunoglobulin are indicated for rapidly progressive disease or life-threatening flares.

- **NSAIDs:** These are helpful for patients with mild arthritis or serositis. However, their use may be limited by concurrent renal disease.
- **Antimalarials (hydroxychloroquine):** These decrease disease activity, flares, and mortality, improve lipid profiles, and decrease the risk of diabetes mellitus, atherosclerosis, and severe infections. They are used to treat mild symptoms of arthritis or rash.
- **Steroids:** Topical and/or low-dose oral glucocorticoids may be used for mild to moderate disease, but avoid long-term treatment due to unwanted side effects. High-dose oral or IV steroids remain the mainstay of treatment for severe initial disease manifestations and flares or to induce remission in lupus nephritis. Corticosteroid adverse effects may mimic NP complications.
- **DMARDs:** These facilitate tapering of glucocorticoid doses to avoid chronic adverse effects. They are especially helpful with hematologic, musculoskeletal, renal, or NP complications.
  - — Azathioprine: Safe in pregnancy and often used for new mild to moderate disease and as maintenance treatment following severe flares.
  - — Methotrexate: Alternative to azathioprine when musculoskeletal or mucocutaneous symptoms are prominent.
  - — Mycophenolate mofetil: Preferred in moderate to severe disease refractory to other treatments; used in conjunction with steroids to induce remission of lupus nephritis.
  - — Cyclophosphamide (alkylating agent): Used for severe disease manifestations or with life-threatening flares.

- **Biologic agents:**
  - — Belimumab (B-lymphocyte stimulator-specific inhibitor): In 2019, this became the first FDA-approved medication for cSLE therapy in children younger than 5 years (improved outcomes when used in combination with standard therapy).
  - — Rituximab (anti-CD19 monoclonal Ab): Used off-label; particularly effective in treating cytopenias, NP, cutaneous, and refractory lupus.

Complications

Disease Flares

Consult a rheumatologist for guidance on treatment of cSLE disease flares. Flare scores facilitate classification of disease flares (mild, moderate, or severe), which is essential to conducting randomized withdrawal trials (primary outcomes are time to flare or the proportion of patients who experience a flare).

Systemic Infections

Consider patients with cSLE to be immunocompromised with functional asplenia and dysregulation of the adaptive and innate immune systems. Many medications used to treat cSLE exacerbate this infection risk. Give special consideration to infection from encapsulated bacterial organisms, systemic cytomegalovirus, herpes zoster, *Pneumocystis jirovecii (PJP)*, and *Cryptococcus*. Immunize patients with cSLE against encapsulated organisms, avoid live-attenuated immunizations without rheumatology approval, and order PJP prophylaxis based on the degree of immunosuppression and the medication(s) being used.

Neuropsychiatric Complications

Monitor for NP manifestations, which can occur at any point in time and are heterogeneous, making diagnosis of these complications a challenge. The most common in descending order are headaches, seizures, cognitive dysfunction, depression, psychosis, cerebrovascular disease, and acute confusional state. Neuropsychiatric complications affect morbidity, mortality, education, work, socialization, and quality of life, and they can occur in the absence of changes in the serum markers. Due to the diversity of symptoms and limited studies, treatment is challenging. Current therapies include antipsychotics and antidepressants and therapies directed at inflammation or at prevention of thrombotic or ischemic events.

Renal Disease

Consult a nephrologist for evaluation, biopsy planning, and management, as renal health is a key predictor of long-term survival in cSLE. Aggressively treat

hypertension and/or proteinuria, targeting a normal blood pressure. Review all nephrotoxic medications, dose appropriately, order a renal diet, and strictly monitor fluid balance. Monitor the response to therapy in lupus nephritis with a first morning void spot urine protein to creatinine ratio and serum creatinine.

Thrombotic Events

A patient with cSLE and antiphospholipid Ab is at increased risk of thromboembolic events; initiate anticoagulation prophylaxis (see Chapter 46, Deep Venous Thrombosis). Low-dose aspirin is useful in decreasing risk, and heparin or low–molecular weight heparin can treat or prevent thrombosis, depending on the risk factors. A heparin drip may be indicated for severe thrombotic events.

Indications for Consultation

- **Rheumatology:** All patients
- **Hospital medicine:** Based on care coordination needs
- **Nephrology:** Renal involvement and/or hypertension
- **Ophthalmology:** Initial (and annual) dilated funduscopic examination to monitor disease and treatment adverse effects
- **Psychology/psychiatry:** Possible NP involvement

Disposition

- **Transfer to a center with a pediatric rheumatologist:** Serious SLE-related complication
- **Telehealth consultation:** If access to a pediatric rheumatologist is limited
- **Intensive care unit transfer:** Severe sepsis, non–fluid responsive shock, progressive MAS, dialysis, heparin drip, plasma exchange, ischemic or thrombotic event
- **Discharge criteria:**
  - — Timely follow-up with a rheumatologist available
  - — Disease flare: Symptoms improving, medication regimen established
  - — Systemic infection: Clinical improvement with targeted antibacterial or antiviral therapy
  - — Renal insufficiency/failure: Creatinine level stable or improving, adequate urine output and blood pressure control, timely follow-up with a nephrologist available
  - — Thrombotic event: Clinical improvement with stable anticoagulant dosing

Follow-up

- **Primary care:** Within 1 week
- **Rheumatologist:** Within 1 to 4 weeks, depending on condition at discharge

- **Nephrologist:** Within 1 to 4 weeks, as needed
- **Various subspecialties:** As needed

Pearls and Pitfalls

- Suspect cSLE in an adolescent female with some combination of constitutional symptoms (fever, generalized lymphadenopathy, weight loss), mouth sores, rash (malar and/or photosensitive), and arthritis.
- Elevation in the ESR occurs during a flare.
- An acute CRP elevation suggests systemic infection, serositis, or MAS.
- A multidisciplinary approach to the inpatient treatment of patients with cSLE includes a pediatric rheumatologist, hospitalist, psychologist, and nephrologist, as well as other consultants depending on symptoms and complications.
- Medications used in the treatment of cSLE have serious side effect profiles, and many are used off-label. Treatment decisions must be made judiciously, weighing the risk-benefit ratio, in close consultation with a pediatric rheumatologist.

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Infectious Disease

CHAPTER 61

Acute COVID-19 Disease

Introduction

Pandemic COVID-19, the disease caused by SARS-CoV-2, primarily affects the respiratory, gastrointestinal, endovascular, and neurologic systems. Children of all ages can be affected, generally with milder disease than adults. Risks for hospitalization include unvaccinated status, age younger than 2 years, age 12 to 17 years, obesity, chronic respiratory diseases, asthma, and immunosuppression.

Clinical Presentation

History

Most often, a patient who will require hospitalization due to acute COVID-19 disease presents with fever and/or chills. Other complaints may include pneumonia (dry, nonproductive cough; shortness of breath; hypoxia; respiratory distress), gastroenteritis (abdominal pain, nausea, vomiting, diarrhea), dehydration, myalgias, headache, seizures, and loss of smell and/or taste. In some cases, COVID-19 is detected incidentally when a patient is being hospitalized for another reason.

Ask about recent travel, particularly to areas with high COVID-19 activity, contact with someone diagnosed with the disease, and COVID-19 vaccine status.

Physical Examination

The patient may present as significantly ill, with fever, tachycardia, tachypnea, and hypoxia. Assess the patient's perfusion, which may be adversely affected by decreased oral intake, vomiting, diarrhea, and tachypnea. Poor perfusion, in the context of a newly identified murmur, hepatomegaly, jugular venous distention, or widened cardiac silhouette on chest radiographs, raises the concern of heart failure and the need for caution with fluid resuscitation.

A patient with acute COVID-19 pneumonia is usually tachypneic, with or without wheezing or rales. Hypoxia and breathlessness on walking are common features. The child may appear anxious and/or agitated, ominous signs of respiratory distress and impending respiratory failure.

Perform serial abdominal assessments. Auscultate for bowel sounds and palpate for focal versus diffuse tenderness, rigidity, and rebound tenderness and other peritoneal signs to identify an acute surgical abdomen. COVID-19

typically does not present with a surgical abdomen, although MIS-C (see Chapter 65, Multisystem Inflammatory Syndrome in Children [MIS-C]) can mimic one.

Laboratory Workup

Focus the initial laboratory workup on confirmation of current infection with SARS-CoV-2, identification of new-onset organ dysfunction, measurement of the degree of systemic inflammation versus immune suppression, and evaluation of bacterial coinfection.

Obtain nasopharyngeal swab specimens for nucleic acid amplification tests (NAATs) with real-time polymerase chain reaction to SARS-CoV-2 RNA, if not done prior to admission. Although antigen testing of SARS-CoV-2 is less sensitive than NAATs, it can be performed rapidly or even as a point-of-care test. If the antigen testing is negative, but COVID-19 is likely, obtain NAATs. Also obtain a complete blood cell count, basic metabolic panel, liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels), C-reactive protein, lactate dehydrogenase, ferritin, procalcitonin, erythrocyte sedimentation rate, troponin T, creatinine kinase myocardial band, prothrombin time, partial thromboplastin time, fibrinogen, and a blood culture. An arterial blood gas is indicated if the patient requires more than 0.40 Fio_2 of supplemental oxygen to maintain their oxygen saturation above 94%.

Obtain chest radiographs if the patient's oxygen saturation is less than 90% on room air. Although not all patients with COVID-19 have radiographic findings, ground-glass opacities and focal consolidations are the commonly seen pathologies. Other important findings include parapneumonic effusions, pneumothoraces, and cardiomegaly, as these may indicate the presence of an unforeseen co-infection, a treatable air leak syndrome, or new-onset heart dysfunction, respectively.

Differential Diagnosis

Other causes of significant respiratory distress that may present similarly to acute COVID-19 include pneumonia (typical and atypical bacterial, viral, chemical), pneumonitis, and electronic cigarette (vaping)–associated lung injury. Other considerations are heart failure from another etiology, myocarditis, sepsis, pulmonary emboli, and autoimmune and connective tissue diseases, such as systemic lupus erythematosus and anti–glomerular basement membrane (anti-GBM, or Goodpasture) disease.

Consider MIS-C in a patient with shock-like presentation or with abdominal pain mimicking appendicitis.

Treatment

A primary pillar of management is infection control and disease prevention. Isolate any patient with active SARS-CoV-2 infection with a respiratory component, with standard droplet, contact, airborne, and eye protection protocols for anyone entering the room. Limit the degree of patient contact and the number of times someone enters the patient's room. Place the patient in a negative pressure room if they have respiratory disease, especially if they will be receiving aerosolizing modalities (nebulized medical treatments, high-flow nasal cannula, continuous positive airway pressure, bilevel airway pressure).

The cornerstones of treatment are early use of steroids and remdesivir, based on disease severity and age, while preventing thrombosis with early ambulation. Monitor the vital signs, including the oxygen saturation, and trend the inflammatory markers (as outlined previously) every 48 to 72 hours.

Provide supplemental oxygen, either by face mask or nasal cannula, to maintain an oxygen saturation of at least 90%. If the patient has severe disease, with marked tachypnea or increased work of breathing, provide noninvasive ventilatory support (see Chapter 97, Airway Management and Respiratory Support). Although hospital policies vary, noninvasive ventilatory support is best given and monitored continuously in an intensive care setting, with pulmonary and/or critical care consultation. Treat with appropriate antibiotics (see Chapter 100, Community-Acquired Pneumonia) if there is a concern for a bacterial pneumonia.

Ensure adequate hydration if the patient cannot take sufficient fluids orally. Give an isotonic fluid, with 10 to 20 mEq/L (10–20 mmol/L) of potassium chloride, at a rate sufficient to maintain a urine output of 1 to 2 mL/kg/h. Acute kidney injury is common in COVID-19, so monitor the electrolytes and remove the potassium if the patient is oliguric or anuric.

The patient may be at increased risk for deep venous thrombosis and pulmonary emboli, especially if the D-dimer is rising or the level is greater than 1 mcg/mL (5.476 nmol/L). Consult with a hematologist to decide whether to administer anticoagulation therapy based on risk factors such as obesity, cardiac disease, cancer, recent surgery, immobility, indwelling central lines, and critical illness (see Chapter 46, Deep Venous Thrombosis). If pharmacologic venous thromboembolism prophylaxis is warranted, give low–molecular weight heparin, 0.5 mg/kg per dose, every 12 hours if the patient's creatine clearance is greater than 30 mL/min. Also, encourage mobilization and provide nonpharmacologic modalities, such as pneumatic compression stockings.

Consult with an infectious disease specialist to decide about the use of an antiviral agent, such as remdesivir, for a patient 28 days or older and weighing at least 3 kg. Give an intravenous (IV) loading dose of 200 mg on the day of admission, followed by 100 mg every 24 hours afterward, typically for 5 days total.

Although definitive data in children are lacking, low-dose steroids have been associated with decreased mortality, especially in moderate to severe disease. Give oral or IV dexamethasone to a patient who requires noninvasive or invasive ventilatory support. The dose is 0.15 mg/kg (maximum 6 mg), administered once daily, orally or IV, until the patient is discharged from the hospital, or for a maximum of 10 days, whichever is shorter.

Indications for Consultation

- **Cardiology:** Concern for heart failure or MIS-C
- **Hematology:** Risk of a thromboembolic event and the need for prophylaxis
- **Infectious diseases:** Consideration of antiviral treatment
- **Nephrology:** Acute kidney injury
- **Neurology:** Persistently abnormal neurologic examination
- **Pulmonology:** Need for noninvasive or invasive ventilatory support
- **Rheumatology:** Concern for MIS-C

Disposition

- **Intensive care or subspecialty unit transfer:** Hemodynamic instability, acute respiratory failure requiring invasive ventilation, concern for serious cardiovascular disease, shock, acute kidney injury, persistent abnormal neurologic findings
- **Acute rehabilitation facility:** Need for weaning of respiratory support or intensive physical and occupational therapy
- **Discharge criteria:** No oxygen requirement, tolerating oral medications, maintaining hydration orally

Follow-up

- **Primary care provider:** 1 to 3 days
- **Subspecialists:** As per the diagnosis, generally 1 to 2 weeks

Pearls and Pitfalls

- Regardless of one's vaccination status, always use personal protective equipment (N95 mask, gloves, gown, eye protection, and physical barriers) whenever in direct contact with patients with a suspected or confirmed case of COVID-19.

- The risk of serious illness, hospitalization, and death from COVID-19 is significantly reduced if the patient has received a complete primary vaccine series.
- Recommendations change frequently. Check the NIH website for the latest treatment guidelines: https://www.covid19treatmentguidelines.nih.gov.

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CHAPTER 62

Fever in Infants Younger Than 60 Days

Introduction

Fever in an infant younger than 60 days is defined as a rectal temperature 38 °C (100.4 °F) or higher without evidence of a localized infection such as pneumonia, bronchiolitis, cellulitis, or abscess. In this age group, fever may be the only presenting sign of urinary tract infection (UTI), bacteremia, or bacterial meningitis, with UTI being the most prevalent of these (> 10% of cases). Bacteremia (< 2% of cases) and bacterial meningitis (< 0.5% of cases) are rare and now categorized as invasive bacterial infections (IBIs), with infants 21 days and younger at highest risk.

The most likely organisms causing UTI, bacteremia, and meningitis in the first 60 days after birth include *Escherichia coli,* group B *Streptococcus* (GBS), and *Streptococcus pneumoniae*. Less common but important bacterial organisms are *Staphylococcus aureus, Klebsiella*, *Salmonella*, and *Enterococcus. Listeria monocytogenes* is an exceedingly rare cause of fever in an otherwise well-appearing infant. The most common viral etiologies of fever in infants aged 8 to 60 days include enteroviruses, rhinoviruses, and respiratory syncytial virus.

An otherwise well-appearing febrile infant requires evaluation for bacterial infection and possible empiric antimicrobial treatment while awaiting culture results. However, full evaluation and treatment for all infants younger than 60 days with fever may result in unnecessary costs and iatrogenic complications. Therefore, use risk stratification criteria by age to guide evaluation and empiric treatment. The most recent febrile infant guidelines use the following age groups: 8 to 21 days, 22 to 28 days, and 29 to 60 days. Exclusion criteria include age 7 days or younger, gestational age younger than 37 weeks, clinical bronchiolitis, and medical complexity.

Appropriate antibiotic treatment is indicated if a possible bacterial source for the fever is diagnosed on clinical evaluation. Also, treat with antibiotics, pending culture results, an ill-appearing infant without a source identified after completing a full sepsis workup (blood, urine, cerebrospinal fluid [CSF] cultures).

Clinical Presentation

History

Fever in an infant includes a rectal temperature of 38 °C (100.4 °F) or higher at home within the past 24 hours, even if the infant remains afebrile in the clinical setting. Ask about risk factors for infection such as preterm gestation,

underlying medical conditions, and maternal history of GBS and herpes simplex virus (HSV). Note any recent changes in infant behavior that may indicate illness, such as feeding, urine output, bowel habits, and level of alertness. A history of respiratory distress, vomiting, rashes, or skin lesions may be a clue to the source of infection or indicate the severity of illness. Assess exposure history including known contact with sick persons, day care attendance, and recent travel. Ask about what the family has done to address the fever or other symptoms, including possible use of antipyretics. Assess the family's ease of access to health care, ability for close follow-up, and level of medical literacy.

Physical Examination

The physical examination findings will be unremarkable in most infants presenting with fever, although it is important for assessing the severity of illness and identifying any localizing signs that may indicate an underlying etiology. Particularly concerning findings, which then exclude the infant from the guidelines, include irritability, lethargy, hypotonia, bulging fontanelle, tachypnea, grunting, apnea, mottled skin, cyanosis, poor capillary refill, jaundice, soft-tissue swelling, and difficulty moving an extremity, although meningeal signs may be absent in an infant with meningitis. Vesicular lesions involving the skin, eye, or mouth can occur with an HSV infection, which is also excluded from the guidelines. A temperature higher than 38.5 °C ($>$ 101.3 °F) increases the concern for a bacterial infection.

Laboratory Workup

Obtain a full laboratory evaluation (blood culture, complete blood cell count [CBC], urinalysis [UA], urine culture, and CSF) for an infant younger than 8 days and any infant with a concerning history, appearance, or physical examination findings. For the well-appearing infant 8 to 60 days of age, with an unremarkable physical examination, the extent of the laboratory workup is guided by age-based risk stratification.

Obtain serum inflammatory markers (Table 62–1), including a CBC with differential, C-reactive protein (CRP), and procalcitonin (PCT), if the results will influence further workup or treatment. The absolute neutrophil count is the most useful component of the CBC, but the CRP is more accurate. PCT is the best independent predictor of bacteremia and bacterial meningitis, although this test is not universally available and the results might be too late to affect management decisions.

Perform a lumbar puncture (LP) only if the infant is considered high risk by age, clinical findings, or laboratory values. Send the CSF for cell count, protein and glucose levels, and bacterial culture (Table 62–2). Send CSF for

Table 62–1. Abnormal Values for Urinalysis and Inflammatory Markers

Category	Test	Value
Urinalysis	Leukocyte esterase	Present
	WBC count	> 5/HPF or > 10/ mm^3 (> 0.01 × 10^9/L)
Inflammatory markers	Temperature	> 38.5 °C (> 101.3 °F)
	Absolute neutrophil count	> 4,000 or > 5,200/ mm^3 (> 4.0 or > 5.2 × 10^9/L)
	CRP	> 20 mg/L
	PCT	> 0.5 ng/mL

Abbreviations: CRP, C-reactive protein; HPF, high-power field; PCT, procalcitonin; WBC, white blood cell.
Derived from Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics*. 2021;148(2):e2021052228.

Table 62–2. Normal Cerebrospinal Fluid Values

Laboratory Finding	Age (days)	Range
WBCs/ mm^3	1–28	0–18
	29–60	0–8.5
Protein mg/dL	1–28	15.8–131.0
	29–60	5.5–105.5
Glucose	1–28	30.0–61.0
	29–60	20.6–65.5
RBCs/ mm^3	1–28	0–236
	29–60	0–64.5

Abbreviations: RBCs, red blood cells; WBCs, white blood cells.
Adapted from Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics*. 2021;148(2):e2021052228.

enterovirus polymerase chain reaction (PCR) during the summer and/or when there is a pleocytosis. If these results are available in a timely fashion, a positive PCR may allow for early discontinuation of empiric antibiotics. CSF with a large number of red blood cells (RBCs) may be due to a traumatic tap or HSV, although the absence of RBCs does not rule out HSV. The CSF white count is accurate with up to 10,000 RBCs present. Regardless, CSF with a high RBC count can still be sent for bacterial culture and HSV PCR.

Obtain a chest radiograph only if the infant has respiratory symptoms. Send a respiratory pathogen panel (RPP) only if the results would change management. A positive RPP does not affect risk stratification for bacterial infection but may allow for earlier discharge. Obtain a stool culture if there are persistent watery, mucoid, or bloody stools.

If the infant has risk factors for HSV (Box 62–1), obtain HSV studies: surface swabs of mouth, nasopharynx, conjunctivae, and anus for HSV culture or PCR; serum alanine aminotransferase and HSV PCR; and CSF HSV PCR.

Box 62–1. HSV Risk Factors

History
Maternal fever from 48 hours before to 48 hours after delivery
Maternal history of HSV lesions

Clinical Presentation
Apnea
Focal neurological signs
Hypothermia
Mucocutaneous vesicles
Seizures

Laboratory Values
CSF pleocytosis with a negative Gram stain
Elevated alanine aminotransferase
Leukopenia
Thrombocytopenia

Abbreviations: CSF, cerebrospinal fluid; HSV, herpes simplex virus.
Derived from Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics.* 2021;148(2):e2021052228.

Age-Based Laboratory Summary

Ages 8 to 21 Days

Obtain a sterile urine (via catheterization or suprapubic aspiration) for UA, and then send a urine culture if the UA is positive for leukocyte esterase on dipstick or more than 5 white blood cells per high-power field (WBC/HPF) on microscopy. A positive culture is defined as more than 10,000 colony-forming units of a uropathogenic organism. Obtain blood for culture and inflammatory markers, such as WBC, CRP, or PCT, which may help with determining the duration of treatment. Perform an LP and send the CSF for culture, cell count, and glucose and protein levels. Also order enteroviral testing if there is a pleocytosis.

Ages 22 to 28 Days

Obtain a UA, urine culture, blood culture, and inflammatory markers (as outlined for ages 8–21 days). Elevated inflammatory markers, in the context of a negative UA, can help inform the decision to start empiric antibiotics and/or perform an LP.

Ages 29 to 60 Days

Obtain a UA, urine culture, blood culture, and inflammatory markers (as outlined for ages 8–21 days). Do not perform an LP if the inflammatory markers are normal.

Differential Diagnosis

Most well-appearing patients will have an infectious etiology for the fever, but assume that a neonate younger than 8 days has a vertically acquired perinatal infection until proven otherwise.

Disseminated or central nervous system (CNS) HSV is a concern in a neonate with sepsis syndrome or seizures with or without a vesicular rash. Approximately three-quarters of infants who contract HSV are born to women with no reported history or clinical findings suggestive of genital HSV infection during or preceding pregnancy. Initial signs of HSV can occur any time between birth and 6 weeks, although almost all infected infants with disseminated or CNS disease or disease limited to the skin, eyes, and/or mouth develop clinical symptoms within the first month after birth. Consider disseminated or CNS HSV in a neonate with sepsis syndrome, negative bacterial culture findings, seizures, liver dysfunction, coagulopathy, and/or CSF pleocytosis.

Other possible etiologies of fever include a focal abscess, cellulitis, omphalitis, GBS lymphadenitis, osteomyelitis, pertussis, malignancy, and nonaccidental trauma.

Treatment

Empirically treat with intravenous (IV) antibiotics an infant younger than 21 days, as well as any infant with a concerning history, overall appearance, or physical examination findings. For the well-appearing febrile infant with an unremarkable physical examination and reassuring laboratory results, use the age-based risk stratification to guide empiric antimicrobial treatment.

The choice of empiric antibiotics depends on the patient's age, most likely source of infection, and local antibiogram (see Table 62–3). Administer all empiric antimicrobials parenterally (IV or intramuscular [IM]), except when treating an isolated UTI in an infant 29 to 60 days of age. Empiric therapy must cover gram-negative and gram-positive organisms, including *E coli*, GBS, and *S pneumoniae*. This can be accomplished with a third-generation cephalosporin (ceftriaxone or ceftazidime) or a combination of ampicillin and an aminoglycoside. Use ampicillin when coverage for *Listeria* or enterococcal species is indicated. Synergy between ampicillin and gentamicin may offer additional coverage against GBS and *Enterococcus*. Do not use ceftriaxone in an infant younger than 7 days, if the patient has hyperbilirubinemia, or if they are receiving an IV calcium-containing solution. Add vancomycin for an infant older than 28 days with suspected bacterial meningitis. Discontinue empiric antibiotics when all cultures are negative at 24 to 36 hours. If a pathogen is identified through positive culture or PCR, tailor treatment accordingly.

Not every well-appearing, febrile infant younger than 60 days requires empiric treatment. Use the patient's age and laboratory results to guide the decision to initiate parenteral antibiotics. If cultures could not be obtained, use the other laboratory results to determine the treatment duration. The risk of IBI is higher with abnormal inflammatory markers and a temperature higher

Table 62–3. Antibiotics by Age and Suspected Source of Infection

Suspected Source of Infection	8–21 Days Old	22–28 Days Old	29–60 Days Old
UTI	Ampicillin IV/IM (150 mg/kg/d administered in doses given every 8 h) *and either* Ceftazidime IV/IM (150 mg/kg/d administered in doses given every 8 h) *or* Gentamicin IV/IM (4 mg/kg administered every 24 h)	Ceftriaxone IV/IM (50 mg/kg/dose every 24 h)	Ceftriaxone IV/IM (50 mg/kg/dose every 24 h) Oral medications: Cephalexin (50–100 mg/kg/d administered in doses given every 4 h) *or* Cefixime (8 mg/kg every 24 h)
Bacteremia	Ampicillin IV/IM (150 mg/kg/d administered in doses given every 8 h) *and either* Ceftazidime IV/IM (150 mg/kg/d administered in doses given every 8 h) *or* Gentamicin IV/IM (4 mg/kg administered every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h)
Bacterial meningitis	Ampicillin IV/IM (300 mg/kg/d administered in doses given every 6 h) *and* Ceftazidime IV/IM (150 mg/kg/d administered in doses given every 8 h)	Ampicillin IV/IM (300 mg/kg/d administered in doses given every 6 h) *and* Ceftazidime IV/IM (150 mg/kg/d administered in doses given every 8 h)	Ceftriaxone IV (100 mg/kg/d either every 24 h or divided into doses administered every 12 h) *or* Ceftazidime IV/IM (150 mg/kg/d administered in doses given every 8 h) *and* Vancomycin IV (60 mg/kg/d divided into doses administered every 8 h)

Abbreviations: IM, intramuscular; IV, intravenous; UTI, urinary tract infection.

Adapted from Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8 to 60 days old. *Pediatrics.* 2021;148(2):e2021052228.

than 38.5 °C (> 101.3 °F), but meningitis is rare in an otherwise well-appearing infant with a negative blood culture.

If the history, clinical presentation, or laboratory results are concerning for HSV infection, treat empirically with IV acyclovir (60 mg/kg/d divided into doses administered every 8 hours) (Box 62–1). Initiate maintenance IV fluids to prevent acyclovir-related acute kidney injury, and discontinue the acyclovir when the CSF HSV PCR result is negative. Side effects of acyclovir include anemia, neutropenia, and thrombocytopenia, as well as increased serum bilirubin and transaminase levels.

Age-Based Treatment Summary

Ages 8 to 21 Days

Treat with empiric antibiotics (Table 62–3).

Ages 22 to 28 Days

Treat with empiric antibiotics if the infant has a positive UA, CSF parameters are concerning for bacterial meningitis, or the LP was indicated but CSF could not be obtained or is not interpretable. If the UA and CSF are within normal limits, but at least 1 inflammatory marker is abnormal (including temperature > 38.5 °C [> 101.3 °F]), it is reasonable but not necessary to treat empirically while awaiting culture results. Alternatively, observe the infant in the hospital without treatment. If the UA, inflammatory markers, and CSF (if obtained) are all within normal limits, or the CSF is positive for enterovirus (EV), it is reasonable to observe in the hospital without empiric treatment. If CSF is obtained and is within normal limits, observation may be completed at home if the family can follow up within 24 hours. This approach is guided by shared decision-making with the infant's caregiver(s), but treat the infant with 1 (IV or IM) dose of empiric antibiotics prior to discharge.

Ages 29 to 60 Days

Treat with empiric antibiotics if the infant has CSF parameters that are concerning for bacterial meningitis, or if the LP was indicated but CSF could not be obtained or is not interpretable. If the CSF is within normal limits, but the inflammatory markers are abnormal, it is reasonable, but not necessary, to treat empirically. If the UA is positive, with normal inflammatory markers and CSF, treat for a UTI with oral antibiotics. If the UA, inflammatory markers, and CSF (if obtained) are all within normal limits (or the CSF is positive for EV), empiric antibiotic treatment is not indicated while awaiting culture results. If the UA and inflammatory markers are within normal limits, observation may be completed at home if the family can follow up in 24 hours. Once again, this approach is guided by shared decision-making with the infant's caregiver(s), but the infant does not require empiric antibiotics.

Indications for Consultation

- **Infectious diseases:** Atypical presentation and/or clinical course

Disposition

- **Intensive care unit transfer:** Hemodynamic instability despite administration of IV fluids and antibiotics; significant respiratory distress, apnea, or seizure

- **Discharge criteria:** All cultures negative at 24 to 36 hours; infant is alert, consolable, feeding well, and making adequate urine, and has no respiratory distress; close follow-up arranged

Follow-Up

- **Primary care:** In 2 to 3 days if discharged home after cultures returned negative at 24 to 36 hours; in 24 hours if discharged home for close observation while awaiting culture results

Pearls and Pitfalls

- Birth via cesarean section does not eliminate the risk of neonatal HSV.
- HSV CSF PCR findings may be negative during the first few days of the illness. Treat empirically and perform serial CSF testing if there is a high degree of clinical suspicion for HSV.
- The presence of blood in the CSF is not significantly associated with the rate of HSV meningoencephalitis.
- Obtain enterovirus testing during the warmer months if the patient has a CSF pleocytosis.
- A rectal temperature higher than 38.5 °C (> 101.3 °F) is considered a positive inflammatory marker for purposes of risk stratification.
- Persistent fever despite standard empirical antibiotic coverage is most likely secondary to a viral infection and not an atypical bacterial disease.
- *Neisseria meningitidis* is a rare cause of bacterial infection in this age group and may signal an underlying complement deficiency or asplenia.

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CHAPTER 63

Fever in the International Traveler

Introduction

The ready access to overseas travel is associated with an increased risk of exposure to pathogens not endemic to the United States. Maintaining a high index of suspicion, timely recognition and management, and containment of these infections are essential for the health of the individual and the community. However, common infections of the upper respiratory and urinary tracts, pneumonia, viral gastroenteritis, influenza, and infectious mononucleosis will be the etiologies of fever among most children with a recent travel history. Therefore, the most important aspect of care of the recent traveler is a careful history and physical examination. Seek signs of common infections, but be aware of the most important life-threatening infections related to travel, and treat these empirically on the basis of initial findings while the evaluation proceeds.

Malaria

Malaria is caused by 1 of 5 species of intraerythrocytic parasites of the genus *Plasmodium* (*Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae,* and *Plasmodium knowlesi*) and is spread by female mosquitoes of the *Anopheles* genus. Malaria is endemic throughout the tropics, and about one-half of the world's population lives in areas where transmission occurs. In the United States, there are approximately 2,000 cases of malaria each year, almost all of which are a result of travel from the global endemic areas of Africa and Southeast Asia. Always consider malaria as a possible cause of unexplained fever in an international returnee from a tropical destination.

Dengue

Dengue (also known as "breakbone fever") is an acute febrile illness caused by infection with 1 of 4 dengue virus (DENV) serotypes. Transmission most commonly occurs through the bite of *Aedes* mosquitoes (*Aedes aegypti* and *Aedes albopictus*). Because dengue viremia can last about 7 days, transmission can also occur through exposure to infected blood, organs, or other tissues. Neonates can contract the virus through perinatal transmission from infected mothers, as well as possibly through human milk.

Dengue is endemic throughout the tropics and subtropics and is a leading cause of febrile illness among travelers from Latin America, the Caribbean, and Southeast Asia. However, because human-to-human transmission is

possible, there have been outbreaks in nonendemic regions, such as Europe and North America.

Enteric Fever

Enteric fever is an umbrella term for the clinically indistinguishable typhoid and paratyphoid fevers. Typhoid fever is caused by *Salmonella* serovar Typhi (*Salmonella* Typhi), whereas paratyphoid fever is caused by *Salmonella* serovar Paratyphi A, B, or C.

Enteric fever is prevalent in resource-limited areas of the world with poor sanitation and overcrowding, including the Indian subcontinent, south central and Southeast Asia, and southern Africa. It is limited to humans and acquired by ingestion of contaminated food or drink. A traveler who received the typhoid vaccine is still at risk, as it is generally only about 50% to 80% effective.

Clinical Presentation

History

Malaria

Ask about prophylaxis medication, mosquito bites, high-grade fevers, chills, rigors, sweats, and headache in a patient with a history of travel to a malaria-endemic area. The symptoms may begin as early as 7 days after initial exposure but may also occur as late as several months afterward. Patients may report cyclic fever (every 2 or 3 days), but absence of this pattern does not rule out malaria. Rarely, a patient with *P falciparum* can present with intravascular hemolysis that leads to anemia, hemoglobinuria, and renal failure (also known as "blackwater fever"). Cerebral malaria can also develop with *P falciparum* infection. Relapse may occur with both *P vivax* and *P ovale* infection.

Dengue

Dengue presents with the abrupt onset of fever, anywhere from 3 to 14 days after a potential exposure. The fever can be biphasic and last up to 1 week. The patient may also have severe headache, retroorbital pain, myalgia, arthralgia, and bone pain.

The course of disease typically has 3 phases: febrile, critical, and convalescent. The critical phase begins at defervescence and lasts up to 48 hours. Although most patients show clinical improvement during this phase, up to 5% develop severe dengue, with complaints consistent with substantial plasma leakage. Warning signs for severe dengue include generalized edema, severe abdominal pain and vomiting, hepatomegaly, hemoconcentration, shortness of breath, and lethargy. Serious bleeding, including hematemesis, hematochezia, melena, or menorrhagia may also be present. Severe disease is more

likely if the patient had a previous infection and is now experiencing a repeat infection, rather than with initial exposure.

Enteric Fever

After an incubation period of 1 to 4 weeks, enteric fever presents with either isolated fever or fever with abdominal pain. Initially, the fever tends to be intermittent, with a stepwise pattern, and it may then become continuous. There may be a history of chills, anorexia, headache, abdominal pain, rash, diarrhea (possibly bloody), or conversely, constipation. Severe complications, such as intestinal hemorrhage or perforation, can occur in the second or third week of the illness.

Physical Examination

Malaria

The patient is typically ill appearing but not toxic, although there may be pallor or jaundice in severe cases. Splenomegaly is a common finding. Signs of severe disease include shock, altered sensorium, seizures, and organ system failure (eg, renal, respiratory, and hepatic).

Dengue

Oropharyngeal and facial erythema may be noted in the first 48 hours of symptoms. A macular or maculopapular rash may be present, and the patient may have petechiae, ecchymoses, purpura, or mild mucosal bleeding. Physical findings of severe dengue include edema (central or peripheral), decreased breath sounds because of pleural effusions, and signs of shock, such as narrowing pulse pressure, hypotension, or signs of end-organ hypoperfusion.

Enteric Fever

The classic, but uncommon, rash is rose spots, which are macular, salmon-colored lesions over the chest and abdomen. Other findings include mild hepatosplenomegaly. In severe cases, intestinal bleeding and perforation, altered mental status, and possibly shock can be seen.

Laboratory Workup

If any of these 3 diseases is being considered, obtain a complete blood cell count (CBC) with white blood cell differential and platelet count, liver transaminase levels, and, if the patient appears toxic, blood culture.

Malaria

Findings include anemia, and in severe cases, thrombocytopenia or hypoglycemia can be seen. The Centers for Disease Control and Prevention (CDC) provide resources to assist with malaria diagnosis, including serology,

polymerase chain reaction (PCR) assays, microscopy, and drug-resistance testing. Contact the Malaria Hotline for Healthcare Providers (1-770-488-7788 or 1-855-856-4713 [toll free] or 1-770-488-7100 [after hours]; or via e-mail: malaria@cdc.gov). The standard of reference for diagnosis is a peripheral blood smear to look for parasites. Obtain both thick and thin smears to identify and quantify the parasitemia, as parasite load is important to determine malaria severity and risk of complications. If the pretest probability of malaria is high, 3 negative test sets are necessary to rule out the diagnosis.

A rapid diagnostic test is available as an initial screen; if positive, start empirical therapy. If the test is negative but clinical suspicion remains high, repeat the smears and CBC to exclude the diagnosis.

Some state laboratories will perform PCR assays, which can detect low levels of parasitemia (0.5–5.0 parasites/mcL).

Dengue

Findings may include leukopenia, thrombocytopenia, hyponatremia, and increased transaminase levels. Erythrocyte sedimentation rate and C-reactive protein level are typically normal. Signs of end-organ damage, such as transaminase levels greater than 1,000 IU/L, raise a concern for severe disease.

In the United States, reverse transcriptase–PCR for dengue virus (DENV) genomic sequences, obtained within 5 days of symptom onset, is diagnostic in a patient with compatible clinical and travel history. Immunoglobulin M (IgM) anti-DENV can be detected with enzyme-linked immunosorbent assay (ELISA) after 5 days of illness and is the appropriate test for a patient who presents more than 1 week after fever onset. However, consider potentially cross-reactive flaviviruses (West Nile, yellow fever, Japanese encephalitis, Zika) in a patient with positive IgM findings from a single sample (rather than acute- and convalescent-phase samples) and a compatible history.

Molecular and immunoassay testing is available from commercial reference laboratories, state public health laboratories, and the CDC (1-787-706-2399; https://www.cdc.gov/dengue/healthcare-providers/testing/testing-guidance.html).

Enteric Fever

There is no standard of reference for diagnosis. If the clinical presentation is compatible with enteric fever, initiate empirical treatment while awaiting blood culture results. Nonspecific findings include leukocytosis or leukopenia, anemia, and mildly elevated transaminases. Cultures of blood (more sensitive if there are multiple samples) and stool are not always positive. In rare cases, duodenal aspirate and bone marrow cultures may be performed with varying success, even after several days of incubation. Serologic testing (Widal test) and ELISA are not useful in the acute setting.

Differential Diagnosis

There is much overlap among malaria, dengue, and enteric fever. However, always consider common local infectious illnesses, such as influenza, adenovirus, acute COVID-19 disease, multisystem inflammatory syndrome in children, pneumonia, and bacteremia with sepsis. In children with the appropriate travel history, also consider chikungunya virus, meningitis, leptospirosis, and Zika virus.

Treatment

Malaria

For the most up-to-date treatment recommendations, see the current edition of the American Academy of Pediatrics *Red Book* or the CDC malaria guidelines (https://www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf). It is necessary to know where the disease was transmitted to guide therapy, as the CDC has up-to-date information about worldwide resistance patterns. Consult with an infectious diseases expert, because treatment recommendations change quickly in relation to resistance, and conditions in specific locations can affect treatment choices. If an infectious diseases expert is not immediately available, contact the CDC Malaria Hotline (see Laboratory Workup). *P falciparum* infections can be severe, and *P vivax* and *P ovale* require eradication to prevent future relapse. Primaquine and tafenoquine cannot be used in pregnancy and are associated with hemolytic anemia in those with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Prior to use, quantitative G6PD testing is needed to confirm normal activity.

Dengue

There is no specific treatment for dengue. Maintain the patient's hydration level and avoid nonsteroidal anti-inflammatory drugs because of the risk of hemorrhagic disease. Treat the fever with acetaminophen. Prevent febrile patients from getting more mosquito bites because they increase the risk of further transmission.

Enteric Fever

The goal of treatment is to shorten the duration of the illness. Administer 14 days of parenteral ceftriaxone (50–75 mg/kg once daily for 14 days; maximum, 2 g/d) or oral azithromycin (10 mg/kg/d for 1–2 weeks; maximum, 500 mg/d). Note that recently there has been an increase in *S Typhi* resistance to fluoroquinolones, so the CDC recommends caution with their use as empiric treatment. If a diagnosis is established early in the course of uncomplicated typhoid, oral therapy may be sufficient. Culture results and knowledge

of regional resistance patterns, if available, can be used to guide antibiotic choices. Watch for intestinal and extraintestinal complications of enteric fever. For more information, visit www.cdc.gov/typhoid-fever/.

Indications for Consultation

- **Infectious diseases:** All patients with malaria, dengue, and enteric fever

Disposition

- **Intensive care unit transfer:** Coma, encephalopathy, signs of severe end-organ (liver, kidney) involvement, shock, intestinal perforation or severe bleeding, severe malaria (parasitemia > 5% of red blood cells, cerebral malaria)
- **Discharge criteria**
  - **Malaria:** For *P falciparum* malaria, discharge once the parasite load is less than 1% and the patient is clinically stable. For nonfalciparum species, discharge once the patient is maintaining hydration orally. Discuss eradication therapy in cases of *P vivax* infections.
  - **Dengue:** Patient is afebrile, vital signs are stable, and warning signs of severe dengue have resolved.
  - **Enteric fever:** Complete parenteral therapy. In uncomplicated cases with good clinical response, complete the last few days of therapy at home.

Follow-up

- **Primary care:** Within a few days of discharge to assess clinical status and look for complications
- **Infectious diseases:** As indicated by local providers; especially important in areas where providers are less familiar with these diseases and future complications

Pearls and Pitfalls

- Treat for malaria empirically if a patient with a negative smear result has a recent possible exposure and no other plausible diagnosis.
- Remember to rule out serious causes of infections, such as meningococcemia or pneumococcal sepsis.
- Dengue, malaria, and typhoid are notifiable diseases.
- Initiate empirical treatment for typhoid while awaiting culture results.
- Cultures of blood, bile, or bone marrow are most likely to yield *Salmonella* bacteria, whereas stool cultures are frequently negative.
- Relative bradycardia in the context of fever is seen in adults with enteric fever but is not common in children.

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CHAPTER 64

Fever of Unknown Origin

Introduction

Fever of unknown origin (FUO) is defined as a temperature higher than 38.3 °C (101.0 °F) for at least 2 weeks, without a definitive cause, despite a thorough clinical evaluation. There is a vast number of causes of FUO, with infections (especially in a patient < 6 years old) and rheumatologic diseases (in older children) accounting for up to 60% of diagnoses. Fever of unknown origin most often represents a common disease process that presents in an uncommon fashion, such as an occult viral (Epstein-Barr virus [EBV], cytomegalovirus) or bacterial (osteomyelitis, urinary tract infection, missed appendicitis with abdominal abscess) infection. Although rare etiologies may sometimes be considered and diagnosed, initially evaluate the patient for the more conventional illnesses. For about one-third of patients, a definitive diagnosis is never confirmed despite thorough evaluation.

Clinical Presentation

History

The diagnosis of the etiology of FUO relies on an exhaustive and repeated history being obtained from the patient and all caregivers (Box 64–1).

A detailed pattern of the height and duration of fevers may provide clues, as in juvenile idiopathic arthritis (JIA) or periodic fever syndromes, but otherwise rarely leads to a diagnosis.

Include a perinatal history for infants younger than 90 days. Also obtain a social history for excluding fictitious fevers and Munchausen syndrome by proxy.

Physical Examination

Perform a thorough and repetitive physical examination for new clues to aid in the diagnosis. A consistent approach to the examination allows for recognition of salient and evolving changes. Discuss each examined organ system with the family. They may fear a particular diagnosis, such as cancer or HIV, or equate a detailed, prolonged examination of a given organ system with specific pathology.

Evaluate the child when both febrile and afebrile, as physical examination findings may differ. The evanescent rash of JIA often occurs only with fever, and the heart murmurs of acute rheumatic fever or endocarditis will often be accentuated when the patient is febrile. An absence of sweating during fever occurs with familial dysautonomia or atropine exposure.

Box 64–2 outlines the elements of the physical examination.

Box 64–1. History-Taking for Fever of Unknown Origin

- Associated symptoms (eg, arthralgia, cough, diarrhea, pain, vomiting)
- Contact with sick persons
- Medications
  - — New and chronic
  - — Over-the-counter
  - — Herbal supplements
- Exposure to pet animals
  - — Amphibians (salmonellosis)
  - — Kittens (bartonellosis)
  - — Reptiles
- Exposure to farm animals (brucellosis, leptospirosis, Q fever)
- Exposure to common insects/pests (arboviral infections, rat bite fever)
- Consumption of unpasteurized milk or cheese (*Mycobacterium bovis*)
- Exposure to wild game meat/blood (tularemia)
- Pica (*Toxocara* infection, toxoplasmosis)
- Camping or hiking (anaplasmosis, ehrlichiosis, Lyme disease)
- Travel
  - — International (malaria, tuberculosis)
  - — Within the United States (blastomycosis, coccidiomycosis, histoplasmosis, Lyme disease, Rocky Mountain spotted fever)
- Risk factors for sexually transmitted infections
  - — Herpes simplex virus
  - — HIV
  - — Lymphogranuloma venereum
- Poor growth or abdominal symptoms (IBD)
- Frequent or unusual infections (immunodeficiency)
- Family history
  - — Autoimmune disorders
  - — Familial dysautonomia
  - — Immunodeficiencies
  - — Periodic fever syndromes
- Immunization history

Abbreviation: IBD, inflammatory bowel disease.

Laboratory Workup

Tailor the laboratory and radiographic evaluation individually, after taking a meticulous history and performing a detailed physical examination. A baseline complete blood cell count (CBC) with manual differentiation may be helpful as a screening test. Whereas a high white blood cell count with neutrophilic predominance and/or bandemia suggests an infectious or inflammatory process, depression of 2 cell lines with the presence of abnormal cells is worrisome for a malignant process. Inflammatory markers, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and now procalcitonin, aid in stratifying the possible etiologies. An ESR greater than 30 mm/h often indicates infectious,

Box 64–2. Physical Examination in Fever of Unknown Origin

- Growth parameters (growth delay may suggest an inflammatory process such as IBD or immunodeficiency)
  - Height
  - Weight
  - Head circumference (when appropriate)
- Head, eyes, ears, nose, and throat
  - Signs of sinusitis or rheumatologic/autoimmune disease (eg, mucosal ulcerations)
- Ophthalmic changes
  - Bulbar conjunctivitis (often purulent with infection; nonpurulent with Kawasaki disease, leptospirosis)
  - Chorioretinitis (cytomegalovirus, toxoplasmosis, syphilis)
  - Icterus (liver dysfunction, hemolytic anemia)
  - Palpebral conjunctivitis (measles, coxsackievirus, tuberculosis, EBV, bartonellosis, lymphogranuloma venereum)
  - Proptosis (tumor, infection, thyrotoxicosis, Wegener granulomatosis)
  - Red, weeping eyes (connective tissue disease, especially polyarteritis nodosa)
  - Uveitis (sarcoidosis, systemic lupus erythematosus, Kawasaki disease, Behçet disease, JIA)
- Oral cavity
  - Inspect and palpate all teeth for caries
  - Evaluate for tonsillar hypertrophy/absence
- Abdomen (examine when child is relaxed)
  - Palpate for masses and hepatosplenomegaly
- Chest
  - Auscultate for new heart murmurs (acute rheumatic fever, endocarditis)
  - Auscultate for rales (pneumonia)
  - Auscultate for rubs (pleuritis, pericarditis)
- Skin
  - Malar or discoid rash (systemic lupus erythematosus)
  - Petechiae, Janeway lesions, splinter hemorrhages (endocarditis)
- Lymph nodes
  - Lymphadenopathy (cytomegalovirus, bartonellosis, Epstein-Barr virus, lymphoma)
- Musculoskeletal
  - Evidence of arthritis and/or arthralgia (osteomyelitis, JIA, malignancy)
  - Severe pain involving multiple joints out of proportion to visible swelling (may represent leukemia)
  - Abnormal gait (may represent infection or malignancy of the lower extremities or a problem with the spine [diskitis, vertebral osteomyelitis, tumor])
  - Generalized muscle tenderness (may suggest dermatomyositis, trichinosis, arboviral infection)
  - Evaluate joint space above and below any suspected abnormality
- Neurologic system
  - Failure of pupillary constriction (hypothalamic dysfunction)
  - Hyperactive reflexes (thyrotoxicosis)
  - Absence of fungiform papillae (familial dysautonomia)

Abbreviations: EBV, Epstein-Barr virus; JIA, juvenile idiopathic arthritis.

autoimmune, or malignant disease; an ESR greater than 100 mm/h suggests tuberculosis, Kawasaki disease, malignancy, or autoimmune/rheumatologic disease. In contrast, CRP/procalcitonin levels tend to be markedly increased during infectious processes and less so with malignancies and autoimmune diseases.

Obtain a blood culture if the patient is ill appearing, there is concern for a serious bacterial infection, or the patient has no localizing signs. The history of travel or other exposures, or symptoms such as an evanescent rash, may raise the clinical suspicion for an unusual or slow-growing organism. Notify the microbiology laboratory and obtain serial blood cultures while the patient is febrile. Obtain a urinalysis and urine culture to rule out an occult urinary tract infection and a comprehensive metabolic panel to screen for any renal or hepatic disease. The role of infectious polymerase chain reaction (PCR) assays is evolving. Obtain PCR based on clinical suspicion of a specific infection or to decrease further testing.

Perform other tests in Tier 1 from Box 64–3, if indicated (*Bartonella* titers if there is contact with a kitten or consistent physical examination findings; immunoglobulins if there is a history of frequent infections). If fever persists without a diagnosis despite Tier 1 evaluation and observation for several days, repeat the CBC with differential, CRP/procalcitonin/ESR, and any tests from Tier 1 that yielded abnormal results; also perform Tier 2 tests where indicated.

Box 64–3. Laboratory Tiers for Fever of Unknown Origin

Tier 1 Tests

CBC with manual differential and blood cultures
Comprehensive metabolic panel
Inflammatory markers (CRP, procalcitonin level, ESR)
Specific serologic tests (EBV, cytomegalovirus, *Bartonella* infection)
Respiratory or gastrointestinal PCR assay
Quantitative serum immunoglobulins
Urinalysis and urine culture
Stool for blood/leukocytes and culture
Chest radiography
Tuberculin skin test (purified protein derivative) or interferon-γ release assay if the patient is > 2 years old or has received Bacille Calmette-Guerin

Tier 2 Tests

Repeat selected Tier 1 tests
Upper and/or lower gastrointestinal endoscopy[a]
Syphilis,[b] *Toxoplasma,*[b] hepatitis viruses, *Brucella,*[b] Lyme,[b] and tularemia titers[b]
Multiple blood cultures
Computed tomography of the sinuses
Abdominal ultrasonography
Lumbar puncture[c]
Echocardiography
Biopsy of lymph nodes or specific sites and bone marrow biopsy[d]

Abbreviations: CBC, complete blood cell count; CRP, C-reactive protein; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; PCR, polymerase chain reaction.

[a] Perform if the patient has suspicious symptoms, such as loose stools or mucus or blood in the stools and abdominal pain.

[b] Perform in patients exposed to endemic areas or those with a history of exposure.

[c] Perform in an infant or toddler with significant headache, abnormal neurologic examination findings, or bulging fontanel.

[d] Perform for unexplained hematologic abnormalities, such as bicytopenia or pancytopenia, blast cells or other abnormal cells on a peripheral smear, or underlying conditions that predispose the patient to malignancy (eg, Down syndrome).

Obtain a chest radiograph in the initial evaluation to rule out pneumonic processes or hilar adenopathy suggesting pulmonary tuberculosis or malignancy. Regional complaints of discomfort determine the need for further imaging. Consult with radiology to develop a plan to image for possible musculoskeletal infections and intraabdominal abscesses or malignancies. The role of newer imaging modalities, such as fluorodeoxyglucose positron emission tomography scans, in the evaluation of pediatric FUO is yet to be determined by prospective studies.

Differential Diagnosis

First, differentiate FUO from fever without source, pseudo-FUO, factitious fever, and deconditioning. Fever without source is an acute (< 3–5 days) febrile illness, in which the origin of the fever is not initially apparent after obtaining a careful history and performing a physical examination. In pseudo-FUO, there are serial infections in which the fevers abate and recur, but vague symptoms persist. Have the caregiver use a calendar or diary to record symptoms, maximum temperature, and route and method of obtaining the temperature. True fevers that are measured with a thermometer and persistent are more likely to represent FUO. In contrast, the pattern for pseudo-FUO is high fevers for several days, followed by low fevers or reporting that the child "felt warm" with mild, persistent symptoms (slight congestion, improving cough) for several days. The pattern then repeats. Deconditioning is often seen in the adolescent. After a well-defined, self-limited acute illness, the patient develops low-grade or subjective fevers, becomes inactive, and generates increasing concern from extended family members. Vitality and stamina decrease, but true fevers do not persist.

Next, assess the patient for life-threatening or severe diseases. The severity of the disease, and not the anxiety of the family or the referring physician, dictates the appropriate pace of the evaluation. The differential diagnosis is summarized in Table 64–1.

Treatment

Most often, hospitalization is indicated to expedite the evaluation. Reserve empirical antibiotic therapy for a patient who is toxic or has a compromising underlying condition and/or a deteriorating clinical course. Up to 80% of patients will have received 1 dose of antibiotics prior to admission, making the diagnosis more challenging. Avoid prescribing medications such as nonsteroidal anti-inflammatory drugs, because they may mask clues to diagnosis, particularly some malignancies. Reserve their use for symptomatic care on an as-needed basis, as well as for rheumatologic disease.

Table 64–1. Differential Diagnosis of Fever of Unknown Origin

Diagnosis	Clinical Features
Bacterial Infections	
Bartonella infection	Exposure to kittens Lymphadenopathy Cranial nerve palsy Macular star
Lyme disease	Erythema migrans rash Oligoarticular arthritis (especially the knee) Cranial nerve palsy (cranial nerve VII)
Occult abscess	History of antibiotic use Daily fever spike Pain Poor dentition (dental abscess)
Osteomyelitis	Refusal to bear weight Bone point tenderness ↑ CRP/ESR
Salmonellosis	Relative bradycardia (pulse doesn't increase with fever) Vomiting and diarrhea (may be bloody) Rose spots and cough (typhoid)
Sinusitis	Cough and postnasal drip Facial erythema or tenderness Swollen, erythematous nasal turbinates
Fungal Infections (all can cause influenza-like illness, hilar adenopathy, pulmonary infiltrates, and dermatologic and central nervous system involvement, usually in an immunocompromised patient)	
Blastomycosis	Travel to Southeast and Central United States
Coccidioidomycosis	Travel to Southwest United States
Histoplasmosis	Travel to Mississippi, Ohio, and Missouri River valleys Hepatosplenomegaly in toddlers Erythema nodosum in adolescents
Parasitic Infections	
Malaria	Travel to endemic areas Rigors, hepatosplenomegaly Hemolytic anemia
Toxoplasmosis	Lymphadenopathy (especially cervical) Pharyngitis, myalgia
Tick-Borne Infections (all can cause headache, myalgia, thrombocytopenia)	
Babesiosis	Hemolytic anemia
Ehrlichiosis/anaplasmosis	Nausea, variable rash (or no rash) in a truncal distribution, leukopenia, ↑ liver transaminases
Viral Infections	
EBV, cytomegalovirus	Pharyngitis, generalized lymphadenopathy, hepatomegaly Atypical lymphocytosis
Hepatitis viruses	Possible travel history Blood/body fluid exposure ↑ Liver transaminases and bilirubin levels

Table 64–1. Differential Diagnosis of Fever of Unknown Origin, continued

Diagnosis	Clinical Features
Collagen Vascular Diseases	
Acute rheumatic fever	History of streptococcal infection Migratory polyarthritis Carditis (new murmur)
JIA	Quotidian fever spikes alternating with subnormal temperatures Lymphadenopathy Evanescent salmon-colored rash Arthritis (may not be present initially)
Systemic lupus erythematosus	Alopecia, arthritis, malar rash Cytopenia Hematuria
Hereditary Diseases	
Anhidrotic ectodermal dysplasia	Lack of sweating with fever Dental defects, abnormal facies, sparse hair
Fabry disease	Angiokeratomas (flat or raised red-black telangiectasias) Burning pain and paresthesia of the feet and legs
Familial Mediterranean fever	Serositis (especially peritonitis) Arthritis or arthralgia
Malignancy	
Leukemia	Bruising, pallor Bone pain ↑ Lactate dehydrogenase and uric acid levels
Neuroblastoma	Proptosis, abdominal mass Opsoclonus-myoclonus (dancing eyes, dancing feet) ↑ Urine catecholamine levels
Other	
Drug fever	Consider all medications, even eye drops Lack of other symptoms Normal CRP and ESR
Factitious fever	Thermometer manipulation or injection of pyrogens May need video surveillance
Hemophagocytic lymphohistiocytosis	Splenomegaly Cytopenia ↓ Fibrinogen, ↑ ferritin and triglyceride levels
IBD	Growth restriction Abdominal pain Arthritis, erythema nodosum, uveitis
Typical Kawasaki disease	Nonpurulent bulbar conjunctivitis Erythematous polymorphic rash Swollen hands and feet Oral changes
Multisystem inflammatory syndrome in children	Clinical presentation may be very similar to Kawasaki disease Gastrointestinal symptoms: abdominal pain, vomiting, diarrhea Myocarditis

Abbreviations: CRP, C-reactive protein; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; IBD, inflammatory bowel disease; JIA, juvenile idiopathic arthritis.
↑ indicates increased level; ↓, decreased level.

Specific treatment depends on the final diagnosis: antibiotics for bacterial disease; steroids, anti-inflammatory agents, and biological agents for rheumatologic disease/inflammatory bowel disease (IBD); drug discontinuation for drug fever; and education and psychological or psychiatric referral for factitious fever.

If the etiology is not determined or is a virus other than a treatable cause (such as HIV), construct a detailed follow-up plan for the family. This must include symptomatic treatments, both pharmacologic and nonpharmacologic, such as the appropriate use of antipyretic medications, the application of cool cloths/bathing, and the avoidance of potentially harmful cultural techniques to reduce fever (cupping); imposing activity restrictions (taking heat-related illness precautions while fever persists, avoidance of abdominal trauma with splenomegaly); conducting routine follow-up with the primary care pediatrician shortly after discharge; and reviewing indications for emergent visits (severe abdominal pain with EBV that could represent splenic rupture or new signs or symptoms). Communication with the primary care physician regarding evaluation findings and ongoing care can help to decrease parental and physician anxiety and prevent unnecessary readmission.

Indications for Consultation

- **Infectious diseases:** Uncertain diagnosis in a patient who appears toxic or has been exposed to suspicious foods, animals, places, or activities that are associated with infections; immunocompromised patient; need for ongoing specialized outpatient management or follow-up
- **Ophthalmology:** Difficult eye examination or concern for a diagnosis with potential eye involvement (endocarditis, uveitis, IBD, chorioretinitis, JIA)
- **Various subspecialists:** Based on "most likely diagnosis" information obtained from repeated history and physical examination findings

Disposition

- **Intensive care unit transfer:** Clinical deterioration, respiratory distress, hypotension, monitoring of parents to rule out factitious fever
- **Discharge criteria:** Patient afebrile for 48 hours or longer with nontoxic appearance; either the diagnosis is confirmed and continued fever is expected or there is no specific diagnosis after critical inpatient testing has been performed and appropriate consultation obtained, with close outpatient follow-up arranged

Follow-up

- **Primary care:** Within 2 to 3 days
- **Various subspecialists:** Based on the ultimate diagnosis

Pearls and Pitfalls

- The key to the ultimate diagnosis of FUO lies in repeated assessment of both the history and the physical examination findings, not in increasing the extent of the laboratory workup.
- More often than not, FUO represents a common disease process that appears in an uncommon fashion at presentation.

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CHAPTER 65

Multisystem Inflammatory Syndrome in Children (MIS-C)

Introduction

Initial reports from the COVID-19 pandemic suggested that children were less susceptible to the disease. Subsequently, a severe and novel pediatric disorder, termed *multisystem inflammatory syndrome in children* (MIS-C), was described. Although the exact pathophysiology is currently unknown, the temporal relationship of MIS-C to acute COVID-19 disease suggests that the pathogenesis involves postinfectious immune dysregulation with an exaggerated immune response, leading to cytokine storm and hyperinflammation in multiple organs.

Most patients with MIS-C have had a prior infection with, or an exposure to, someone with acute COVID-19 disease in the 2 to 4 weeks prior to developing signs and symptoms. MIS-C primarily occurs in healthy 6- to 12-year-olds. In contrast to acute COVID-19 disease, comorbidities are unusual, with the most common being obesity, asthma, allergic rhinitis, cardiac, or an underlying hematologic disorder.

Many patients, particularly adolescents with prominent cardiac involvement, will become critically ill and require transfer to an intensive care unit (ICU). Coronary artery aneurysms may develop in 10% to 20% of such patients.

Clinical Presentation

Several national and international health care organizations have published case definitions to help identify patients with MIS-C. Although the definitions are similar, the one cited most often is the Centers for Disease Control and Prevention (CDC) case definition (Table 65–1). The most common clinical features are summarized in Box 65–1.

History

Determine whether the patient had an illness compatible with acute COVID-19 disease, or contact with someone who had the disease, in the previous 2 to 4 weeks. Ask about the duration of fever and any associated vomiting, diarrhea, and rash.

Physical Examination

A patient with MIS-C is usually quite irritable and ill appearing. Priorities on the physical examination include the vital signs for indications of shock; peripheral perfusion (warmth, capillary refill); respiratory pattern and effort;

Table 65–1. Centers for Disease Control and Prevention Case Definition for Multisystem Inflammatory Syndrome in Children

Age
< 21 years
Clinical Criteria
Fever ≥ 38 °C (100.4 °F) or subjective fever (no minimum duration) Severe illness necessitating hospitalization Evidence of systemic inflammation indicated by C-reactive protein ≥ 30 mg/dL *and* New onset of 2 or more organ systems involved • Cardiac involvement indicated by — Left ventricular ejection fraction < 55% *or* — Coronary artery dilatation, aneurysm, or ectasia *or* — Troponin elevated above laboratory normal range • Mucocutaneous involvement indicated by — Rash *or* — Inflammation of the oral mucosa *or* — Conjunctivitis or conjunctival injection *or* — Extremity findings (erythema or edema of the hands or feet) • Shock • Gastrointestinal involvement indicated by — Abdominal pain *or* — Vomiting *or* — Diarrhea • Hematologic involvement indicated by — Platelet count < 150,000 cells/mcL *or* — Absolute lymphocyte count < 1,000 cells/mcL
Laboratory or Epidemiologic Evidence of SARS-CoV-2 Infection
Detection of SARS-CoV-2 RNA in a clinical specimen up to 60 days prior to or during hospitalization, using a diagnostic molecular amplification test (eg, polymerase chain reaction), *or* Detection of SARS-CoV-2 specific antigen in a clinical specimen up to 60 days prior to or during hospitalization, *or* Detection of SARS-CoV-2 specific antibodies in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization
No Alternative Diagnoses

Adapted from Centers for Disease Control and Prevention. Multisystem inflammatory syndrome (MIS). Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C). Updated May 20, 2021. Accessed April 3, 2022. https://www.cdc.gov/mis/mis-c/hcp.

cardiac examination for a new murmur or signs of congestive heart failure or myocarditis; abdominal examination (for signs of an alternative diagnosis); and mucocutaneous examination.

Laboratory Workup

The diagnosis of MIS-C is challenging. If MIS-C is a diagnostic consideration, obtain a complete blood cell count (check for lymphopenia and thrombocytopenia), comprehensive metabolic panel, C-reactive protein, SARS-CoV-2

Box 65–1. Common Clinical Signs and Symptoms Associated With Multisystem Inflammatory Syndrome in Children

Cardiovascular
Arrhythmia
Hypotension, poor peripheral perfusion
Myocarditis
Pericardial effusion (friction rub, distant heart sounds)
Pulmonary edema (hepatomegaly, jugular venous distention, rales)

Dermatologic
Mucocutaneous involvement (conjunctival injection, oral ulcers, rash)
Periorbital edema
Swollen hands or feet

Gastrointestinal
Abdominal pain, nausea, vomiting
Hepatitis

Hematologic
Deep vein thrombosis
Extremity ischemia
Pulmonary embolism

Neurologic
Altered mental status
Decreased hearing or vision
Headache
Seizures
Stroke (acute weakness)

Respiratory
Chest pain/tightness
Cough
Localized rales or decreased breath sounds
Pleural friction rub
Shortness of breath
Sore throat
Wheezing

Systemic Inflammation
Fatigue
Lymphadenopathy
Myalgias
Weakness

polymerase chain reaction and antibodies, and troponin. Also obtain an electrocardiogram and echocardiogram. Other tests should be performed as necessary to consider or rule out an alternate diagnosis such as Kawasaki disease.

Differential Diagnosis

MIS-C can resemble other entities associated with a hyperinflammatory response, such as Kawasaki disease, toxic shock syndrome, macrophage activation syndrome, and sepsis (Table 65–2).

Although the CDC and other organizations have established criteria for diagnosis, these criteria are fairly nonspecific and subject to change. One of the CDC criteria is that there be "no alternative plausible diagnosis." Therefore, the team caring for the patient is left with the difficult decision between not missing MIS-C versus excessive testing.

Treatment

Most children with MIS-C present severely ill, with approximately 60% to 70% requiring ICU transfer. Many will need fluid resuscitation, respiratory and inotropic support, anticoagulation, and probably immunomodulatory therapies.

Treatment protocols are continuously evolving and may differ among institutions; therefore, assess each patient individually. Mild cases may be admitted to the general pediatric service, but it is imperative that they be

Table 65–2. Differential Diagnosis of Multisystem Inflammatory Syndrome in Children

Diagnosis	Clinical Features
Acute COVID-19 disease	Comorbidities far more common Conjunctivitis uncommon Fewer GI symptoms, especially abdominal pain Rash more common Lower SARS-CoV-2 antibody titers Severe respiratory disease more likely
Appendicitis	Abdominal imaging usually diagnostic Abdominal pain initially periumbilical, then migrates to the right lower quadrant Diarrhea less common
Kawasaki disease	GI symptoms uncommon, especially abdominal pain Less dramatic elevations of C-reactive protein, D-dimer, and ferritin Peak incidence at 1–2 years of age; most patients are younger than 5 years Shock is uncommon, except in Kawasaki disease shock syndrome Thrombocytosis
Stevens-Johnson syndrome	Erythema multiforme with involvement of 2 or more mucous membranes Identifiable trigger (sulfonamides, anticonvulsants, β-lactam antibiotics, nonsteroidal anti-inflammatory drugs)
Sepsis	Likely source of infection: positive culture(s) or chest radiograph
Toxic shock syndrome	May have end organ damage with renal involvement with ↑ blood urea nitrogen/creatinine level or increased transaminase levels Presence of inciting bacterial agent (*Staphylococcus, Streptococcus*) Signs of shock, including hypotension

Abbreviation: GI, gastrointestinal.
↑ indicates increased level.

monitored closely, as rapid deterioration can occur. Transfer a patient with moderate or severe disease to an ICU. These patients are usually quite ill and are best managed by a multidisciplinary team. Although there are institutional algorithms that are based on clinical experience and local expert consensus, to date there have not been any large, randomized studies addressing management.

Based on the biochemical and clinical similarities of MIS-C and Kawasaki disease, intravenous immunoglobulin and steroids (see Chapter 59, Kawasaki Disease) have been used successfully, with rapid clinical improvement and reduction in inflammatory markers in most patients. There is limited experience with other immunomodulators, such as anakinra for interleukin-1 blockade and infliximab (anti–tumor necrosis factor blockade).

Indications for Consultation

- **Allergy/immunology:** Suspected MIS-C; consideration of immunomodulator treatment
- **Cardiology:** Suspected MIS-C; need for inotropic support

- **Hematology:** Need for anticoagulation (prophylaxis versus therapeutic dosing)
- **Infectious disease:** Suspected MIS-C versus bacterial sepsis
- **Neurology:** Persistent or serious neurologic symptoms
- **Rheumatology (if available):** Suspected MIS-C, for consideration of immunomodulator therapy

Disposition

- **ICU transfer:** Need for invasive respiratory support, inotropic therapy, anticoagulation, or immunomodulator administration
- **Discharge criteria:** No longer requiring respiratory support or intravenous therapies; adequate oral intake

Follow-up

- **Allergy/immunology, hematology, rheumatology (if involved):** As per individual protocols
- **Cardiology:** All patients
- **Primary care:** 1 to 2 weeks

Pearls and Pitfalls

- Patients with MIS-C tend to be older than those with other febrile illnesses.
- Abdominal pain can be severe, mimicking an acute abdomen.
- Absolute lymphopenia is a very common finding.
- Compared to an acute COVID-19 illness, conjunctivitis, oral mucosa changes, and gastrointestinal symptoms are more common.
- Despite the significant morbidity of MIS-C, the mortality is less than 2%.

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CHAPTER 66

Sepsis

Introduction

Sepsis historically has been defined as infection and the presence of systemic inflammatory response syndrome (SIRS). However, the SIRS criteria have poor sensitivity and specificity for both adult and pediatric sepsis. In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), designed primarily for adult patients, defined the following:

- *Sepsis:* Life-threatening organ dysfunction caused by a dysregulated host response to infection.
- *Septic shock:* Sepsis *and* underlying circulatory and cellular/metabolic abnormalities that are profound enough to substantially increase mortality. Practically, this means the presence of sepsis with hemodynamic instability requiring fluid resuscitation to stabilize blood pressures.

"Organ dysfunction" in pediatric patients is still ambiguous, as the various pediatric scoring systems in use are primarily laboratory based and have not been used as predictive tools outside of a critical care environment. Thus, the definition of sepsis has undergone many transformations, and a formal pediatric definition is still forthcoming from the Surviving Sepsis Campaign. For practical purposes, it remains essential to identify changes in perfusion, mental status, heart rate, and blood pressure, as well as temperature instability, as part of the clinical picture for sepsis screening.

While the etiology of sepsis varies with patient age, immune status, and geographic location, most cases in children in high-resource countries are caused by bacterial infections, although viruses and fungi are also implicated. Excluding neonatal sepsis (see Chapter 62, Fever in Infants Younger Than 60 Days), the most common cause of pediatric severe sepsis is pneumonia, followed by bacteremia. Other illnesses (pyelonephritis, osteomyelitis, appendicitis, meningitis) can progress to sepsis, and the pathogenic organism can thus range from being gram-positive (*Streptococcus pneumoniae*, *Staphylococcus aureus*) to gram-negative (*Escherichia coli, Neisseria meningitidis*) or anaerobic (*Bacteroides* species), as well as respiratory syncytial virus, influenza, SARS-CoV-2, and herpes virus. An immunocompromised patient may have a fungal (particularly *Candida* species) or other viral (cytomegalovirus, herpes zoster) infection.

Clinical Presentation

History

Perform a careful review of the symptoms. Fever pattern, cough, dyspnea, emesis, diarrhea, abdominal pain, dysuria, headache, rash, and focal pain or swelling will yield clues to the type of underlying infection. Recent urine output or mental status may help determine where the patient is on the spectrum of sepsis, severe sepsis, and septic shock. Frequent recurrent infections, chronic diarrhea, and failure to thrive may suggest an immunodeficiency and the possibility of a pathogen.

Travel to lower-resource countries suggests the possibility of infections such as *Salmonella* Typhi, malaria, dengue, and yellow fever. Travel within the United States can raise the concern for exposure to leptospirosis (Hawaii), Rocky Mountain spotted fever (Southeast United States), and chikungunya virus (Florida, Puerto Rico, U.S. Virgin Islands).

Physical Examination

Carefully assess and frequently reassess vital signs, with special attention to

- Fever or hypothermia (temperature $<$ 36.0 °C [$<$ 96.8 °F] or $>$ 38.5 °C [$>$ 101.3 °F])
- Tachypnea
- Tachycardia or bradycardia (adjust the heart rate for fever): for each 1.0 °C (1.8 °F) above 38.5 °C (101.3 °F), subtract 10 beats/min from the heart rate

Capillary refill time longer than 2 seconds, weak pulse, hypotension, decreased urine output, and altered mental status for the patient's age are sensitive indicators for abnormal end-organ perfusion with shock. Bradycardia and hypothermia are ominous signs. Focus the remainder of the rapid first physical examination on identifying sources for sepsis to direct the initial antimicrobial choice.

Laboratory Workup

The 2 goals of laboratory studies are to identify the etiology of infection and to assess the severity of organ dysfunction. Some evaluations, such as C-reactive protein (CRP) level, may be most helpful when repeated to trend the severity of the infection or response to interventions. Indicated basic studies, similar to those for the patient in shock (see Chapter 13, Shock), include

- Complete blood cell count with differential (note bandemia, toxic granulocytes, thrombocytopenia, anemia; smear for hemolysis or abnormal cells)
- Blood culture (aerobic and anaerobic)
- Urinalysis and urine culture

- Basic metabolic panel with liver enzyme evaluation
- Lactate level (≥ 4 mmol/L is consistent with high risk for sepsis)
- Venous blood gas panel (often includes ionized calcium, sodium, glucose, hemoglobin, and potassium level assessment)
- CRP or procalcitonin level
- Chest radiograph
- Electrocardiogram (when pericarditis/myocarditis is suspected)
- Coagulation panel (when disseminated intravascular coagulation is suspected)
- Cerebrospinal fluid studies, viral polymerase chain reaction test, and bacterial culture (if meningitis/encephalitis is suspected; also consider reserving extra fluid for possible specialty viral/fungal/parasitic testing)
- Viral respiratory panel (when respiratory infection is suspected)
- Gastrointestinal pathogen panel (when persistent or significant diarrhea is present)

Differential Diagnosis

The differential diagnoses of sepsis are summarized in Table 66–1.

Treatment

Initiate treatment for sepsis within the first 3 hours of symptom recognition; promptly resuscitate septic shock within 1 hour of initial diagnosis. Stabilize the patient by using Pediatric Advanced Life Support pathways to address circulation, airway, and breathing. Immediately provide oxygen to all patients.

Standard therapy for all types of sepsis is fluid resuscitation to the point of hemodynamic stability. However, new guidelines consider high-risk patients who may suffer complications from fluid boluses. Therefore, withhold fluid resuscitation in the setting of fluid overload, but give maintenance fluid to a normotensive patient in a resource-limited setting (ie, no access to intensive care). Obtain immediate intravenous (IV) access, preferably at 2 sites, but if that is not possible, place an intraosseous line. For all other patients without risk from fluid resuscitation, push boluses of 10 to 20 mL/kg of isotonic crystalloid (normal saline or lactated Ringer solution) over 15 to 20 minutes. Repeat boluses as necessary until there is clinical improvement, including normalization of the blood pressure, capillary refill, pulse, and urine output. Consider epinephrine/norepinephrine, in an intensive care setting, if shock persists after 40 to 60 mL/kg of fluid boluses. As noted, clinical outcome may be negatively affected by fluid overload, especially in a patient with underlying cardiac disease or certain infectious diseases (dengue, malaria, and other illnesses found in resource-limited countries). If any signs of fluid overload (new hepatomegaly or pulmonary rales) develop, start an inotrope instead of continuing fluid resuscitation.

Table 66–1. Differential Diagnosis of Sepsis

Diagnosis	Clinical Features
Hemodynamic Instability	
Anaphylaxis	Urticaria and/or angioedema Wheezing and/or acute respiratory distress Emesis, abdominal pain Hypotension
Adrenal crisis	History of previous steroid use or underlying primary deficiency Nausea/emesis Shock unresponsive to IV fluids Patient may have hyponatremia with hyperkalemia
Congestive heart failure	Tachypnea/diaphoresis during feeds (infant) Cardiomegaly Hepatomegaly or pulmonary congestion (rales)
Fever and Systemic Signs	
Kawasaki disease	Nonpurulent conjunctivitis Mucosal changes (strawberry tongue, cracked lips) Polymorphous rash Cervical adenopathy Hand/foot swelling
Multisystem inflammatory syndrome in children (MIS-C)—complication of prior acute COVID-19 disease	Fever Laboratory evidence of inflammation At least 2 organ systems involved (eg, renal, gastrointestinal, cardiac, skin) Hemodynamic instability Recent clinical or lab evidence of SARS-CoV-2 infection
Inborn errors of metabolism	Symptoms may present at birth, with concurrent illness, or when infant starts fasting through the night Emesis, lethargy, altered mental status May have ↓ glucose level, ↑ ammonia level, and/or metabolic acidosis
Periodic fever syndromes	Often other family members are affected Child is well between episodes that occur at regular intervals Abdominal pain, rash, and joint pain are all common
Sympathomimetic ingestion	Psychosis/irritability in a young child Hypertension, mydriasis, diaphoresis
Dysautonomia/neurologic storming	History of underlying central nervous system disease Increased dystonia Hypertension, tachycardia
Narcotic or baclofen withdrawal	Hypertension, tachycardia Diarrhea Irritability

Abbreviation: IV, intravenous.
↑ indicates increased level; ↓, decreased level.

Initiate antibiotics based on the most likely underlying infection, within the first hour of recognition of symptoms for septic shock, or within 3 hours for the diagnosis of sepsis-associated organ dysfunction without shock. Do not interrupt the fluid resuscitation for antibiotic administration, and do not withhold antibiotics if the culture specimens cannot be obtained expeditiously, especially the cerebrospinal fluid if the patient is not stable enough to undergo a lumbar puncture. Consequently, empirical antibiotic choices are broad, but narrow the spectrum once an organism and/or source is identified. See Table 66–2 for antibiotic choices based on the common etiologies of sepsis. For infants younger than 60 days, see Chapter 62, Fever in Infants Younger Than 60 Days.

Disposition

- **Intensive care unit (ICU) transfer:** Hemodynamic instability despite administration of antibiotics and fluid resuscitation (typically after 40–60 mL/kg isotonic fluids in 1 hour) or pressor support required, respiratory failure, evidence of multiorgan dysfunction

Table 66–2. Initial Empirical Antibiotic Choices

Type of Infection	Antibiotic(s) of Choice
Previously healthy patient Community-acquired pneumonia Pyelonephritis Bacterial meningitis	IV ceftriaxone 50 mg/kg every 24 h; use 100 mg/kg/d if meningitis is suspected (4-g/d maximum) *and* Vancomycin 15 mg/kg per dose every 8 h (give first dose regardless of renal status)
Medically complex patient with risk of aspiration/anaerobic infections	IV ampicillin/sulbactam 50 mg/kg per dose every 6 h (maximum, 3 g per dose) *or* IV clindamycin 13 mg/kg per dose every 8 h (4.8-g/d maximum) *or* IV meropenem 20 mg/kg per dose every 8 h (3-g/d maximum, except for meningitis [6-g/d maximum]) *and if MRSA infection is suspected* Vancomycin (dosing as above)
Intra-abdominal infection	IV meropenem 20 mg/kg per dose every 8 h (3-g/d maximum) *or* IV piperacillin/tazobactam, 100 mg piperacillin/kg per dose every 8 h (maximum, 3.375 g per dose)
Immunocompromised patient Neutropenic (due to chemotherapy or underlying immunodeficiency) Cystic fibrosis	Ensure pseudomonal coverage with IV cefepime 50 mg/kg per dose every 8 h (maximum, 2 g per dose) *or* Carbapenems (ie, meropenem; dosing as above) *and if clinically indicated* MRSA coverage with vancomycin (dosing as above) and fungal coverage (consult with an infectious diseases specialist)

Abbreviations: IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*.

- **Institutional transfer:** Need for ICU or specialist consultation not available locally
- **Discharge criteria:** Patient hemodynamically stable with infection identified and therapy demonstrating consistent clinical improvement

Follow-up

- **Primary care:** 2 to 3 days
- **Infectious diseases:** 1 to 2 weeks if long-term antibiotic therapy is prescribed

Pearls and Pitfalls

- Hypotension is a *late finding* of sepsis and uncompensated shock. Diagnose and treat shock when it is compensated, by using heart rate, perfusion, and core temperature.
- Carefully review the patient's vaccination status.
- Perform titrated fluid resuscitation with the goal of normalizing blood pressure, perfusion, and possibly heart rate, while being alert for signs of fluid overload (new rales, hepatomegaly). In a resource-limited setting, and in the absence of hypotension, start maintenance IV fluids only.
- Narrow the antimicrobial therapy as soon as possible to avoid development of organism resistance.
- Sepsis is usually the end result of a process that develops over many hours. It can often be recognized early by identifying at-risk patients and monitoring for the initial clinical changes.

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Ingestions

CHAPTER 67

Gastrointestinal Foreign Body

Introduction

About 75% of gastrointestinal (GI) foreign body ingestions occur in children younger than 5 years. Other high-risk patient populations include children with developmental delays, psychological disorders, GI anatomical anomalies, or motility disorders.

Coins are the most common foreign bodies ingested by children in the United States. The most frequent site where GI foreign bodies lodge is in the esophagus, at one of the areas of anatomic narrowing: 60% to 70% are at the thoracic inlet at the upper esophageal sphincter, 10% to 20% are in the midesophagus at the level of the aortic notch, and about 20% are just above the lower esophageal sphincter. Beyond the esophagus, foreign bodies are less likely to be retained, but areas of higher risk are the gastric outlet, c-curve of duodenum, and the ileocecal valve. Other less common objects include toys or toy parts, needles and pins, chicken or fish bones, and other food.

Batteries, magnets, and sharp and long objects require special consideration because of the higher risk for complications. Button batteries larger than 2 cm in diameter have the highest risk of retention. They can conduct electricity if retained in the esophagus, causing liquefaction necrosis and perforation that can develop within hours. Late complications can then include esophageal stricture, tracheoesophageal fistula, and vascular-esophageal fistula.

Depending on number and size, magnets pose dangers of perforation, necrosis, or vessel rupture, if the bowel wall becomes entrapped between multiple magnets or metallic objects are attracted to the magnets. The risk is particularly high with magnets made of rare earth metals, which are 10 times more powerful than regular ones.

Recently, there has been an increase in the ingestion of detergent pods, which contain concentrated alkaline solutions. These can cause liquefaction necrosis, perforation, and bleeding, with tissue damage that is most common in the esophagus but can occur anywhere from the oropharynx to the duodenum. There is a risk of subsequent stricture formation 2 to 8 weeks after ingestion.

There is a high risk of perforation with sharp objects throughout the GI tract, especially if the object is longer than 3 cm or has been retained for more than 24 hours. Objects longer than 2.5 cm may not pass through the pylorus, whereas larger ones (> 6 cm) may not pass through the duodenal c-loop.

Clinical Presentation

History

The presenting symptoms depend on the type and size of the foreign body, as well as the location and duration of impaction. The most common symptoms of esophageal foreign body are sore throat, refusal to eat or drink, drooling, dysphagia, substernal discomfort or a sensation of a foreign body, retching, vomiting, coughing, and difficulty breathing. For objects that pass beyond the esophagus, most patients are asymptomatic but may experience abdominal pain, distention, vomiting, and feeding intolerance. The presence of fever is concerning because it suggests deep ulceration or perforation. There may be a history of a choking episode, the caregiver may have witnessed the ingestion, or the patient may self-report it. However, up to one-third of patients are asymptomatic, and in as many as 40% of cases, there is no history of ingestion. If possible, determine the time since the ingestion, because a longer duration (> 24 hours) is associated with greater risk of complications.

If magnet ingestion is a concern, attempt to ascertain if more than one magnet was ingested or if other metallic foreign bodies were ingested along with the magnet(s).

Physical Examination

The physical examination findings may be normal, or there may be drooling, stridor, or wheezing. Neck swelling, erythema, or crepitus is concerning for esophageal perforation. If the object has passed the esophagus, the physical examination is most likely normal, unless there is a complication. Rarely, a vascular-esophageal fistula can develop, presenting as massive hematemesis.

Laboratory Workup

Regardless of the suspected location of the object, the initial evaluation includes anteroposterior and lateral radiographs of the neck, chest, and abdomen. Coins in the esophagus appear as a circle on frontal views and as a line on lateral views. To distinguish a button battery from a coin, look for a double ring sign (circle within a circle) on the frontal view radiograph. On the lateral radiograph, look for a "step-off" sign, which represents the button battery contour between the positive and negative poles. A radiolucent object will not be visualized on plain radiographs, but its presence may be suggested by compression or displacement of adjacent structures. If the history and physical examination findings are consistent with an esophageal foreign body but the radiographic findings are normal, obtain a contrast-enhanced esophagram to rule out a radiolucent foreign body or proceed to esophagogastroduodenoscopy. Order

chest computed tomography (CT) if the patient has significant respiratory distress that may be secondary to erosion or extraluminal extension. A handheld metal detector is another option for identifying and localizing coins and other metallic objects. For high-risk radiolucent objects, CT, magnetic resonance imaging, or ultrasonography are more helpful than radiography.

Differential Diagnosis

The differential diagnosis of an esophageal foreign body is summarized in Table 67–1.

Treatment

Treatment of a foreign body depends on the type, location, and size of the object; symptoms; and the risk of complications, which is a primary driver of management. In up to 80% to 90% of cases, an esophageal foreign body will

Table 67–1. Differential Diagnosis of an Esophageal Foreign Body

Diagnosis	Clinical Features
Drooling/Dysphagia	
Mediastinal mass	Difficulty breathing Recurrent lung infections
Peritonsillar abscess	Trismus, "hot potato" voice Uvula deviated to the contralateral side
Retropharyngeal abscess	Fever, drooling Anterior bulging of the posterior pharyngeal wall Limited neck hyperextension
Cough/Choking/Cyanosis	
Bronchiolitis	Upper respiratory infection prodrome, followed by respiratory distress and wheezing
Gastroesophageal reflux	Intermittent regurgitation Sandifer syndrome
Pneumonia	Fever, cough, tachypnea Infiltrate on chest radiograph
Stridor/Wheezing	
Croup	Hoarseness, barking cough Stridor
Laryngotracheomalacia	Positional inspiratory stridor Presentation occurs early in life
Abdominal Pain/Vomiting	
Gastroenteritis	May have fever and/or diarrhea
Bowel obstruction	Bilious emesis Radiography: air-fluid level

pass spontaneously, whereas 10% of objects must be removed endoscopically; fewer than 1% of cases will require a surgical procedure. Most objects identified past the esophagus will pass without complication, usually within hours of the ingestion.

For an esophageal foreign body, permit a period of observation of up to 24 hours if the patient is asymptomatic and has no history of esophageal or tracheal abnormality and the foreign body is not a high-risk object (Table 67–2). Give the patient nothing by mouth, provide continuous cardiac monitoring with pulse oximetry, and administer maintenance intravenous fluids. If the patient remains asymptomatic, repeat the radiography in 12 to 24 hours. Discharge the patient if the object spontaneously passes into the stomach. However, if drooling, substernal chest pain, vomiting, difficulty swallowing, or respiratory distress develops, or if the object does not progress

Table 67–2. High-Risk Objects

Foreign Body	Management: Esophagus	Management: Stomach/Intestinal Tract
Button battery	Immediate removal	Immediate removal: age < 5 years or battery > 2 cm Observe for passage with serial radiographs within 48 hours if low risk
Coin	Remove (depends on the presence of symptoms)	If symptomatic: remove immediately If asymptomatic: repeat radiography at 2 and 4 weeks If still retained at 4 weeks, refer for removal
Long (> 6 cm) or large object	Immediate removal	Remove within 24 hours, as these objects are unlikely to pass through duodenum or ileocecal valve Sharp, long, or large objects within stomach warrant endoscopic removal If asymptomatic, obtain serial radiographs and remove if it fails to progress
Magnet	Immediate removal	Determine if single, multiple, or single with metallic FB Consult surgery if > 12h since ingestion, symptomatic and beyond stomach, multiple magnets, or single with metallic FB If out of reach of endoscopy: Monitor in hospital for passage Perform serial abdominal examinations
Sharp object Fish bone, needle	Immediate removal	Stomach: Immediate removal Consult GI/surgery if in intestines, follow radiographically, and remove surgically if no forward progression for 3 days
Detergent pod	Endoscopy within 24h	None

Abbreviations: FB, foreign body; GI, gastrointestinal.

after 24 hours, consult with an otolaryngologist, gastroenterologist, or surgeon to coordinate a removal procedure. Arrange for *immediate* removal if the object is high risk or the patient cannot manage their secretions or exhibits develops acute respiratory symptoms. Do not prescribe motility agents, such as glucagon or laxatives.

Depending on institutional skills and preferences, removal options for an esophageal foreign body include rigid esophagoscopy and flexible endoscopy. Regardless of the technique used, the success rate for removal of an esophageal foreign body is 95% to 100%. If several hours have elapsed while coordinating the removal procedure, repeat the radiographs just prior to confirm the position of the foreign body.

For a foreign body located past the esophagus, the size of the object and presence of symptoms or GI anatomic anomalies determines treatment. An object lodged in the stomach that is more than 3 to 6 cm long or more than 2.5 cm wide is less likely to pass through the pylorus and duodenum and therefore requires removal. Otherwise, observe an asymptomatic patient if the foreign body is not high risk for complications. Remove a penetrative object retained in the stomach as soon as possible; a patient with a nonpenetrative object can be observed as an outpatient for 4 to 6 weeks.

During the postremoval period, observe the patient for signs of complications from the procedure, such as bleeding, vomiting, stridor, respiratory distress, or hypoxia. If there is no drooling or difficulty breathing, start a trial of clear liquids to ensure that the patient can now swallow appropriately.

Indications for Consultation

- **Gastroenterology, otorhinolaryngology, surgery, or radiology:** Depending on who performs the procedure at a given institution and the location of the foreign body

Disposition

- **Intensive care unit transfer:** Impending respiratory failure or signs of shock
- **Discharge criteria:** Normal respiratory status, no oxygen requirement, no drooling, adequate oral intake

Follow-up

- **If object required removal:** 1–2 weeks with the physician that performed the procedure
- **If object is in the stomach and can be safely observed for passage:** 1–2 weeks with primary pediatrician, until object clears, for up to 4 weeks

Pearls and Pitfalls

- If the foreign body passes into the stomach, instruct the caregivers to watch for signs of abdominal pain, bleeding, or vomiting.
- The patient may continue to complain of a foreign body sensation for several days after removal.
- Food impaction in an older child or adolescent can be caused by eosinophilic esophagitis.
- Caregivers may want to check stool to ensure expulsion or recovery of the ingested object, but failure to recover the object does not mean that it has been retained, especially in an otherwise asymptomatic patient.
- Esophageal injury following button battery removal can persist for days, placing the patient at risk for a vascular-esophageal fistula, presenting with difficulty swallowing, chest pain, or hematemesis.

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Toxic Exposures

Introduction

Children and youth are exposed to large number of potentially toxic substances. This has a major impact on child health, especially among children living in poverty. In 2020, 58% of calls to poison control centers and 7% of toxin-related fatalities involved patients younger than 20 years. Younger patients (< 6 years) have better outcomes because they usually present promptly to a health care facility, have fewer comorbid conditions, are exposed to a single substance, and are not trying to harm themselves. However, some substances are potentially fatal in small doses (Box 68–1).

Clinical Presentation

History

Ask about the timing and onset of symptoms, timing and amount of exposure, and available sources of exposure, including prescription and over-the-counter medications, household/cosmetic products, alcohol, cannabis, nicotine, illicit drugs, pesticides, and herbal/alternative and traditional/cultural medications. Determine occupational exposures, encounters with venomous/poisonous animals, or exposures to plants. Use historical data and available pharmacy information to determine maximum exposures. Assess intent regarding exposure. Ask about underlying medical conditions (renal or liver disease) that may affect drug metabolism.

Physical Examination

Be aware that some toxic effects have delayed onset (Table 68–1). Physical examination findings are summarized in Table 68–2.

Box 68–1. Toxins That Are Potentially Fatal in Small Doses

Antidysrhythmics	Methyl salicylate
Antimalarials (chloroquine, hydroxychloroquine, quinine)	Opioids
β-antagonists	Organophosphates (parathion)
Calcium channel antagonists	Phenothiazines
Camphor	Sulfonylureas
Clonidine	Theophylline
Clozapine	Tricyclic antidepressants
Diphenoxylate-atropine	

Table 68–1. Toxins With Potential for Delayed Toxicity	
Toxin	**Toxicity**
Amanita species mushrooms	Hepatic failure
Acetaminophen	Hepatic and renal failure
Brodifacoum	Bleeding
Buprenorphine-suboxone	Respiratory failure
Bupropion	Seizures
Colchicine	Gastrointestinal toxicity, multiorgan failure
Diphenoxylate-atropine	Respiratory failure
Diquat	Renal failure, multiorgan failure
Iron	Hepatic, multiorgan failure
Lead	Encephalopathy, seizures, anemia
Paraquat	Pulmonary fibrosis, multiorgan failure
Salicylates	Encephalopathy, seizures, arrhythmias, renal failure, multiorgan failure
Sulfonylureas	Hypoglycemia
Sustained-release β-antagonists	Hypotension, bradycardia
Sustained-release calcium channel antagonists	Hypotension, bradycardia

Table 68–2. Findings in Toxic Exposures	
Symptom	**Substance/Syndrome**
Vital Signs	
Bradycardia	Cholinergics (organophosphates, carbamates), β-blockers, calcium channel blockers, digoxin, opioids, sedatives, clonidine
Bradypnea	Opioids, sedatives, clonidine, cholinergics
Hypertension	Sympathomimetics, elemental mercury, serotonin syndrome, GABA agonist withdrawal
Hyperthermia	Anticholinergics, sympathomimetics, serotonin syndrome, malignant hyperthermia, neuroleptic malignant syndrome, GABA agonist withdrawal (ethanol, benzodiazepines, barbiturates, baclofen, γ-hydroxybutyrate)
Hypotension	Calcium channel blockers, β-blockers, digoxin, clonidine, opioids, TCAs
Hypothermia	Opioids, hypoglycemic agents, carbon monoxide, β-blockers
Tachycardia	Sympathomimetics, anticholinergics, serotonin syndrome, GABA agonist withdrawal, TCAs
Tachypnea	Sympathomimetics, anticholinergics, salicylates, hydrocarbons
Neurologic/Mental Status	
Agitation	Sympathomimetics, anticholinergics, serotonin syndrome
Hallucinations/delusions	Sympathomimetics, anticholinergics, dextromethorphan, lysergic acid diethylamide, cannabinoids, phencyclidine, psilocybin, *Salvia divinorum*
Sedation	Opioids, sedatives, carbon monoxide, hydrocarbon inhalants

Table 68–2. Findings in Toxic Exposures, continued	
Symptom	**Substance/Syndrome**
Seizures	Sympathomimetics, anticholinergics, TCAs, antipsychotics, caffeine, isoniazid, propoxyphene, tramadol, theophylline
Head, Eyes, Ears, Nose, Throat	
Dry mucosal membrane	Anticholinergics
Miosis	**C:** carbamates, clonidine; **O:** opioids, organophosphates, olanzapine; **P:** phenothiazines; **S:** sedatives
Mydriasis	Sympathomimetics, anticholinergics
Sialorrhea/drooling	Cholinergics, caustics
Visual loss	Methanol
Cardiopulmonary	
Myocarditis	Ipecac (chronic exposure)
Pulmonary edema (noncardiogenic)	Salicylates, opioids, organophosphates, carbamates
Torsades de pointes (prolonged QT interval)	TCAs, methadone, antipsychotics, erythromycin, cisapride, diphenhydramine (see list at https://crediblemeds.org)
Ventricular tachycardia (prolonged QRS)	Cocaine, TCAs, anticholinergics, halogenated hydrocarbons, propranolol, propoxyphene
Wheezing/dyspnea	Hydrocarbons, organophosphates, carbamates
Gastrointestinal	
Constipation	Anticholinergics, opioids
Diarrhea	Caustics, cholinergics, ipecac, iron, cathartics
Emesis	Caustics, cholinergics, ipecac, ethanol, plants, mushrooms, iron
Hepatotoxicity	Acetaminophen, *Amanita* species mushrooms, phenytoin, ethanol, iron, valproic acid
Pancreatitis	Ethanol, salicylates, valproic acid
Hematologic and Renal	
Bleeding/bruising	Coumadin, brodifacoum (found in certain rat poisons)
Nephrotoxicity	Ethylene glycol, nonsteroidal anti-inflammatory drugs, aminoglycosides

Abbreviations: GABA, γ-aminobutyric acid; TCA, tricyclic antidepressant.

Laboratory Workup

The laboratory workup of a suspected toxic exposure depends on the specific clinical situation. In general, order a blood glucose level, basic metabolic panel, creatine phosphokinase level, liver transaminases, bilirubin, prothrombin time and partial thromboplastin time (Table 68–3), and electrocardiogram, and provide continuous pulse oximetry. If there is an unknown exposure or suicidal intent, also obtain acetaminophen, ethanol, and salicylate levels and a urine drug screen. For an unconscious patient, order neuroimaging, chest radiography, and ammonia. Base other testing on suspected

Table 68–3. Metabolic Findings Associated With Certain Toxins	
Electrolyte Abnormality	**Possible Toxins**
Anion gap metabolic acidosis	Methanol, metformin, iron, isoniazid, ethylene glycol, salicylates, carbon monoxide, cyanide, toluene
Hyperchloremia	Sodium chloride
Hyperglycemia	Sympathomimetics, calcium channel blockers
Hyperkalemia	Digoxin
Hypernatremia	Sodium salts, baking soda, sodium phosphate, drug-induced diabetes insipidus
Hypoglycemia	Insulin, sulfonylureas, β-blockers, ethanol
Hypokalemia	Sympathomimetics, toluene, insulin, albuterol
Hyponatremia	Lithium, diuretics, drug-induced syndrome of inappropriate antidiuretic hormone
Metabolic alkalosis	Baking soda
Normal anion gap metabolic acidosis	Topiramate, toluene

toxin, history, physical examination, and initial laboratory findings. Order a pregnancy test for a postpubertal female.

Send urine and blood samples to the laboratory for storage, if malicious poisoning with an unknown substance is suspected. Use these samples for future testing with the guidance of subsequent clinical course, history, and consultant expertise (poison control center, medical toxicologist).

Differential Diagnosis

At presentation, some toxic exposures can appear the same as common pediatric illnesses. Seizures from sympathomimetics or bupropion are indistinguishable from generalized seizures. Sympathomimetics, anticholinergics, lead encephalopathy, and serotonin syndrome can mimic infectious meningitis. Consider carbon monoxide poisoning in the evaluation of new-onset migraine or tension headaches. Hydrocarbon ingestion can be confused with an asthma exacerbation. Early acetaminophen or iron poisoning and viral gastroenteritis will appear with comparable symptoms. Liver injury from viral hepatitis and acetaminophen toxicity can have the same clinical and laboratory pattern. Dehydration and sodium chloride toxicity can appear with similar symptoms and laboratory findings. Some poisons appear with constellations of symptoms called *toxidromes* (Table 68–4).

Treatment

The initiation of Pediatric Advanced Life Support, if necessary, and supportive care are mainstays of treatment. Discuss treatment and antidote (Table 68–5)

Table 68–4. Common Toxidromes

	Sympathomimetic	Opioid	Anticholinergic	Cholinergic
Toxins	Cocaine, amphetamines, pseudoephedrine, methylenedioxypyrovalerone	Heroin, morphine, codeine, fentanyl, methadone	Diphenhydramine, tricyclic antidepressants, atypical antipsychotics, carbamazepine, *Datura* species	Organophosphates, carbamates
Temperature	Hyperthermia	Hypothermia	Hyperthermia	—
Pulse	Tachycardia	Bradycardia	Tachycardia	Bradycardia
Blood pressure	Hypertension	Hypotension	—	—
Respiratory rate	Tachypnea	Bradypnea, apnea	—	Dyspnea (pulmonary edema), tachypnea
Skin	Diaphoresis	—	Dry	Diaphoresis
Neurologic symptoms	Agitation, seizures	Sedation, coma	Agitation, seizures, coma	—
Ocular symptoms	Mydriasis	Miosis	Mydriasis	Miosis
Gastrointestinal symptoms	—	Constipation	Constipation	Emesis, diarrhea
Genitourinary symptoms	Urinary retention	—	Urinary retention	Enuresis
Mnemonic symptoms	Mimics "fight-or-flight" response	—	"Mad as a hatter, hot as a hare, blind as a bat, red as a beet, dry as a bone"	**S**alivation **L**acrimation **U**rination **D**efecation **G**astrointestinal upset **E**mesis

administration with a poison center (800-222-1222) or medical toxicologist. Reserve gastrointestinal decontamination (activated charcoal, gastric lavage, whole-bowel irrigation) for the following select cases, if recommended by the consultant:

- Activated charcoal (1–2 g/kg; maximum, 50 g): potentially fatal toxin (calcium channel blocker, tricyclic antidepressant), presentation within 1 hour of ingestion, and no aspiration risk
- Gastric lavage: potentially life-threatening toxin that can be withdrawn through a gastric tube (liquid such as organophosphates, ethylene glycol, methanol), presentation within 1 hour of ingestion, and no aspiration risk
- Whole-bowel irrigation (polyethylene glycol 3350 and electrolyte lavage solution, 25 mL/kg/h, 2-L/h maximum, until desired effect is achieved): potentially life-threatening toxin (iron, lead, arsenic) and no aspiration risk

Table 68–5. Select Antidotes	
Toxin	**Antidote**
Carbon monoxide	Oxygen
Cyanide	Hydroxocobalamin
Digoxin	Digoxin-specific Fab
Ethylene glycol, methanol	Fomepizole
Heparin	Protamine
Iron	Deferoxamine
Isoniazid	Pyridoxine
Lead	Succimer, calcium disodium edetate, dimercaprol
Local anesthetics (cardiotoxicity)	IV lipid emulsion (info at http://lipidrescue.org)
Organophosphates and carbamates	Atropine and pralidoxime
Toxin-induced methemoglobinemia	Methylene blue
Sulfonylureas	Octreotide
Warfarin, brodifacoum	Vitamin K, fresh frozen plasma

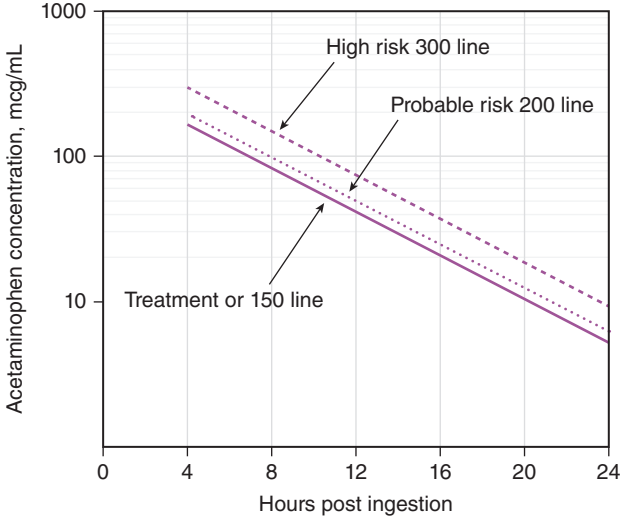
Abbreviation: IV, intravenous.

Treat toxin-induced agitation or seizures with intravenous (IV) lorazepam (0.05–0.10 mg/kg per dose, 2–4-mg maximum). Treat seizures refractory to lorazepam with IV phenobarbital (10–20 mg/kg per dose, 1-g maximum).

Use naloxone (0.1 mg/kg, repeat every 2 minutes as needed; maximum, 2 mg per dose) for altered mental status or respiratory failure from opioids and for opioid-induced hypotension, particularly when the hypotension is refractory to standard therapies. Do not use flumazenil for non–life-threatening benzodiazepine ingestion because it can cause seizures from benzodiazepine withdrawal. Reserve flumazenil (0.01 mg/kg per dose; 0.2-mg maximum) for confirmed benzodiazepine ingestion with respiratory failure, without co-ingestion of substances that will lower seizure threshold and without a history of chronic benzodiazepine use.

Administer IV N-acetylcysteine (NAC) (150 mg/kg/h for 1 hour, then 12.5 mg/kg/h for 4 hours, then 6.25 mg/kg/h for a minimum of 16 hours) for an acute acetaminophen ingestion with a serum concentration above the acetaminophen toxicity nomogram treatment line (Figure 68–1). In an acute ingestion, discontinue NAC after the 21-hour infusion if the acetaminophen concentration is undetectable and if the aspartate transaminase (AST) and alanine transaminase (ALT) levels are within normal limits. If the acetaminophen remains detectable, or the AST or the ALT levels are elevated, continue IV NAC at 6.25 mg/kg/h until the acetaminophen is undetectable, the AST and ALT are at 50% of peak or decreasing and below 1,000 U/L, and the international normalized ratio (INR) is less than 2.

Figure 68–1. The Rumack-Matthew nomogram is a useful tool in guiding the management of an acute acetaminophen overdose when the time of ingestion is known and the patient presents within 24 hours.



From Nadler A, Fein DM. Acetaminophen poisoning. *Pediatr Rev*. 2018;39(6):316–318.

Administer IV NAC (150 mg/kg/h for 1 hour, then 12.5 mg/kg/h for 4 hours, then 6.25 mg/kg/h until discontinuation parameters have been met) for a patient with a chronic acetaminophen ingestion with a detectable acetaminophen concentration or with evidence of liver injury/decreased function, or with hepatotoxicity in a patient with an unknown ingestion. Consult with a medical toxicologist or poison center, as a longer course of NAC may be required in these scenarios, and length of treatment and discontinuation parameters may vary.

Also consult a medical toxicologist or poison center about running the IV NAC infusion at a faster rate when the patient has a high initial acetaminophen concentration ($\geq$ 300 mcg/mL 4 hours postingestion). Also consult about the indications for hemodialysis if a patient presents with a very high acetaminophen concentration ($\geq$ 700 mcg/mL 4 hours postingestion).

To enhance the elimination of salicylates, initiate serum alkalinization for a salicylate concentration greater than 40 mg/dL (2.896 mcmol/L) or a detectable salicylate concentration with metabolic acidosis, altered mental status, seizures, and/or tinnitus. Put 150 mEq (150 mmol) of sodium bicarbonate in

1 L 5% dextrose in water and administer the IV fluids at 1 to 2 times maintenance requirements. The goals are a serum pH level of 7.40 to 7.45 and a urine pH level of 7.5 to 8.0 while monitoring the patient carefully for hypokalemia.

Elimination of salicylates, ethylene glycol, methanol, caffeine, and theophylline are enhanced by hemodialysis.

Institute suicide precautions and consult a psychiatrist if there is suicidal or unclear intent.

Indications for Consultation

- **Medical toxicology (if available):** All patients with symptoms that require antidotes or enhanced elimination
- **Poison center (800-222-1222):** All patients
- **Psychiatry:** Suicidal or unclear intent, substance use, factitious disorder imposed on another
- **Social work:** Home or self-safety concerns

Disposition

- **Intensive care unit transfer:** Seizure, cardiac arrhythmia, hypotension, agitation, respiratory failure
- **Discharge criteria:** Patient is asymptomatic and any toxin-induced organ injury has resolved; psychiatric and social disposition is established; observation period is met for toxins with delayed toxicity

Follow-up

- **Primary care:** 1 to 3 days
- **Psychiatry:** If needed, 1 to 3 days (if the patient was not admitted to an inpatient psychiatry unit)

Pearls and Pitfalls

- Fosphenytoin and levetiracetam are ineffective for most toxin-induced seizures.
- Avoid premature disposition for a patient who has ingested a substance with delayed toxicity (salicylates, acetaminophen, bupropion, sulfonylureas, ethylene glycol, methanol, sustained-release [SR] β-blockers, SR calcium channel blockers).
- Acetaminophen toxicity nomogram is only for acute ingestion of the regular product, not the extended-release product or chronic ingestion.
- Do not discontinue NAC in acetaminophen toxicity when the acetaminophen concentration is undetectable but hepatotoxicity is worsening.

- IV NAC can increase the prothrombin time and increase the INR as high as 1.9.
- Establish trends by obtaining serial serum concentrations with salicylate or iron ingestion.
- Salicylate concentrations are often reported in units of milligram percent or milligrams per deciliter, rather than milligrams per liter.
- Know which drugs are included in serum or urine drug screenings, and use caution when relying on screening tests to prove toxicity, predict prognosis, or rule exposures in or out.
- Be aware of substances that can cause false-positive drug screening results (eg, antihistamines, central nervous system stimulants, decongestants, dextromethorphan, poppy seeds).
- Always consider that an adolescent has taken more than one drug.

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Maltreatment

CHAPTER 69

Child Abuse: Physical Abuse and Neglect

Introduction

Child maltreatment encompasses neglect, physical abuse, sexual abuse, and emotional abuse. Neglect is the most prevalent form of child maltreatment, though due to its very nature it is the presentation seen least frequently among hospitalized children. Failure to thrive (FTT) is the most common presentation of neglect, but neglect may also manifest as a lack of supervision, such as when a patient ingests an unsecured or unsafely stored toxic substance. Medical and dental neglect refers to harm resulting from the caregiver failing to continue needed treatment or management of a child's medical condition, such as not refilling prescriptions or missing medical appointments. See Box 69–1 for the factors necessary for the diagnosis of medical neglect.

According to the Child Abuse Prevention and Treatment Act (CAPTA) of 1988, child abuse "means at a minimum any recent act or failure to act on the part of a parent or caretaker, which results in death, serious physical . . . harm, . . . or an act or failure to act which presents an imminent risk of serious harm." Although the definition of physical abuse varies among states, all must meet, at a minimum, the CAPTA definition.

Psychosocial risk factors for abuse include isolation of the family, employment instability, neighborhood violence, social unrest, and restrictions experienced during the COVID-19 pandemic. Adolescent parenthood, substance use, single parenthood, maternal depression, and family violence can also adversely affect safe parenting. Individual risk factors include prematurity and low birth weight. Child abuse is not limited to one societal group and cuts across all cultural and socioeconomic strata.

Identification of children who have been abused is critical because they may be repeatedly abused. As many as one-third of patients who are

Box 69–1. Factors Necessary for the Diagnosis of Medical Neglect

The patient is harmed or at risk of harm because of lack of health care.
The recommended health care offers significant net benefit to the patient.
The anticipated benefit of the treatment is significantly greater than its morbidity, so that reasonable caregivers would choose treatment over nontreatment.
It can be demonstrated that access to health care is available and not used.
The caregiver understands the medical advice given.

From Jenny C; American Academy of Pediatrics Committee on Child Abuse and Neglect. Recognizing and responding to medical neglect. *Pediatrics*. 2007; 120(6):1385–1389.

diagnosed as having experienced physical abuse have evidence of old injury at the time of diagnosis, with the most likely perpetrator being a parent.

Clinical Presentation

History

Accurate and detailed documentation is critical. Quote the child's own words when possible.

Ask about social support at home and any family stressors. In addition, assess the parent's affective behavior toward the patient by gently asking questions about how the parent responds to the child when a need is expressed. Ask how the caregiver typically disciplines the child or deals with difficult behaviors. To build trust and rapport, acknowledge stressors, frustration, job loss, poverty, and medical problems that the parent or parents may face.

It is critically important to carefully review the child's medical, developmental, birth, family, and social histories, including the number of previous reports to child protective services (CPS), if known. Determine who, other than the parents, are regular caregivers, as well as their relationship to the family, how long the family has known them, and if other children are cared for along with the patient (because other children may also be at risk). In addition, inquire about the child's gross motor development, speech, temperament, sleep schedule, and behavioral issues.

Trauma may not be part of the chief complaint or initial history of a child who has experienced abuse. The patient may instead present with apnea, an altered level of consciousness, new-onset afebrile seizures, vomiting, a change in the feeding pattern, recurrent high-risk brief resolved unexplained events, or simply an unexplained or unwitnessed injury. If emesis or increased sleep is reported, can they be differentiated from the patient's usual condition (eg, reflux) or an acute viral illness? Has any swelling or bruising appeared? Has there been a recent change in activity, such as decreased use of an arm or failure to bear weight?

In a case of trauma, obtain and document a step-by-step mechanism of injury from the caregiver and the child, if verbal, although the patient may be reticent to talk about the events. With physical abuse, the stated mechanism of injury is often inconsistent with the physical examination findings, so determining the exact mechanism is a priority. A history that is inadequate to explain the injury, whether because it makes no sense with respect to mechanism, severity, or timing, or because the child is not developmentally able to have sustained the injury under their own power, is suspicious for inflicted trauma.

Important questions include: Is the story compatible with the developmental abilities of the child? What was the patient doing just before and just after the event? Who saw the patient last before the event, and what was the patient's status? Who saw the patient most immediately postevent, and what was the status then? Can anyone speak to if/how the patient's status changed over time after the event? If the patient has fallen, inquire about the prefall and postfall position, the reported fall distance, and the type of surface that the child's body hit.

Obtaining an accurate history can be particularly challenging when the parent/caregiver has a developmental disability, communication difficulties, behavioral issues, or mental illness. In such a case, consult with a trained interviewer, such as a child abuse expert, social worker, psychologist, or psychiatrist, and involve a trained interpreter if needed.

Physical Examination

Perform the examination with the child undressed and a chaperone present. Measure and plot the height, weight, and, if age appropriate, head circumference. Chronic abuse or neglect can be reflected in abnormal growth parameters, especially reduced weight and length (neglect) and increased head circumference (chronic subdural hematomas). See Chapter 36, Failure to Thrive, for the approach to a patient with FTT. A patient with a known genetic syndrome may have been persistently below the standard curves but recently had a further decrease in growth velocity.

Document bruising, petechiae, obvious patterns, and other skin findings with a digital camera (preferred) or body diagram, and include a measuring device in the picture. Suspicious sites for inflicted skin injury include the ears, neck, jaw, and soft-tissue prominences such as the cheeks, abdomen, and buttocks. Any bruise in a nonambulatory child is concerning for abuse. Also perform a thorough oral examination of the palate, the gum plates and teeth, and the frenula of the lips and tongue. Oral injury such as frenulum tears, perioral bruising, or facial petechiae may represent a suffocation event or direct facial impact.

In a child with potential neglect from calorie deprivation, document (with photographs) diminished fat stores, such as the thighs, buttocks, rib cage, and face. Record the overall neuromuscular tone, because these children are often delayed in achieving gross motor milestones. Note the neurodevelopmental level (eg, head lag, ability to sit or stand), and compare to normal for age.

After 1 to 2 days, reexamine areas that are tender but do not have visible signs of injury, as it may take that much time for bruises to appear. A patient with abdominal injury may have an equivocal abdominal examination, most

often without visible bruising. In contrast to long bones, rib and metaphyseal fractures may not present with tenderness to palpation.

Although up to 80% of infants with abusive head trauma have retinal hemorrhages, funduscopy is not a useful screening study for occult head injury. Rather, arrange a dilated funduscopic examination, ideally within 24 to 48 hours of the event, to evaluate for comorbid retinal hemorrhage, retinal detachment, or vitreous hemorrhage in a patient with either intracranial or external ocular injury.

Laboratory Workup

For physical abuse, use Table 69–1 to guide the choice of laboratory and radiology examinations.

Obtain a complete blood cell count, looking for an acute anemia (acute trauma), thrombocytopenia, or an abnormal smear to identify mimics of abuse, such as leukemia. Also obtain liver enzymes to assess for occult abdominal injury, but amylase and lipase determinations are less helpful. Liver injury is the most common abdominal injury and may manifest as a rapid elevation of enzymes, falling hemoglobin, and vital sign changes. If the patient presents with bruising or central nervous system hemorrhage, screen for a bleeding diathesis by obtaining a platelet count, prothrombin time, activated partial thromboplastin time, von Willebrand antigen and activity, levels of factors VIII and IX, and, if there is an intracranial hemorrhage, a disseminated

Table 69–1. Laboratory and Radiologic Evaluation of Suspected Abuse

Laboratory Test/Radiologic Examination	< 12 Months	12–36 Months	> 3 Years
Complete blood cell count, aspartate transaminase/alanine transaminase, prothrombin time/partial thromboplastin time	Always	Always	Per history or physical examination
CT abdomen	Per history, physical examination, and laboratory results		
Dilated indirect funduscopic examination	Any patient with intracranial bleeding or external ocular injury		
Head CT (rule out intracranial bleed)	Always if < 6 mos	With signs of inflicted trauma	
MR imaging of brain (first choice for infants in some centers)	Follow-up for an abnormal head CT as needed		
MR imaging C-spine	Any patient with intracranial bleeding concerning for abusive head trauma		
Skeletal survey (when stable)	Always	Always if < 24 mos	Per history or physical examination

Abbreviations: C-spine, cervical spine; CT, computed tomography; MR, magnetic resonance.

intravascular coagulation panel (D-dimer and fibrinogen levels). If the patient has fractures that are suspicious for abuse, obtain calcium, phosphorus, and alkaline phosphatase levels. An osteopenia workup may be indicated for an ex-preterm patient to determine if the patient's osteopenia could predispose to fractures.

Radiology Examinations

Order head computed tomography (CT) if there is a concern for an intracranial bleed. Magnetic resonance (MR) imaging can further define the extent of the bleed and offer good detail on associated parenchymal injury. Most pediatric centers now use low-dose radiation for head CTs in accordance with the Image Gently protocol (www.imagegently.org).

Indications for a skeletal survey are summarized in Box 69–2. Because a skeletal survey is not typically an urgent study, if possible defer it until the patient is clinically stable and skilled pediatric radiology personnel are available. Obtain a repeat skeletal survey in 2 weeks to document missed occult fractures that subsequently demonstrate callus formation.

Differential Diagnosis

Abuse is more likely if the caretaker's explanations are absent, vague, variable (from the same historian or between caretakers), or inconsistent with the pattern of injuries or the developmental capabilities of the patient. Consider cultural practices and healing traditions that may leave marks, burns, or bruises, such as coining, spooning, or holding the child upside down to hit the feet, also known as "caida de mollera." The intention of these cultural practices is to heal or treat a perceived illness rather than to inflict injury.

Suspect abuse if a child is found unconscious without a clear explanation provided. Consider inflicted trauma if a nonambulatory infant has any

Box 69–2. Indications for Obtaining a Skeletal Survey

- Age < 2 years with obvious abusive injuries
- Age < 2 years with any suspicious injury, including
  - Bruises or other skin injuries in nonambulatory infants
  - Oral injuries in nonambulatory infants
  - Injuries not consistent with the history provided
- Infant with unexplained, unexpected sudden death (consult with medical examiner/coroner first)
- Infant or young toddler with unexplained intracranial injuries, including hemorrhage and hypoxic-ischemic injury
- Siblings < 2 years of age and household contacts of an abused child
- Twin of an abused infant or toddler

Adapted from Christian CW; American Academy of Pediatrics Committee on Child Abuse and Neglect. The evaluation of suspected child physical abuse. *Pediatrics.* 2015;135(5):e1337–e1354.

bruising. In contrast, a cruising toddler will typically have bruising on extensor surfaces (shins) or over bony prominences, such as the forehead or chin. Recurrent injuries are suspicious for abuse if there is no clear and consistent explanation from the caregiver. Injuries that are also concerning for abuse include multiple, complex, diastatic, or occipital skull fractures, as well as extraaxial bleeding or heterogeneous hematomas on brain imaging. Some fracture types in infants, such as posterior rib fractures or classic metaphyseal fractures, are highly suspicious for inflicted injury.

If inflicted trauma is a concern, obtain CT or MR imaging for a patient with new onset seizures. If there is persistent altered mental status (AMS), a CT scan can confirm the presence of an intracranial hemorrhage. Infections, such as meningitis or encephalitis, can cause AMS or seizures, as well as vomiting. There may be a history of fever, headache, cold symptoms, or rash. Ingestion and purposeful administration of a toxic substance are other etiologies of AMS and seizures.

Above-average weight gain while under observed care and receiving large amounts of *ad lib* intake is suspicious for nutritional neglect. Consider food insecurity, poverty, and domestic violence, which may contribute to nutritional problems and access to appropriate foods.

See Table 69–2 for differential diagnosis of child abuse and neglect.

Treatment

Stabilization of circulation, airway, and breathing is always the priority. Ensure that the patient is hemodynamically stable before being sent for neuroimaging. If there is concern for head injury or other trauma, consult the appropriate surgical services, and for all other injuries, treat according to the standards of care. Carefully document all findings and management decisions using objective language.

Caring for a child who has been battered is emotionally unsettling and can lead to strong protective feelings in medical staff that may compromise objectivity. The role of the medical team is to focus on the health and support of the child, not to investigate a potential crime or judge a perceived perpetrator. Consult with CPS and the appropriate hospital administration to limit family visitation if the hospital staff are threatened by a caretaker or the safety of other patients is jeopardized. However, parental visitation cannot be broadly denied unless CPS decides it is necessary for the protection of the child.

Child Safety and Protection

If there is any *reasonable suspicion* of abuse or neglect, report the case to the local social services. It is not necessary to have a specific perpetrator or

Table 69–2. Differential Diagnosis of Child Abuse and Neglect

Diagnosis	Clinical Features
Abdominal Injury	
Volvulus with malrotation	Bilious vomiting Surgical abdomen
Bleeding	
Glutaric aciduria type 1	Macrocranium Subdural hematoma, frontotemporal atrophy Sparse retinal hemorrhages
Hemophilia	Positive family history Hemarthrosis ↑ Partial thromboplastin time
Hemorrhagic disease of the newborn	History of no vitamin K prophylaxis, or home birth Exclusively breastfed Parenchymal cerebral hemorrhage and mucosal bleeding
Idiopathic thrombocytopenic purpura	Petechiae Thrombocytopenia
Cutaneous Findings	
Coining	Erythematous, linear abrasions over back/extremities
Cupping	Bruises are perfectly circular and appear in a pattern
Congenital melanocytic nevi (formerly *Mongolian spots*)	Nontender macules No change in appearance when reexamined
Failure to Thrive (See Chapter 35, Failure to Thrive)	
Fractures	
Osteogenesis imperfecta	Transverse long-bone and rib fractures Blue sclerae (not seen in all types) Macrocephaly, numerous Wormian bones, gracile or osteopenic long bones
Rickets	History of prematurity History of poor vitamin D and/or calcium intake ↓ Calcium, ↑ alkaline phosphatase Exclusively breastfed; minimal sun exposure Uniform changes at costochondral junctions and all long bones on radiograph Frontal bossing (severe)

↑ indicates increased level; ↓, decreased level.

hypothesis in mind. In addition, the privacy provisions of the Health Insurance Portability and Accountability Act *do not apply,* because communication to appropriate child protection agencies is necessary to protect children. Know your state laws, found on the U.S. Department of Health and Human Services website at https://www.childwelfare.gov/topics/systemwide/laws-policies/state/.

Indications for Consultation

- **Child protection team:** All patients
- **Dietitian:** FTT
- **Genetics:** Suspected glutaric acidemia type 1 or osteopenic bone disease, such as osteogenesis imperfecta, or FTT that fails to respond to provision of adequate calories
- **Hematology:** Suspected coagulopathy
- **Neurosurgery:** Intracranial injury, displaced skull fracture, or spinal injury
- **Ophthalmology:** If a dilated funduscopic examination is indicated
- **Orthopaedics:** Evaluation and management of fractures
- **Surgery:** Suspected intra-abdominal injury

Disposition

- **Intensive care unit transfer:** Unstable vital signs or AMS
- **Discharge criteria:** Injuries stable or improved; CPS identified a safe environment to which the child may be discharged; follow-up plan established

Follow-up

- **Primary care:** 2 weeks from the original imaging, for repeat skeletal survey for a patient younger than 2 years, biopsychosocial follow-up, vaccine catch-up, other primary care needs, etc
- **Developmental-behavioral pediatrician:** As needed for problems with regression, fears, tantrums, aggression, and sleep problems
- **Early intervention or Head Start:** As needed for developmental delay
- **Mental health services:** As needed for signs of depression, posttraumatic stress

Pearls and Pitfalls

- A short fall (< 3 feet) can result in a simple, linear skull fracture with scalp bruising and swelling but rarely causes multiple, complex, diastatic, or occipital skull fractures or an intracranial injury.
- Children who do not cruise do not bruise.
- *Reasonable suspicion* of abuse is sufficient to report the case to the local child protection authorities. A useful strategy when a child abuse and neglect team conducts the evaluation is to make a report if even one member of the team feels it is necessary.
- Maintain a high index of suspicion, particularly with infants, as many abused children are seen for their injuries by medical professionals prior to abuse being diagnosed. One bruise in a nonambulatory infant strongly correlates with other concomitant injuries.

- The age of a bruise cannot be determined by the physical examination or color.
- Consent is not needed to take pictures for medical-legal documentation.

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CHAPTER 70

Sexual Abuse

Introduction

Sexual abuse is defined as sexual activities involving a child that the child cannot comprehend, activities for which the child is developmentally unprepared and cannot give consent, and/or activities that violate the law or social taboos of society. *Sexual assault* is one type of sexual abuse and has been defined in a 2003 National Institute of Justice report as "a range of acts, including the sexual penetration of a youth's vagina or anus by a penis, finger, or object; the placement of another person's mouth on a youth's sexual parts; the touching of a youth's sexual parts by another person or the forcing of a youth to touch others' sexual parts; or the unwanted penetration of others by a youth." Most identified perpetrators of sexual abuse are male, with adolescents implicated in at least 20% of cases.

Clinical Presentation

History

Sexual abuse can present in a variety of ways, including parental concern alone, nonspecific physical symptoms, the presence of a sexually transmitted infection (STI), and frank disclosure of the abuse by the child. If there are signs or symptoms concerning for abuse, interview the caregiver and the patient separately. Attempt to determine if there is a legitimate concern of sexual abuse, but defer obtaining a full history to a trained forensic interviewer. For example, ask the patient, "Has anything ever happened to your body that made you feel weird, or scared, or confused?" If the patient answers "yes," follow up with, "Tell me about that."

If the patient has recently arrived in the United States, ask how he or she traveled here and what happened after arrival. Questions that can help screen for human trafficking include: "Can you tell me about what happened to you when you traveled to the United States? Has anyone ever asked you to have sex in exchange for something you wanted or needed (money, food, shelter, or other items)? Have you been threatened or harmed if you try to quit or leave your situation? Did anyone where you stay ever make you feel scared or unsafe?"

A thorough review of systems is necessary, including asking questions about abdominal pain, dysuria, enuresis, encopresis, bleeding, discharge, phobias, difficulty sleeping, possible physical trauma, and exposure to adult or pornographic material. Also ask about homicidal or suicidal ideation.

Symptoms potentially concerning for sexual abuse include rectal or genital bleeding and developmentally unusual sexualized behavior.

If there is enough information to raise a concern that inappropriate contact has occurred, contact child protective services (CPS) and/or law enforcement depending on the mandated reporting laws in the area in which the abuse occurred. Arrange for a separate, detailed interview to be conducted by a trained professional, with a trained interpreter present, if necessary. This can occur in the hospital by contacting the child protection team or a social worker. Occasionally, it may be appropriate to delay the interview until the child can be seen at a children's advocacy center (CAC) if follow-up can be arranged within a short period of time, CPS has determined that the patient is safe from the perpetrator after discharge, the disclosure is of remote contact, and the child has no physical complaints. Regardless, the hospital team must obtain a history pertinent to the diagnosis and treatment of any medical diagnoses secondary to the abuse. This includes the type of abuse, when the last incident occurred, the type of contact that happened, any signs or symptoms of STIs, and the date of menarche and last menstrual period in females. Do not interview a patient younger than 3 years, but document any spontaneous utterances in quotation marks, such as, "You won't hurt my pee-pee like John did, will you?"

Physical Examination

If the incident(s) occurred more than 72 hours (prepubertal child) or 120 hours (pubertal adolescent) prior to presentation, and there are no genitourinary symptoms, the examination may be deferred until the patient can be seen at a CAC equipped with trained examiners and a colposcope. Collection of forensic evidence is warranted when the last episode of abuse occurred within the age-specific time frame noted above, if the child is acutely injured, or if the history includes the potential for exposure to bodily fluids. Perform the examination in accordance with the protocols for sexual assault survivors to properly collect the evidence. Many institutions have a pediatric sexual assault nurse examiner (SANE-P) or child abuse pediatrician available to perform the genital and rectal examination with colposcopic viewing and photography. Ideally, arrange for the presence of a supportive adult, ideally of the patient's choice, who is not involved in the allegations of abuse.

If no designated examiner is available, start with explaining the examination to the patient and parent/guardian, if present. Inspect the oropharynx and skin for signs of trauma or infection. Note the child's affect and development, although there is no standard reaction to sexual assault on the part of survivors and the patient's demeanor cannot be used to determine the veracity of their

disclosure. The patient may be poorly interactive, sad, withdrawn, or, in contrast, smiling and engaged with the examiner.

During the genitourinary examination, note the patient's sexual maturity rating and describe each part of the genitalia, breasts, perineal region, anus, and buttocks as necessary, with accompanying drawn diagrams. Have a SANE-P or child abuse expert assist with forensic photography to ensure correct procedures are followed. The best way to visualize the hymen and female genitalia is by means of labial traction. Place the patient in the frog-leg or lithotomy position, grasp each of the labia majora with the thumb and forefinger, and gently pull toward the examiner (as if pulling up a sock). If performed correctly, the examination is painless, and the hymen will become more three-dimensional in relation to the introitus and vaginal canal. However, the hymen can have a variety of normal configurations that may require specialized training to recognize.

It is uncommon to discover physical examination findings that are diagnostic of sexual abuse, even among those who have experienced chronic sexual abuse. Concerning findings include abrasions or bruising of the inner thighs and labia; trauma to the labia minora, fossa navicularis, posterior fourchette, or posterior hymen; interruption of the posterior hymen; and absent hymeneal tissue. In the assessment for genital injury, anal injury is the most rarely identified. Anal bruising, lacerations, or scars can also be consistent with an acute sexual assault.

Laboratory Workup

Regardless of the acts described, complete a forensic evidence collection kit, if not already performed in the emergency department, if the abuse has occurred in the past 72 to 120 hours or if there is a possibility of direct contact with blood or body fluids. Never force the child to undergo evidence collection. To decide on testing for STIs, consider the following:

- Was there oral, genital, or rectal contact with bodily secretions? Digital fondling alone is unlikely to transmit an STI.
- How common are STIs in the community?
- Whether the child is symptomatic does not affect the decision to test, as most infections in children are asymptomatic.

Typical STI testing includes obtaining samples to test for gonorrhea, chlamydia (throat swab for culture and urine nucleic acid amplification testing [NAAT]), testing for *Trichomonas vaginalis*, Venereal Disease Research Laboratory or rapid plasma reagin screening for syphilis, and HIV. Note that NAAT is now approved for testing of all extragenital sites. Also perform

a pregnancy test for patients at Tanner Stage 3 or higher of female sexual maturity. Pregnancy or the presence of sperm or semen is diagnostic of sexual contact. A positive test result for gonorrhea, chlamydia, trichomoniasis, syphilis, or HIV is diagnostic of child abuse when vertical transmission has been excluded. Because it is unusual for a prepubertal survivor to present immediately after the abuse occurred, select tests on a case-by-case basis in consultation with a child abuse expert.

Differential Diagnosis

Normal behavior surrounding genitalia is playful, driven by curiosity, and sometimes involves other children of the same age range. Sexually reactive behaviors may include a child who attempts to force another child, whether younger or an age peer, to engage in sexual behaviors or a child who performs insertive acts on themselves, on toys, or on playmates, although this may be normative behavior. As with many medical conditions, a diagnosis of sexual abuse does not rely solely on the physical examination findings. Often, a clear and consistent history is sufficient to assign the diagnosis.

In the case of genital abnormalities, consult a child abuse specialist or pediatric gynecologist who has the expertise to categorize abnormalities.

Reporting

The threshold for reporting possible sexual abuse is low. A reasonable suspicion of sexual abuse is sufficient for any health care provider to report the case to the local CPS, who then has the responsibility for conducting a thorough investigation. If the report is made in good faith, the provider is immune from liability.

Treatment

Antibiotics

Treatment for STIs depends on the type of contact with the alleged perpetrator. Order prophylactic antibiotics if there was a possible exposure to bodily fluids in a pubertal (or older) patient, but prophylaxis is rarely indicated for a prepubertal survivor. See Chapter 3, Sexually Transmitted Infections, for treatment regimens.

HIV Prophylaxis

If there is concern for HIV, contact a retrovirologist or infectious diseases expert for guidance with postexposure prophylaxis. An additional useful resource is the PEPline (888-448-4911; nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/).

Unintended Pregnancy

It is critical to address pregnancy prophylaxis within 5 days following the assault of a postpubertal female. Discussions regarding the best individual response to manage that risk should include the patient's support system when possible, including family members or a supportive adult who is not involved in the allegations of abuse, and ideally a familiar medical professional who has a long-standing relationship with the patient. Engaging the patient's support system is important in the discussion of the options to address an unintended pregnancy, because the patient is in a vulnerable state while deciding an outcome that is life-changing.

Child Safety and Protection

If there is any *reasonable suspicion* of abuse or neglect, report the case to the local CPS agency to address the child's safety and protection. It is not necessary to have a specific perpetrator or hypothesis in mind. In addition, the Health Insurance Portability and Accountability Act does not apply to mandated reports because communication to appropriate child protection agencies is necessary to protect the patient. Follow the state laws, which can be found on the U.S. Department of Health and Human Services website at www.childwelfare.gov/systemwide/laws-policies/state/.

There are more than 900 CACs in the United States. They function as centralized locations for survivors of child maltreatment and violence and their families. Children's advocacy centers provide coordination among community agencies and professionals, including law enforcement, CPS agencies, prosecution entities, medical organizations, survivor advocacy groups, and mental health services. To find a CAC, go to https://www.nationalchildrensalliance.org/cac-coverage-maps.

If the patient is a victim of human trafficking, ensure that the patient is not left alone. Separate the patient from their companion and call security as needed. Consult a social worker and call CPS and the National Human Trafficking Resource Center at 888-373-7888. You may also call the Homeland Security Investigations Tip Line at 866-347-2423 (24 hours a day, 7 days a week, with over 300 languages and dialects available) or submit a tip online at www.ice.gov/tips.

Indications for Consultation

- **Child protection team:** Suspected sexual abuse or genital abnormality
- **SANE-P, if available:** Suspected sexual abuse or assault
- **Psychiatry:** Suicidal or homicidal ideation
- **Social work:** Suspected sexual abuse
- **Pediatric gynecology:** Genital abnormality or injury

Disposition

- **Intensive care unit transfer:** Unstable vital signs or altered mental status
- **Discharge criteria:** CPS has identified a safe environment into which the child may be discharged; a follow-up plan has been established

Follow-up

- **Primary care:** 1 to 2 weeks
- **CAC:** 3 to 5 days to complete information gathering, establish care with mental health services, and screen for STIs, if indicated
- **Pediatrician who is expert in child abuse:** 3 to 4 weeks for surveillance laboratory testing and follow-up examination, if the local CAC does not have a clinical component
- **Mental health services:** 1 to 2 weeks, if not available at the nearest CAC, or referrals not provided by CAC

Pearls and Pitfalls

- The diagnosis of sexual abuse can be assigned on the basis of a clear and consistent history, such that a normal physical examination finding does not rule out sexual abuse.
- A reasonable suspicion of sexual abuse is sufficient to report the case to the local child protection authorities.
- Document observations thoroughly and clearly, using quotations when possible. Detailed notes will help inform protective agencies and law enforcement, as well as facilitate effective testimony in court.
- Use a colposcope or camera when conducting a physical examination and collecting evidence.
- Genitalia, especially female genitalia, have many variations of normal. If there is uncertainty about the findings of a physical examination, consult a child abuse expert or pediatric gynecologist.

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Nephrology

CHAPTER 71

Acute Glomerulonephritis

Introduction

The term *acute glomerulonephritis* (AGN) encompasses the spectrum of diseases that lead to variable degrees of inflammation in the glomeruli. It can be an isolated, self-limited illness or the first presentation of chronic glomerulonephritis (GN). Clinical manifestations can vary from asymptomatic microscopic hematuria to acute nephritic syndrome, characterized by abrupt onset of gross hematuria, proteinuria, and edema, often with hypertension and some degree of renal insufficiency.

Postinfectious AGN (PIAGN) is the classic example of AGN and the most frequent cause in children. It most commonly occurs after a pharyngitis or skin infection with group A *Streptococcus,* although it can be seen after many other bacterial, mycobacterial, viral, fungal, or parasitic infections. Postinfectious AGN classically presents 7 to 14 days after pharyngitis or up to 3 to 12 weeks after pyoderma. It typically occurs in school-aged children and is rare before 2 years of age.

Berger disease, or immunoglobulin A (IgA) nephropathy, occurs most often in patients older than 10 years and can frequently present as recurrent episodes of gross hematuria in childhood.

Other causes of pediatric AGN include membranoproliferative (mesangiocapillary) GN and vasculitic diseases, including Henoch-Schönlein purpura (HSP).

Clinical Presentation

History

Painless gross hematuria and edema are the most common presenting symptoms of PIAGN. The patient may report the abrupt development of puffy eyes, or facial or dependent edema, accompanied by foamy, cola-colored urine and decreased urine volume. A patient with PIAGN will often develop hypertension. However, hypertensive emergency, presenting with headaches, seizures, altered mental status, and visual disturbances, is very uncommon. Other rare complaints include dyspnea or cough as a result of pulmonary edema. The gross hematuria and edema of PIAGN usually resolve within 3 to 7 days, with gradual normalization of urine output and blood pressure over the next 2 to 4 weeks.

Ask about recent or concurrent infections to determine the etiology of the AGN. Exacerbations of IgA nephropathy often occur concurrently with mild

infections. Note any other preceding infections, particularly endocarditis, visceral abscess, osteomyelitis, and shunt infection.

Fever and systemic symptoms are typically absent in PIAGN. However, a history of fever, abdominal pain, arthralgia, arthritis, or rash may be present in a patient with a systemic vasculitis, such as systemic lupus erythematosus (SLE) or HSP.

Physical Examination

With the possible exception of increased systolic and/or diastolic blood pressure, the physical examination findings may be normal, although pallor, edema (localized or generalized), and/or pulmonary rales may be noted. There may also be physical findings (eg, hair loss, epistaxis, joint swelling, and rash) specific to a systemic etiology. Carefully assess growth parameters, because chronic kidney disease may initially manifest as AGN.

Laboratory Workup

Hematuria is the hallmark of PIAGN and is defined by the presence of 5 or more red blood cells (RBCs) per high-power field. For any patient presenting with dark urine, perform a complete urinalysis with urine microscopy to distinguish among the various causes of red urine. Red blood cells will be present in GN but not with hemoglobinuria, myoglobinuria, and discoloration from drugs or foods. Gross hematuria is turbid, whereas urine containing myoglobin or hemoglobin is dark but clear. For further differentiation, examine the centrifuged serum, which will be clear in myoglobinuria but have a pink tinge with hemoglobinuria.

Once the presence of RBCs is confirmed, perform a urine culture, complete blood cell count, basic chemistry panel, and complement component 3 (C3) and 4 (C4) assessment. To screen for PIAGN, check the antistreptolysin O (ASO) and antideoxyribonuclease (anti-DNase) titers. A positive ASO result does not confirm the diagnosis of PIAGN but only establishes that either colonization or infection (old or new) with *Streptococcus* has occurred. Moreover, PIAGN that is unrelated to streptococcal infection will feature negative results for both the ASO and anti-DNase antibody. Perform renal/bladder ultrasonography if the patient presents with bright red blood (to rule out a mass) or has recurrent hematuria or a systemic disease.

In PIAGN, the urine will be reddish-brown or cola colored, with dysmorphic RBCs, RBC casts, and often white blood cells. Nonnephrotic-range proteinuria is commonly present (see Chapter 74, Nephrotic Syndrome). Anemia is usually hemodilutional, but PIAGN has been associated with autoimmune hemolytic anemia. Depending on the degree of renal dysfunction, the blood

urea nitrogen (BUN)/creatinine ratio may be increased. The C3 level is decreased in 90% of patients, whereas the C4 level is typically normal. In general, the ASO level is increased in a patient with streptococcal pharyngitis, whereas the anti-DNase titer is high in cases of pyoderma.

If the AGN does not seem to be postinfectious and/or the patient has acute and severe deterioration in renal function (ie, rapidly progressive GN), obtain antibodies to the glomerular basement membrane (anti–glomerular basement membrane; Goodpasture syndrome) or those associated with other forms of vasculitis (anti–neutrophil cytoplasmic antibodies).

Differential Diagnosis

The differential diagnosis of hematuria is extensive, but painless gross hematuria suggests a glomerular etiology. Potential causes can be further classified according to C3 and C4 levels. Glomerulonephritis associated with normal C3 and C4 levels includes IgA nephropathy, Alport syndrome, and HSP, whereas low C3 level occurs in PIAGN, and low C3 and C4 levels occur in membranoproliferative GN, shunt nephritis, and SLE. Additional details for each of these conditions are summarized in Table 71–1.

Table 71–1. Differential Diagnosis of Painless Gross Hematuria

Diagnosis	Clinical Features
Alport syndrome	X-linked dominant inheritance Sensorineural hearing loss Ocular disease: retinopathy, cataracts, lenticonus
Berger disease/IgA nephropathy	Age > 10 y Macroscopic hematuria concurrent with infections ↑ IgA level in 50% of cases; normal complement levels
HSP	Purpuric rash, arthritis, abdominal pain Normal complement levels
Lupus nephritis	Photosensitive malar rash, arthralgia, serositis ↓ C3 and C4 levels (+) Antinuclear antibody, anti–double-stranded DNA
Membranoproliferative GN	Similar to PSAGN Persistent ↓ C3 level with or without ↓ C4 level
PSAGN	Age 2–12 y Pharyngitis or skin infection 1–12 wk prior ↓ C3 level, normal C4 level (+) ASO/anti-DNase
Shunt nephritis	History of shunt Arthralgia, lymphadenopathy, hepatosplenomegaly ↓ C3 level

Abbreviations: anti-DNase, anti-deoxyribonuclease; ASO, anti-streptolysin O; C3, complement component 3; C4, complement component 4; GN, glomerulonephritis; HSP, Henoch-Schönlein purpura; IgA, immunoglobulin A; PSAGN, poststreptococcal glomerulonephritis.
+ indicates positive finding; ↑, increased level; ↓, decreased level.

Treatment

Treatment of PIAGN is largely supportive and focuses on control of hypertension and fluid overload. Because these are primarily caused by enhanced salt and water retention, fluid and salt restriction is the first-line treatment. Limit sodium to 1 to 2 mEq/kg/d (1–2 mmol/kg/d). Fluid restriction varies on the basis of the degree of edema and circulating volume but may be as strict as 1 to 2 times the amount needed to replace insensible losses (400–800 mL/m^2/d).

If further treatment is needed to control volume overload and/or mild to moderate hypertension, administer a loop diuretic (intravenous [IV] furosemide 0.5–1.0 mg/kg every 8 hours). If the hypertension persists, provide a calcium channel blocker such as oral nifedipine (0.25–0.50 mg/kg, every 4–6 hours; maximum, 10 mg per dose) or oral amlodipine (0.05–0.40 mg/kg once daily, 10-mg maximum). Consult with a nephrologist before ordering an angiotensin-converting enzyme inhibitor because there is a risk of decreasing the glomerular filtration rate and causing hyperkalemia.

Initial IV treatment options for a hypertensive emergency include hydralazine (start at 0.1 mg/kg per dose, titrate to the desired blood pressure with 0.2–0.4 mg/kg per dose, 20-mg maximum) or labetalol (0.2–1.0 mg/kg per dose, 40-mg maximum; avoid use with significant acute respiratory disease or asthma). If these measures do not provide adequate control of blood pressure, options include nicardipine (0.5–5.0 mcg/kg/min; start at 0.1–0.2 mcg/kg/min), nitroprusside (0.3–0.5 mcg/kg/min, 10-mcg/kg/min maximum), or labetalol (0.25–3.00 mg/kg/h). If the patient has hypertension and volume overload, administer furosemide (1 mg/kg per dose, 6-mg/kg/d maximum). For any patient treated with IV antihypertensive medications, check the blood pressure at least every 5 to 15 minutes and titrate the infusion to reach the target blood pressure. There are a number of specific guidelines for safe blood pressure reduction. One approach is to target a normal blood pressure in a stepwise fashion by reducing the blood pressure by 25% over the first 8 hours, followed by another 25% over the next 8 to 12 hours, and the remaining 50% over the next 24 hours.

Indications for Consultation

- **Nephrology:** AGN
- **Rheumatology:** Concern for a systemic vasculitis, such as SLE

Disposition

- **Intensive care unit transfer:** Hypertensive emergency, need for dialysis or hemofiltration, need for ventilator support
- **Discharge criteria:** Blood pressure controlled, renal impairment improving

Follow-up

- **Primary care:** 1 week for blood pressure check, BUN/creatinine ratio assessment, and urinalysis
- **Nephrology:** 4 weeks to check C3 level (if it was low)

Pearls and Pitfalls

- Poststreptococcal AGN runs a typical course. Evaluate the patient for other etiologies of AGN if the presentation is unusual in terms of clinical and/or laboratory features.
- Up to 50% of patients with AGN and an abnormal urinalysis result are asymptomatic.
- A patient with hypertensive encephalopathy or acute renal failure may have a marginally abnormal urinalysis result.
- Hematuria is not the only cause of dark-colored urine or a positive heme on a urine dipstick. Confirm the presence of RBCs on microscopy.

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Hemolytic Uremic Syndrome

Introduction

Hemolytic uremic syndrome (HUS) is a disorder characterized by the triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute renal injury. Classically, it follows a prodrome of a diarrheal illness. Most patients will recover completely, but 3% to 5% will progress to renal failure. Most cases occur in children younger than 5 years, often during the summer and fall.

Cases of HUS are classified as either primary (formerly atypical or diarrhea negative) or secondary (formerly typical or diarrhea positive). Approximately 10% of cases of HUS are classified as primary, which include genetic or acquired disorders of regulatory components of the complement system. This form of HUS is less common but has a poorer prognosis, with higher rates of both relapse and progression to end-stage renal disease. Most cases of HUS are classified as secondary and are primarily associated with infections, most commonly Shiga toxin–producing *Escherichia coli* serotypes or other bacteria, such as *Shigella*, *Salmonella dysenteriae*, *Streptococcus pneumoniae*, and HIV. Other rare triggers for secondary HUS include drug toxicities, autoimmune disorders, and pregnancy.

Clinical Presentation

History

Secondary HUS is preceded by a nonspecific diarrheal illness (often bloody) or pneumococcal pneumonia or meningitis. It presents with low-grade fever, nausea, vomiting, abdominal pain, and cramping. A patient with HUS will then develop the sudden onset of pallor, irritability, weakness, and oliguria or anuria. These symptoms occur several days (often 5–7 days) after the onset of the diarrheal illness, typically when the colitis is improving. Approximately one-third of patients may experience neurologic changes at the onset of symptoms, ranging from mild irritability and lethargy to seizures, stroke, or coma.

Physical Examination

Perform a thorough physical examination, because abnormal findings reflect the severity of the cascade of hematologic and renal dysfunction. The patient is often ill appearing, with significant pallor and possibly mild jaundice. There may be petechiae, but purpura is rare. Generalized edema is often present and is more prominent in dependent areas. Nonspecific neurologic findings are

common and include irritability and generalized weakness or fatigue. However, more severe neurologic changes, such as seizures, encephalopathy, coma, or focal neurologic deficits consistent with stroke, may be seen secondary to metabolic derangements or thrombotic events.

Generalized abdominal pain and tenderness are common and are typically related to the inciting infectious colitis. More focal abdominal pain and tenderness can be seen with complications such as hepatitis (right upper quadrant tenderness, hepatomegaly), pancreatitis (epigastric pain and tenderness radiating to the back, severe emesis), intestinal obstruction, intussusception, or perforation (distention, severe emesis, decreased bowel sounds). Cardiovascular complications include severe tachycardia, hypertension, or signs of heart failure (dyspnea, tachypnea, rales, hepatomegaly, cool extremities, delayed capillary refill). These physical findings are secondary to severe anemia, fluid overload, electrolyte abnormalities, and acute renal insufficiency. Myocarditis is a rare complication.

Laboratory Workup

Repeat the complete blood cell count every 8 to 12 hours, to follow the status of the microangiopathic hemolytic anemia. The hemoglobin level is typically less than 8 g/dL (< 80 g/L) and may decrease rapidly as a result of intense, ongoing hemolysis. The cells are normochromic and normocytic, with schistocytes/helmet cells seen on a peripheral smear. Assess the patient for other markers of nonimmune-mediated hemolysis, including increased reticulocyte count, elevated indirect bilirubin and lactate dehydrogenase levels, decreased haptoglobin level, and a negative Coombs test result. The patient may have thrombocytopenia, with a platelet count less than 75×10^9/L (< 75,000/ mm^3), and megakaryocytes on a peripheral smear. Coagulation factors (prothrombin/partial thromboplastin time) typically remain normal. Low complement components 3 and 4 (C3 and C4) levels may be noted in some cases of primary HUS.

During the acute phase, monitor the electrolyte levels every 12 hours to look for hyperkalemia, hyper- or hyponatremia, metabolic acidosis, hyperphosphatemia, and hypocalcemia. The blood urea nitrogen and creatinine levels might be markedly increased, although there is no correlation between the degree of anemia and the severity of the renal disease. The patient may also have increased liver transaminases, as well as hypoalbuminemia from enteric protein losses. If the pancreas is involved, amylase and lipase levels will be increased, and the patient may be hyperglycemic. Also perform a urinalysis to assess the patient for hematuria, proteinuria, and possible red blood cell casts.

Perform a stool Shiga toxin assay, as well as a stool culture for enterohemorrhagic *E coli*. Stool cultures performed more than 6 days into the diarrheal illness may have a low yield, and blood cultures typically have negative results.

Radiology Examinations

Although imaging is not routinely indicated, perform abdominal imaging (anteroposterior abdominal radiography, computed tomography [CT], ultrasonography) if there is a concern for obstruction, perforation, or intussusception. Perform magnetic resonance imaging or non–contrast-enhanced head CT if the patient experiences seizures, coma, or signs of a stroke. Order an electrocardiogram if the patient has severe hyperkalemia, and order an echocardiogram, troponin level, and/or brain natriuretic peptide level if there are signs of congestive heart failure, pericardial effusion, or myocarditis.

Differential Diagnosis

The differential diagnosis of HUS is summarized in Table 72–1.

Treatment

The management of secondary HUS is mostly supportive and includes meticulous attention to fluid and electrolyte balance, based on the patient's intravascular fluid status and renal function. Thus, rehydrate a hypovolemic patient, but restrict fluids in a patient with increased intravascular volume and diminished urine output. Provide insensible losses only (one-third of routine maintenance fluid volume). Early volume expansion targeted to increase body weight by 10% can improve the outcome, with a decreased rate of renal replacement therapy, shorter duration of intensive care, shorter length of stay, and a trend toward decreased central nervous system (CNS) involvement.

Correct electrolyte abnormalities and follow the patient's daily weight. Administer furosemide (1 mg/kg per dose every 6–24 hours) to help maintain some urine output and prevent progression from oliguria to anuria. Antimotility agents and antibiotics are contraindicated and may worsen the disease course. Optimization of nutritional support is essential, preferably by the enteral route, if the clinical status permits.

Despite rigorous management of fluid and electrolyte status, dialysis may eventually be required. Indications for dialysis include severe electrolyte abnormalities (eg, hyperkalemia, acidosis) refractory to medical therapy, symptomatic uremia, or volume overload with persistent anuria that is not responsive to diuretic therapy. In addition, management of nutritional support and transfusions for severe anemia may require administration of large

Table 72–1. Differential Diagnosis of Hemolytic Uremic Syndrome

Diagnosis	Clinical Features
Gastrointestinal Etiology: No Microangiopathic Hemolytic Anemia or Thrombocytopenia	
Appendicitis	Acute onset of periumbilical pain that migrates to the right lower quadrant Diarrhea uncommon Normal blood urea nitrogen/creatinine levels and liver function test results
Infectious colitis	Fever, severe abdominal pain, tenesmus (+) Fecal leukocytes
Inflammatory bowel disease	Diarrhea or constipation Weight loss and/or growth failure Oral ulcers and perianal skin tags/fissures
Henoch-Schönlein purpura	Arthralgia/arthritis Palpable purpura of extensor surfaces of the lower extremities Intermittent severe abdominal pain, which can be due to intussusception Heme (+) stools
Hematologic Etiology	
Bilateral renal vein thrombosis	Flank pain No gastrointestinal symptoms
DIC	Prolonged prothrombin time/partial thromboplastin time ↓ Fibrinogen level, fibrin split products, D-dimer level
Sepsis	Absence of microangiopathic hemolytic anemia Signs/symptoms of infection/systemic inflammatory response system May be associated with DIC
Thrombotic thrombocytopenia	Usually occurs in adults Unlikely if platelet count is 30×10^9/L (<30,000/ mm^3) or if ↑ creatinine level More CNS involvement
Renal Etiology	
Acute glomerulonephritis	Absence of hemolysis No gastrointestinal symptoms
Severe dehydration	Return of renal function with fluid resuscitation No hematologic findings
Vasculitis	Rash, arthralgia/arthritis Gastrointestinal symptoms may occur with gut involvement Persistent systemic symptoms

Abbreviations: CNS, central nervous system; DIC, disseminated intravascular coagulation.
+ indicates positive finding; ↑, increased level; ↓, decreased level.

volumes of fluid, necessitating dialysis, although preemptive dialysis is of no benefit. In the acute phase of renal injury, avoid nephrotoxic drugs, such as angiotensin-converting enzyme inhibitors and nonsteroidal anti-inflammatory medications, because they alter glomerular perfusion.

Transfuse packed red blood cells (5–10 mL/kg) if the hemoglobin level is less than 6 to 7 g/dL (< 60–70 g/L) or if there are signs of cardiovascular

compromise. Transfuse slowly with a posttransfusion goal of a hemoglobin level of 8 to 9 g/dL (80–90 g/L). Monitor the patient closely for signs of fluid overload and treat with furosemide (1 mg/kg per dose), if necessary, before and/or during the transfusion. Avoid a platelet transfusion unless there is a significant hemorrhage or an invasive procedure is necessary. A patient with significant CNS involvement or primary HUS may require eculizumab or plasmapheresis.

Indications for Consultation

- **Cardiology:** Carditis or heart failure
- **Gastroenterology/surgery:** Complications from colitis or acute abdomen
- **Hematology:** Complications from anemia or thrombocytopenia
- **Nephrology:** Suspected or diagnosed HUS
- **Neurology:** Coma, stroke, or seizure

Disposition

- **Intensive care unit transfer:** Severe electrolyte abnormalities, refractory hypertension requiring antihypertensive infusions, status epilepticus, coma, stroke, or heart failure
- **Discharge criteria:** Improving renal function, anemia, and thrombocytopenia, with stable electrolyte levels; adequate oral intake and nutrition; hypertension resolved or stable with oral medication

Follow-up

- **Primary care:** 2 to 3 days
- **Nephrologist:** 1 week; however, long-term follow-up is needed for persistent or recurrent hypertension and proteinuria

Pearls and Pitfalls

- Maintain a high index of suspicion for a patient with a recent diarrheal illness and abrupt onset of pallor or change in urine output or activity.
- Consider obtaining central access early to facilitate management and monitoring of fluid and electrolyte status, nutritional support, hematologic derangements, transfusions, and possible dialysis, through a right internal central venous catheter and not a peripherally inserted central catheter.
- There is no correlation between the severity of the hematologic findings and that of the renal disease.

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CHAPTER 73

Nephrolithiasis

Introduction

Nephrolithiasis accounts for up to 1 in 1,000 pediatric hospitalizations in the United States. Consequences of untreated nephrolithiasis include severe pain, increased risk of infection, and, rarely, kidney injury.

Physiological risk factors for nephrolithiasis include low urine volume, low urine pH level (but alkaline urine pH for calcium carbonate and struvite stones), bacterial urinary tract infection (UTI), increased urinary concentrations of stone-forming metabolites, and reduced concentrations of inhibitors (eg, citrate, magnesium) of stone formation. Metabolic abnormalities cause more than 50% of pediatric renal calculi, with hypercalciuria and hypocitraturia being the most common, especially in younger children. Repeated infection, with or without anatomic abnormality, can also lead to nephrolithiasis in children. Urease-producing bacteria, such as *Proteus, Providencia, Klebsiella, Pseudomonas,* and enterococci, promote renal stone formation by lowering urinary pH level, leading to struvite precipitation and the "staghorn" type of renal stone. A history of surgical correction of genitourinary abnormalities or prolonged immobilization further increases the risk of hypercalciuria with subsequent nephrolithiasis.

Clinical Presentation

History

Nephrolithiasis usually presents with a combination of colicky abdominal pain that may also be generalized, flank pain, back pain, vomiting, and gross hematuria. In the first few months after birth, the symptoms may seem consistent with infantile colic. Ask about a personal or family history of renal disease, UTIs, and other chronic medical conditions, including malabsorption and neurogenic bladder. Determine if the patient is taking any medications that can predispose to stone formation, such as calcium supplements, loop diuretics, acetazolamide, prednisone, adrenocorticotropic hormone, or anticonvulsants. A first-degree relative affected by nephrolithiasis suggests a genetic etiology.

Physical Examination

Examination findings are inconsistent and nonspecific. Abdominal pain with palpation and costovertebral angle tenderness may be present. Usually there is no abdominal guarding or rebound tenderness. The acute pain of renal colic

is classically writhing in nature, with the patient having difficulty finding a position of comfort.

Laboratory Workup

Perform a urinalysis and urine culture to evaluate the patient for hematuria and markers of infection, such as pyuria, leukocyte esterase, nitrites, and bacteria. However, as many as one-third of pediatric patients with nephrolithiasis do not present with hematuria.

Once the presence of a stone is confirmed, it is important to identify the exact type before initiating specific treatment. Arrange for the nursing staff or the patient/parent to strain the urine and send any recovered stones for analysis. A 24-hour urine collection is the best way to identify any abnormal metabolites (calcium, oxalate, phosphate, citrate, magnesium, cystine, xanthine, uric acid). Because this collection may be difficult to perform in a younger patient, send a random urine sample for calcium, citrate, cystine, oxalate, and uric acid evaluation, calculate the metabolite-to-creatinine ratio for each, and compare the ratios to standard values (most useful for calcium-to-creatinine ratio). For example, divide the spot calcium level in milligrams by the spot creatinine level in milligrams to determine the urinary calcium-to-creatinine ratio. (See Table 73–1 for reference values.)

Order further laboratory tests, such as serum electrolyte, calcium, phosphorus, and magnesium levels, on the basis of the clinical picture, stone composition, and urine metabolite evaluation. For example, in a patient with a calcium stone or high calcium-to-creatinine ratio, consider a broad differential for hypercalciuria, including abnormal gastrointestinal absorption of calcium, renal tubular dysfunction, endocrine derangements, and metabolic disorders. This workup may be deferred to the outpatient setting.

Table 73–1. Normal Values for Urine Metabolite-to-Creatinine Ratios

Metabolite Ratio	Age	Normal Range[a]	Diagnoses Associated With Increased Ratios
Calcium-to-creatinine ratio	0–6 mo 6–12 mo 2–18 y	< 0.80 < 0.60 < 0.20	Bartter syndrome, distal renal tubular acidosis, loop diuretics
Oxalate-to-creatinine ratio	0–6 mo 6 mo to 4 y > 4 y to adult	< 0.30 < 0.15 < 0.10	Cystic fibrosis Primary oxaluria
Cystine-to-creatinine ratio	All ages	< 0.02	Cystinuria

[a] Urine metabolite-to-creatinine ratios are calculated with values in milligrams.

Adapted from Gillespie RS, Stapleton FB. Nephrolithiasis in children. *Pediatr Rev.* 2004;25(4):131–139.

Radiology Examinations

Order anteroposterior abdominal radiography as the initial radiologic study, although many stones may be missed if they are small in size or composed of material that is less radiopaque, such as uric acid or cystine. Ultrasonography (US) will most likely demonstrate a clinically significant stone or unilateral hydronephrosis, which provides indirect evidence of an obstructing calculus. The most accurate test is non–contrast-enhanced computed tomography, which is 96% sensitive and 98% specific, although it entails radiation exposure.

Differential Diagnosis

The differential diagnosis for renal colic is broad and includes most of the common causes of significant abdominal pain (Table 73–2).

Treatment

The mainstays of therapy are aggressive intravenous hydration and adequate analgesia. Administer 5% dextrose normal saline with 20 mEq/L (20 mmol/L) KCl at 1.5 to 2 times maintenance levels, provided there is no evidence of

Table 73–2. Differential Diagnosis of Nephrolithiasis

Diagnosis	Clinical Features
Appendicitis	Fever, vomiting Periumbilical pain that migrates to the right lower quadrant Abdominal guarding and rebound tenderness
Cholelithiasis	Risk factors: hemolysis, postpartum status, rapid weight loss Right upper quadrant pain, hyperbilirubinemia (+) Abdominal ultrasonography
Glomerulonephritis	No colic Hypertension Tea-colored urine with red blood cell casts
Intussusception	Intermittent abdominal pain, drawing the legs up No hematuria (+) Guaiac test, currant jelly stools
Malrotation	Vomiting, abdominal distention, no colic No hematuria
Ovarian/testicular torsion	Intermittent lower abdominal pain No hematuria (+) Ultrasonography
Pancreatitis	Epigastric or left upper quadrant pain relieved by leaning forward ↑ Amylase and lipase levels
Pyelonephritis	Fever, toxicity Costovertebral angle tenderness but no colic ↑ White blood cell count Pyuria, bacteriuria, (+) nitrites and leukocyte esterase

+ indicates a positive finding; ↑, increased level.

urinary obstruction and urine output is adequate. This will dilute the stone components and encourage excretion of excess metabolites. In addition, prescribe morphine (0.1–0.2 mg/kg every 2–4 hours; maximum dose, 2 mg for an infant, 4–8 mg for a child, and 10 mg for an adolescent). Nonsteroidal anti-inflammatory drugs, such as ibuprofen (10 mg/kg every 6 hours; maximum, 800 mg per dose) and ketorolac (0.5 mg/kg per dose every 6 hours, 120-mg/d maximum), may be used if there is no evidence of acute kidney injury or history of chronic kidney disease. If infection is suspected, start empirical antibiotic treatment with ceftriaxone (50 mg/kg/d, divided into doses administered every 12 hours; 4-g/d maximum), and then tailor the antibiotics to the culture results.

Obtain a urology consult for significant hydronephrosis from an obstructing stone, a stone larger than 5 mm, or intractable pain. Among the treatment options are medical expulsion treatment, urinary decompression by stent, percutaneous nephrolithotomy, ureteroscopic stone removal, and extracorporeal shock wave lithotripsy.

Consult with a nephrologist to institute specific treatment of nephrolithiasis once the underlying cause of the stone formation is determined. For example, thiazide diuretics reduce calcium excretion and slow the formation of calcium stones.

Indications for Consultation

- **Metabolism/genetics:** Recurrent stones, abnormal urine metabolic profile (if performed)
- **Nephrology:** Recurrent stones, abnormal urine metabolic profile (if performed)
- **Urology:** Hydronephrosis or other stone-related obstruction, recurrent stones

Disposition

- **Discharge criteria:** Adequate oral intake of both fluids and pain medication with normal urine output

Follow-up

- **Primary care:** 1 to 2 weeks
- **Urology and/or nephrology:** 1 week

Pearls and Pitfalls

- The absence of hematuria does not rule out nephrolithiasis.
- If nephrolithiasis is suspected, obtain anteroposterior abdominal radiography or US as the initial imaging study.

- There may be an iatrogenic cause for nephrolithiasis, such as medications and prolonged immobilization.

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CHAPTER 74

Nephrotic Syndrome

Introduction

Nephrotic syndrome (NS) is a consequence of increased glomerular permeability with resultant heavy proteinuria. This leads to hypoalbuminemia, hyperlipidemia, and hypercoagulability. The decreased plasma oncotic pressure and sodium retention predispose the patient to edema when the fluid overload exceeds 3% to 5% of the patient's body weight. Urinary immunoglobulin losses can increase susceptibility to severe infections (peritonitis, pneumonia, sepsis) caused by encapsulated organisms (eg, *Streptococcus pneumoniae,* group B streptococci).

Nephrotic syndrome can be classified according to etiology as either primary (or idiopathic) or secondary. In 85% to 90% of patients, primary NS is caused by minimal-change nephrotic syndrome (MCNS), occurring in school-aged children. Other primary diseases include focal segmental glomerulosclerosis (FSGS) and membranous nephropathy.

Secondary causes include infections (HIV, hepatitis C, hepatitis B, syphilis, malaria, toxoplasmosis, and varicella zoster; acute COVID-19 disease has been reported in several cases of childhood onset of NS) and drugs (nonsteroidal anti-inflammatory drugs, penicillamine, lithium, heavy metals [mercury, gold], pamidronate, interferon-γ). Other etiologies are lymphoma, leukemia, systemic lupus erythematosus (SLE), immunoglobulin A nephropathy, immunoglobulin A vasculitis (Henoch-Schönlein purpura), postinfectious glomerulonephritis (GN), and membranoproliferative glomerulonephritis (MPGN), also known as complement 3 glomerulopathy.

Genetic NS appears within the first 3 months after birth. It can be suspected if a large placenta is found during prenatal ultrasonography (US). Other causes of congenital NS include syphilis, toxoplasmosis, cytomegalovirus, measles, and HIV.

Clinical Presentation

History

Ask about recent weight gain, along with swelling noted in gravity-dependent sites, such as around the eyes, ankles, feet, and genitalia. The patient may note that clothing, especially articles with elastic (underwear, socks) seem tighter or leave lines in the skin. There may be systemic complaints of fatigue and loss of appetite.

In chronic treatment-resistant NS, renal losses of thyroxin-binding proteins and vitamin D–binding protein predispose the patient to the development of hypothyroidism and vitamin D deficiency, respectively.

Physical Examination

The hallmark of NS is edema, which appears in areas of low tissue resistance, such as the periorbital, pedal, pretibial, scrotal, and labial regions, as well as the abdominal cavity (ascites). The edema is characteristically dependent, so that in the morning it is periorbital and later in the day localizes primarily to the lower extremities. The edema can also evolve into the generalized edema of anasarca.

Intravascular hypovolemia causes tachycardia and signs of peripheral vasoconstriction. Nephrotic syndrome can result in severe hypoalbuminemia, which may lead to pleural effusions and dyspnea, as well as ascites, with resultant abdominal pain, umbilical or inguinal hernias, spontaneous bacterial peritonitis, and shock.

Laboratory Workup

If NS is suspected, perform urinalysis and a spot urine test, ideally of the first morning void, for protein-to-creatinine ratio (normal ratio, < 0.2; non–nephrotic-range proteinuria, 0.2–2.0; nephrotic-range proteinuria, > 2). In a toilet-trained child, a 24-hour urine collection can confirm the diagnosis. Nephrotic-range proteinuria in a child is defined as greater than 50 mg/kg per 24 hours, or greater than 40 mg/m^2/h, or greater than 1 g/m^2 per 24 hours. For an adult, it is greater than 3 g per 24 hours.

Although gross hematuria is rare in NS, microscopic hematuria occurs in up to 20% of patients. Membranoproliferative GN can produce a nephritic-nephrotic picture, with hematuria and increased blood pressure, whereas gross hematuria is most often seen in MPGN or acute GN.

Other laboratory tests to perform include

- **Serum electrolyte levels, including calcium, phosphorus, and magnesium:** Hyponatremia can occur secondary to antidiuretic hormone secretion. Hypoalbuminemia predisposes the patient to apparent hypocalcemia, although the ionized calcium level is normal. However, if urinary losses of 25–OH–vitamin D are prominent, true hypocalcemia can also occur.
- **Blood urea nitrogen (BUN)/creatinine ratio:** Intravascular volume depletion predisposes the patient to prerenal azotemia.
- **Total protein and albumin levels:** Hypoalbuminemia lower than 2.5 g/dL (< 25 g/L) is characteristic, with a low total protein level (< 5 g/dL [< 50 g/L]).

- **Lipid profile:** Hyperlipidemia is typical, with increased total serum cholesterol and triglyceride levels.

Additional laboratory testing, to be performed on an individualized basis, includes

- **Complement levels (C3 and C4):** These are normal in MCNS, whereas a low C3 level is associated with GN (both MPGN and postinfectious). Both C3 and C4 are decreased in lupus nephritis.
- **Viral serologic studies to determine an etiology:** HIV antibody, hepatitis B surface antigen, hepatitis C antibody, SARS-CoV-2 in patients with acute respiratory illness or suspected multisystem inflammatory syndrome in children (MIS-C).
- **Antinuclear antibodies (SLE):** Especially in a patient older than 10 years.

Radiology Examinations

During the initial workup, perform renal US to ensure the presence of bilateral normal kidneys while ruling out congenital malformations, renal masses, and renal vein thrombosis.

Differential Diagnosis

Nephrotic syndrome is the most common cause of edema in childhood and the only diagnosis associated with significant proteinuria (Table 74–1). A patient with MCNS usually has normal blood pressure, renal function, and complement levels (Table 74–2). Box 74–1 summarizes the differential diagnosis of periorbital edema.

Table 74–1. Differential Diagnosis of Nephrotic Syndrome

Diagnosis	Clinical Features
Edema	
Cirrhosis/liver disease	Abnormal liver function test results Signs of portal hypertension
Congestive heart failure	S3 gallop Pulmonary edema and/or hepatomegaly Abnormal echocardiogram findings ↑ N-terminal pro-BNP
Protein-losing enteropathy	Diarrhea Failure to thrive ↑ Stool α1-antitrypsin level
Dark-Colored Urine	
Acute GN	Gross hematuria Hypertension more likely Evidence of recent strep infection ↓ C3 level, normal C4 level

Abbreviations: C3, complement component 3; C4, complement component 4; GN, glomerulonephritis; pro-BNP, pro-hormone of brain natriuretic peptide; ↑ indicates increased level; ↓, decreased level.

Table 74–2. Differential Diagnosis of Primary Etiologies of Nephrotic Syndrome	
Diagnosis	**Clinical Features**
Minimal change nephrotic syndrome	Patient age 2–6 y Microscopic hematuria (20% of cases) Responsive to steroids (> 80% of cases)
Focal segmental glomerulosclerosis	Hematuria (60%–80% of cases) Hypertension (20% of cases) Resistant to steroids (80%–85% of cases)
Membranous nephropathy	Patient age > 18 y Hematuria (60% of cases) Venous thromboembolism
Membranoproliferative glomerulonephritis	Hematuria (80% of cases) Hypertension (35% of cases) ↓ C3 level

Abbreviation: C3, complement component 3.
↓ indicates decreased level.

Box 74–1. Differential Diagnosis of Periorbital Edema	
Infectious	**Noninfectious**
Dacryocystitis (unilateral)	Angioedema (unilateral or bilateral)
Eyelid insect bite (unilateral or bilateral)	Neoplasm (unilateral or bilateral)
Orbital or periorbital cellulitis/abscess (unilateral)	Dacryocystitis (unilateral)
Preseptal cellulitis (unilateral)	Seasonal allergy (bilateral)
	Trauma (unilateral or bilateral)

Treatment

Initial Presentation

Because the most likely cause of NS is MCNS, initially treat all patients with steroids, after performing a purified protein derivative skin test or interferon-γ release assay blood test to rule out tuberculosis. Use prednisone 60 mg/m^2/d (administered once per day or divided into doses delivered twice a day; 60-mg/d maximum). For most patients with MCNS, the proteinuria will clear by the third week of oral prednisone treatment. However, proteinuria may persist for 7 to 10 days after initiation of steroids, so being proteinuria free is not a discharge criterion. Maintain the daily steroids for 6 weeks, after which continue with 40 mg/m^2 per alternate day for 6 weeks (maximum 40 mg), without any additional taper.

Manage edema with dietary sodium restriction (< 2 g/d or 1–2 mEq/kg/d [1 mEq = 23 mg sodium]). If the patient has pulmonary edema, ascites, or severe edema that affects ambulation, administer a single dose of intravenous (IV) furosemide (1 mg/kg), along with fluid and sodium restriction, and monitor

the response. If there is no improvement, administer IV low-sodium 25% albumin (0.5–1.0 g/kg over 4 hours, maximum 50 g) concomitantly with the furosemide. This regimen can be repeated as frequently as every 8 hours if the patient responds. However, be aware that albumin can cause flash pulmonary edema. Avoid diuretic use in a patient with evidence of significant intravascular volume depletion.

Closely monitor the patient's intravascular volume status and obtain daily electrolyte and BUN/creatinine ratios until there is satisfactory diuresis, with clinical improvement of edema. Monitor the patient's weight daily and the urine output per shift to confirm the response to treatment.

If the patient does not have a good clinical response or has persistent edema and proteinuria after 4 weeks of treatment with prednisone, consult a nephrologist to consider initiating other treatments, such as an angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker, or an immunosuppressant agent such as a calcineurin inhibitor (cyclosporine, tacrolimus) or mycophenolate.

A renal biopsy is indicated if there is no response to treatment within 4 to 6 weeks. Other indications may include steroid-responsive NS with more than 2 relapses in a 6-month period or more than 4 relapses in any 12-month period, unresponsiveness to steroids or immunosuppressants, low serum C3 level at the time of initial presentation of the NS (not related to acute poststreptococcal glomerulonephritis), hypertension at presentation (higher likelihood of FSGS), kidney failure with increased BUN/creatinine ratio, hematuria, age younger than 1 year or older than 12 years at presentation, and presence of infection (hepatitis B or C, HIV, or tuberculosis).

Relapses

The baseline risk of relapse within 6 months of initial treatment with steroids is 60% to 75%. Consult a nephrologist and start a steroid regimen as follows: prednisone 60 mg/m^2 (max 60 mg in a single or 2 divided doses) until the urine is protein free for 5 consecutive days, and then administer 40 mg/m^2 (max 40 mg) on alternate days for 4 weeks.

Complications

A patient with NS is at increased risk of infections. Up to 15% of patients with ascites may develop bacterial peritonitis, usually caused by *S pneumoniae* or *Escherichia coli*. Suspect peritonitis if the patient has ascites and fever, abdominal pain, and/or vomiting, although the presentation may be subtle. Note that a patient taking steroids may be afebrile or have just a low-grade fever. Promptly arrange for abdominal paracentesis to obtain fluid for cell count, Gram stain, and culture. Infected fluid usually has more than 250

white blood cells/mm^3 (0.25×10^9/L). Administer IV ceftriaxone (50 mg/kg every day, 4-g/d maximum) or cefotaxime (150 mg/kg/d, divided into doses administered every 8 hours; 8-g/d maximum) for 10 days. Ascites fluid culture findings may be negative in up to 50% of cases of primary peritonitis. Therefore, complete the course of antibiotics if the clinical presentation and ascites fluid cell count are consistent with peritonitis, regardless of a negative culture result.

Another life-threatening complication is thrombosis related to the decrease in proteins C and S and antithrombin III. There can be pulmonary embolism, manifested by chest pain, dyspnea, tachycardia, or central venous thrombosis manifested by headache and irritability. Renal vein thrombosis will cause flank pain, hypertension, and hematuria.

Indications for Consultation

- **Genetics:** Congenital or infantile NS (< 1 year old)
- **Hematology:** Hypercoagulable event
- **Infectious diseases:** Peritonitis
- **Nephrology:** All patients

Disposition

- **Intensive care unit transfer:** Sepsis, acute kidney injury, severe anasarca, acute pulmonary edema, deep venous thrombosis, or pulmonary embolus
- **Discharge criteria:** No anasarca or respiratory distress and family education complete

Follow-up

- **Primary provider:** Outpatient dipstick monitoring of proteinuria once weekly
- **Nephrology:** 2 to 4 weeks

Pearls and Pitfalls

- The patient may not initially present with edema.
- Nephrotic syndrome is a risk factor for a hypercoagulable state, and venous thromboembolism prophylaxis is indicated for a patient with other concomitant risk factors.
- Most cases are caused by steroid-responsive MCNS, whereas most patients refractory to steroids will have FSGS.

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Pyelonephritis

Introduction

Urinary tract infections (UTIs) may involve the lower (cystitis) or the upper tract (pyelonephritis). Distinguishing between the two, particularly in a patient younger than 2 years, can be difficult. Patients at higher risk for pyelonephritis include infants younger than 6 months, females, uncircumcised males, and children with underlying obstructive urologic abnormalities or bladder and bowel dysfunction.

Clinical Presentation

History

An infant or young child may present with fever and nonspecific symptoms, such as poor weight gain, lethargy or irritability, vomiting, diarrhea, or poor feeding. An older child or adolescent will report fever, urinary problems (eg, dysuria, urinary frequency, incontinence, hematuria), or abdominal/back pain.

Ask about factors that may predispose to UTIs, including a history of abnormal urinary tract system, previous UTIs, chronic constipation, sexual activity (in adolescents), prenatal urinary tract dilatation, stool-withholding behaviors, daytime wetting, diseases predisposing the patient to a neurogenic bladder, and a family history of renal anomalies.

Physical Examination

Assess the vital signs, including temperature and blood pressure, and obtain a weight. Pyelonephritis typically causes a high fever (> 39.4 °C [> 103 °F]), whereas an elevated blood pressure and/or poor weight gain can be consistent with chronic kidney disease. Examine the abdomen for tenderness and mass, as bladder or renal enlargement may be noted with an obstructive process. Gently percuss the costovertebral angle for tenderness, suggestive of pyelonephritis. Examine the external genitalia for anatomic anomalies, signs of irritation, and circumcision status (if appropriate).

Laboratory

If a UTI is suspected, obtain a urinalysis (UA) and culture prior to the administration of antibiotics. If the patient is too young to effectively provide a clean catch specimen, obtain the urine culture via straight catheterization or

suprapubic aspiration. Suprapubic aspiration may result in less contamination, but the success rate is lower than with urethral catheterization unless aided by direct visualization of a full bladder at ultrasonography (US). Do not rely on a bag specimen, which is frequently contaminated, for culture, although a negative finding is likely a true-negative finding.

The diagnosis of a UTI requires both evidence of inflammation on UA and growth of a single pathogen from a urine culture. Confirmation of a UTI in a patient 2 to 24 months of age entails a positive culture of a single uropathogen from a catheter-obtained sample (colony count > 50,000 colony-forming units [CFU]/mL), along with pyuria (> 5 white blood cells per high-power field) and/or bacteriuria at UA. Use a minimum of more than 100,000 CFU/mL for a clean-catch specimen in an older child. A positive UA finding for leukocyte esterase or nitrites is about 88% sensitive, but only the finding for nitrites is highly specific for the diagnosis of UTI.

Additional laboratory tests, such as complete blood cell count and inflammatory markers, are not necessary. However, obtain blood urea nitrogen and creatinine levels when there is a suspicion of severe pyelonephritis or chronic kidney disease. Additional testing will generally be necessary for a febrile infant younger than 60 days (see Chapter 62, Fever in Infants Younger Than 60 Days).

Differential Diagnosis

In a patient presenting with fever without a clearly identifiable source, always consider a UTI, especially if there are any of the risk factors mentioned above. When a source is not identified in a febrile infant or young child, evaluate for UTI as the occult source of infection.

Other common causes of dysuria, urgency, frequency, and/or pyuria include dysfunctional voiding, viral cystitis, vaginitis, vaginal foreign body, and urethritis (eg, from bath products), whereas glycosuria can cause polyuria. Sterile pyuria can occur with Kawasaki disease, Behçet syndrome, lupus, Sjögren syndrome, and chemical urethritis.

In a patient presenting with fever and abdominal pain, consider acute gastroenteritis, appendicitis, streptococcal pharyngitis, and pneumonia. Urinary complaints may also be secondary to vulvovaginitis, urethritis, or urolithiasis.

Treatment

Depending on the patient's clinical presentation, predisposing factors, and UA, antibiotics may be started empirically prior to results of the urine culture. The Gram stain of the urine can provide vital information to guide antibiotic selection. *Escherichia coli* is the most common pathogen in UTIs, although

other gram-negative (*Klebsiella, Pseudomonas, Enterococcus*) and gram-positive organisms (*Staphylococcus saprophyticus*) may be an indication for a different antibiotic selection, based on the local resistance pattern.

Patient Younger Than 2 Months

Initially treat intravenously (IV) with the combination of ampicillin (50 mg/kg administered every 6 hours) *and either* gentamicin (full-term neonates 0–7 days old with normal renal function, 2.5 mg/kg administered every 12 hours; > 7 days old, 2.5 mg/kg administered every 8 hours) *or* a third-generation cephalosporin (cefotaxime 50 mg/kg administered every 12 hours if < 7 days old or every 6–8 hours if > 7 days old, *or* IV/intramuscular ceftriaxone 50 mg/kg administered every 12 hours).

Use this combination at least until bacteremia and/or meningitis is excluded, then continue monotherapy tailored to the sensitivity of the organism until the patient is afebrile for 24 hours and the blood culture result (if obtained) is negative. Complete a 10-day course with oral antibiotics.

Patient 2 Months and Older

If the patient fits the criteria for inpatient treatment of pyelonephritis, start with IV antibiotics. Because most *E coli* bacteria are resistant to ampicillin, use ceftriaxone 50 mg/kg every day (2-g/d maximum) or cefotaxime 150 mg/kg/d, divided into doses administered every 8 hours (6-g/d maximum). If the patient is at increased risk for *Pseudomonas* infection (prior history of *Pseudomonas* UTI, chronic indwelling catheter, neurogenic bladder), administer IV ciprofloxacin 18 to 30 mg/kg/d, divided into doses administered every 8 hours (1.2-g/d maximum), or oral ciprofloxacin 20 to 30 mg/kg/d, divided into doses administered every 12 hours (1.5-g/d maximum). If there is a risk factor for *Enterococcus*, such as genitourinary instrumentation or renal anomaly, or if gram-positive rods are noted on the Gram stain, add ampicillin 100 mg/kg/d, divided into doses administered every 6 hours (4-g/d maximum) empirically. If *Staphylococcus aureus* grows from the urine culture, consider hematogenous spread. Confirm a negative blood culture result and perform a thorough physical examination to look for signs of soft-tissue, joint, pulmonary, or cardiac involvement.

Treat sepsis and complicated pyelonephritis, such as with a renal abscess or in a pregnant adolescent, with a 10- to 14-day course of therapy, based on bacterial identification and sensitivities.

Imaging

Screen a patient with a first febrile UTI with renal/bladder US (RUS). Obtain a follow-up voiding cystourethrogram (VCUG) if the RUS finding suggests

high-grade reflux. For a patient who has not undergone any imaging but presents with a second or third febrile UTI, perform RUS and VCUG. Although RUS is not sensitive for low-grade vesicoureteral reflux (VUR), waiting for a second febrile UTI before performing VCUG balances prompt diagnosis of high-grade VUR with avoidance of invasive testing of these infants, most of whom do not have significant VUR. Also order a VCUG if posterior urethral valves are suspected in a male infant (palpable bladder distention, dribbling urine). A technetium-99m dimercaptosuccinic acid scan is indicated only if recommended by a consulting nephrologist or urologist.

Indications for Consultation

- **Nephrology:** Renal insufficiency, recurrent UTIs, voiding dysfunction
- **Urology:** Renal abscess, urinary tract dilation, ureteropelvic obstruction, ureterovesical junction obstruction, neurogenic bladder, grade III–V VUR, posterior urethral valves

Disposition

- **Intensive care unit transfer:** Septic shock, multisystem organ failure, renal failure
- **Discharge criteria:** Adequate oral intake, effective outpatient treatment regimen available (eg, patient is tolerating oral antibiotics or has a peripherally inserted central catheter placed for multi–drug-resistant organisms that require extended IV antibiotics), complications resolved (eg, shock, abscess, acute renal failure), and radiologic workup arranged (if indicated)

Follow-up

- **Primary care:** Within 1 to 2 weeks to assess completion of the antibiotic course and assess the need for prophylaxis or radiologic studies
- **Urology:** 1 to 2 weeks if there is a known genitourinary abnormality
- **Nephrology (if the patient has renal insufficiency):** 1 to 2 weeks

Pearls and Pitfalls

- Treat underlying bladder or bowel dysfunction with scheduled voids and constipation management, respectively.
- A positive blood culture equals bacteremia and is not an indication for changing management unless the patient is septic.
- Test of cure with a repeat urine culture is not necessary if the patient improves with antibiotics.

- Lack of clinical response suggests bacterial resistance or an underlying obstruction, such as a renal abscess or obstructive stone.

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Neurology

CHAPTER 76

Acute Hemiparesis

Introduction

Acute hemiparesis, or unilateral weakness, can be the presenting symptom of many neurologic diseases. The most concerning are pediatric stroke and intracranial hemorrhage (ICH). The diagnosis of stroke is often delayed due to subtleties in presentation, especially in younger children. In addition, "stroke mimics" such as seizure, infection, and migraine are common in children.

Anatomically, hemiparesis typically implicates the contralateral corticospinal tract, which travels from the cortex through the internal capsule to the medulla, where it decussates contralaterally and descends in the lateral spinal cord. It then synapses on the anterior horn cells, which give rise to the peripheral nerves. Because unilateral spinal cord injury is rare, especially acutely, cerebral pathology is the most common cause for acute hemiparesis.

Clinical Presentation

History

Ask about risk factors for stroke, including personal history of thrombophilia, as well as trauma. Inquire about a family history of hypercoagulability, connective tissue disease, or aneurysm. A history of easy bleeding or idiopathic thrombocytopenic purpura may indicate a bleeding disorder and concern for ICH. Acute fever suggests infection, such as meningitis and cerebral or paraspinal abscess, while recent illness or immunization followed by abrupt neurologic symptoms (including hemiparesis) raises the concern for a demyelinating process (see Chapter 80, Demyelinating Disorders), such as acute disseminated encephalomyelitis (ADEM). Gradual progression of weakness over 1 hour in the setting of headache can be consistent with hemiplegic migraine.

Physical Examination

The presence of fever suggests an infectious or inflammatory process. Hypertension is typical for stroke, both ischemic and hemorrhagic, although a normal blood pressure does not exclude stroke.

Carefully examine motor strength in all 4 extremities and attempt to determine if the weakness is central or peripheral. With rare exception, involvement of the corticospinal tract results in weakness in the ipsilateral limbs or the face. Although monoplegia implies a peripheral nervous system insult, an exception is an anterior cerebral artery infarct that causes unilateral leg weakness.

A patient younger than 12 months has immature myelination of the corticospinal tract and may present with subtle signs of weakness, including slight asymmetry in tone or movement. Careful observation at the bedside is typically more revealing than overzealous examination.

Laboratory Workup

Perform a complete blood cell count and complete metabolic panel, including liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels), which may be abnormal with certain viral infections, such as herpes simplex virus (HSV). If an ICH is suspected or confirmed, obtain a prothrombin time/partial thromboplastin time.

For an ischemic and hemorrhagic stroke, evaluate the patient for systemic lupus erythematosus, vasculitis, or sickle cell disease, if the clinical picture is consistent with one of those conditions. While the hematologic studies for ischemic stroke are not standardized, in the absence of a clear vascular or cardiac etiology, obtain levels of homocysteine, antiphospholipid antibodies, protein C and S, lipoprotein (a), and ferritin, as well as activated protein C resistance. If these are unremarkable, arrange for genetic studies, including factor V Leiden. A tiered approach to diagnosis potentially limits unnecessary and expensive studies, and it is reasonable to defer genetic testing to the outpatient setting, except in the unlikely case that the results will change the acute management.

In addition, for an ischemic stroke, obtain an electrocardiogram and a transthoracic echocardiogram.

If an infectious etiology is a possibility, perform a lumbar puncture (LP) either before or after head computed tomography (CT), unless the patient has a platelet count less than 20,000/mcL ($< 20 \times 10^9$/L) or there is concern for increased intracranial pressure (ICP). Do not defer administration of antibiotics if the LP will be delayed or is difficult to perform. If ADEM is suspected, send cerebrospinal fluid (CSF) for cell count, glucose level, protein level, oligoclonal band screen, myelin basic protein level, and immunoglobulin G (IgG) index (requires simultaneous serum IgG testing).

Radiology Examinations

Imaging is the most informative modality when evaluating a patient with acute hemiparesis. Perform an emergent head CT if there is a concern for an ICH. Arteriovenous malformation is by far the most common cause of ICH in children, so discuss further imaging with a neurosurgeon and radiologist. After 3 to 6 hours, an ischemic stroke may be visible on CT, although magnetic resonance (MR) imaging can identify an ischemic stroke within minutes of symptom onset and is therefore the preferred modality. Magnetic resonance

imaging is also more sensitive for encephalitis, brain dysplasia, and tumor. However, if MR imaging is not available, CT angiography (CTA) is a rapid way to evaluate the patient for thrombosis or dissection.

Contrast-enhanced MR angiography (MRA) of the head can identify a vasculopathy, the most common cause of pediatric acute ischemic stroke. Magnetic resonance angiography of the neck with fat-suppressed imaging can identify arterial dissections, particularly in the setting of trauma.

Differential Diagnosis

The initial priority in a child with acute hemiparesis is the diagnosis of acute ischemic stroke or ICH (Table 76–1). Evaluation of acute ischemic stroke includes looking for cardiac, vascular, infectious, immune-mediated, or hematologic causes.

Seizures are a common neurologic disease in children. Rarely, seizures may be followed by a period of temporary postictal paralysis known as Todd paralysis (see Chapter 82, Seizures).

A cerebral abscess is typically caused by contiguous spread of infection, such as bacteremia, sinusitis, mastoiditis, or a dental abscess. The patient will have new focal weakness, seizures, or altered mental status, with or without fever. Meningitis, either bacterial or viral, and encephalitis can also result in hemiparesis.

Acute disseminated encephalomyelitis is a multifocal, monophasic, demyelinating illness that develops over hours to days. It is typically postinfectious or parainfectious, with viral infections being most common. The patient presents with acute-onset multifocal neurologic disease that may consist of altered mental status, visual loss, ataxia, limb weakness, and seizures. Perform an LP. Typical CSF findings are pleocytosis (>6 white blood cells/mm^3 [$>0.006 \times 10^9$/L]) and increased protein (>25 mg/dL [>0.25 g/L]).

Hemiplegic migraine is a diagnosis of exclusion, after alternative diagnoses such as stroke and seizure have been ruled out. The typical history involves the gradual spread of neurologic symptoms over 20 to 30 minutes, followed by headache. The development of symptoms, visual loss, numbness, and weakness correlates with the progression of cortical depression.

Because many falls in children are secondary to neurologic weakness, do not assume that decreased use of a limb is simply due to pain from trauma.

Treatment

Stroke and Increased Intracranial Pressure

Obtain a nonenhanced head CT emergently. Transfer the patient to the intensive care unit (ICU) and then (if necessary) to a center with immediately available pediatric neurosurgery, as well as diagnostic imaging (MR imaging)

Table 76–1. Differential Diagnosis of Acute Hemiparesis

Diagnosis	Clinical Features	Radiologic Studies
Acute disseminated encephalomyelitis	Abrupt onset of weakness Encephalopathy associated with a febrile illness	MR imaging with and without contrast Demyelination on T2-weighted MR imaging
Acute ischemic stroke	Abrupt lateralizing limb weakness Sensory and/or language impairment Cranial neuropathies	Head CT (nonenhanced acutely) Brain MR imaging Head/neck MRA vs CTA
Brain tumor (complicated by intracranial hemorrhage or seizure)	Prior subtle signs of weakness and headache followed by acute worsening of symptoms	MR imaging with and without contrast
Cerebral abscess	Fever Headache Penetrating trauma Contiguous infection	MR imaging with and without contrast
Complex (hemiplegic) migraine	May have a personal/family history of migraines Gradual spread of neurologic symptoms over 20–30 min, followed by headache	Nonenhanced MR imaging MRA
Encephalitis (especially HSV)	Lateralizing weakness Fever, confusion May have seizures	CT acutely MR imaging with and without contrast
Hypoglycemia	Focal weakness History of diabetes	MR imaging for persistent encephalopathy or limb weakness
Intracerebral hemorrhage	Headache, hypertension, vomiting Altered mental status, seizures Limb weakness	Head CT (nonenhanced acutely) Brain MR imaging Head/neck MRA or CTA
Meningitis (bacterial or viral, including West Nile Virus)	Fever, headache, vomiting Neck/back pain, meningismus	Consider brain or spine MR imaging
Mitochondrial myopathy, encephalopathy, lactic acidosis	Unexplained lateralizing weakness Headache and/or confusion Can appear with seizures	Brain MR imaging (signal intensity changes do not follow a vascular distribution)
Seizure/Todd paralysis	Acute history of paroxysmal movements Weakness or somnolence	MR imaging

Abbreviations: CT, computed tomography; CTA, CT angiography; EEG, electroencephalogram; HSV, herpes simplex virus; MR, magnetic resonance; MRA, MR angiography.

and capability for monitoring ICP. Consult with a neurologist to determine whether to administer intravenous (IV) tissue plasminogen activator (tPA), which has limited use in children because of the frequency of stroke mimics. To maintain an adequate cerebral perfusion pressure for a patient with an acute ischemic stroke, permissive hypertension to 1.5 times the normal value for age is the general rule. In centers without pediatric neurology or neurosurgery, the adult neurology stroke service may be helpful in evaluation and treatment decision-making.

Obtain urgent neurosurgical and neurology consultations if the patient has an ICH (see Chapter 79, Cerebrospinal Fluid Shunt Complications). If the patient is alert, defer intubation so as to avoid sedation and its subsequent effects on the neurologic examination. Provide aggressive blood pressure control in the case of an intracerebral hemorrhage. Urgently treat thrombocytopenia or a coagulopathy with the administration of platelets or fresh frozen plasma, respectively. Monitor the patient closely for signs of deterioration, such as a change in mental status (becoming more difficult to arouse), anisocoria, or worsening limb weakness. An acute alteration in the neurologic examination warrants repeat head CT. If the patient had been receiving chronic anticoagulation therapy, consult with a hematologist to initiate reversal.

If ischemic stroke is either suspected or confirmed and hemorrhage has been excluded, administer aspirin, 5 mg/kg (maximum dose, 325 mg) by mouth. Give the patient nothing else by mouth and administer normal saline fluids, at a maintenance rate, until the patient is evaluated by a speech-language pathologist. Control any fever with acetaminophen (15 mg/kg; maximum, 1,000 mg per dose) and/or cooling blankets, but avoid nonsteroidal anti-inflammatory drugs. Monitor the blood glucose level and maintain it at less than 200 mg/dL (< 11.1 mmol/L). Neurosurgical involvement is not usually necessary in the early management of ischemic stroke. However, given that cerebral edema can worsen in the first 3 to 5 days, alert neurosurgery early in the course in case decompressive craniotomy becomes necessary.

The evaluation for an acute ischemic stroke includes looking for cardiac, vascular, infectious, immune-mediated, or hematologic causes. Perform a thrombophilia evaluation, electrocardiogram, and transthoracic echocardiogram and consult a rheumatologist. Perform an LP to evaluate the patient for immune-mediated vasculitis or viral infections such as varicella, which are treatable causes of viral vasculopathy and strokes in children.

Seizures

The evaluation and treatment of seizures is detailed in Chapter 82, Seizures.

Meningitis

If there is suspicion for bacterial meningitis, treat empirically with IV ceftriaxone and vancomycin at meningitic dosing for 14 to 21 days (see Chapter 66, Sepsis). Note that viral causes of meningitis, particularly West Nile Virus, may cause hemiparesis.

Encephalitis

If there is any concern for HSV encephalitis, initiate acyclovir immediately (10 mg/kg administered in doses every 8 hours for 14–21 days). Note that

while the sensitivity of HSV CSF polymerase chain reaction (PCR) is high, it is not 100%, so a patient with herpes encephalitis can have a negative PCR finding. Therefore, rely on both clinical suspicion and the HSV PCR results to determine whether to initiate and continue acyclovir. Also, the PCR result can remain positive for days after treatment has begun, so an LP performed after the initiation of acyclovir is still useful. The response to acyclovir is not immediate; therefore, a patient who is back to baseline mental status within less than 24 hours of the initiation of treatment is unlikely to have HSV encephalitis. Another treatable form of viral encephalitis is varicella zoster virus (VZV) encephalitis, particularly if there is prior history of a painful or dermatomal rash. Perform VZV PCR and VZV IgG assessment of the CSF.

Cerebral Abscess

Obtain an infectious disease consult and treat empirically with IV antibiotics for 6 to 8 weeks. The choice of antibiotic therapy is based on the presumed source of infection (oral flora, hematogenous spread, postneurosurgical procedure), but in some cases a brain biopsy is necessary for identification of the pathogens. In the setting of significant mass effect, manage increased ICP and consult a neurosurgeon. A focal neurologic examination and concern for increased ICP are contraindications to LP.

Hemiplegic Migraine

See Chapter 81, Headache, but do not use sumatriptan, which causes vasoconstriction and might worsen the hemiplegic migraine.

Acute Disseminated Encephalomyelitis

The first line treatment for all central nervous system inflammatory demyelinating conditions is a high-dose steroid pulse. Give IV methylprednisolone 30 mg/kg/d (maximum 1,000 mg/d) for 5 days, followed by an oral prednisone (start at 1–2 mg/kg/d) taper over 4 to 6 weeks for a patient with residual symptoms. Consult with a neurologist to determine whether additional treatments such as IV immunoglobulin (2 g/kg, administered either as a single dose or over the course of 3–5 days) or plasmapheresis are indicated.

Indications for Consultation

- **Hematology:** Patient with stroke who requires thrombophilia evaluation and/or is receiving anticoagulation therapy
- **Infectious diseases:** Patient with encephalitis, cerebral abscess
- **Neurology:** Acute hemiparesis
- **Neurosurgery:** Hemorrhagic stroke, brain tumor, cerebral abscess
- **Oncology:** Brain tumor

- **Rheumatology:** Acute ischemic stroke not caused by cardiac embolus or dissection

Disposition

- **ICU transfer:** Acute stroke, airway concern, status epilepticus
- **Discharge criteria:** Stable, nonevolving condition; action plan in place for recurrent events (eg, seizures, migraines); adequate plan for administration and monitoring of therapy and rehabilitation (if needed)

Follow-up

- **Primary care:** 3 to 5 days
- **Neurology:** 1 to 2 weeks

Pearls and Pitfalls

- If the patient has a history of recent trauma, consider embolic stroke caused by arterial dissection.
- New hypertension in the setting of hemiparesis is suggestive of stroke.
- Todd paralysis after a seizure implies a focal seizure and is often associated with a structural lesion, such as remote stroke, cortical dysplasia, or a brain tumor.
- Perform CT early if a stroke is suspected to identify a patient for whom tPA is a potential option (within 4.5 hours of symptom onset).
- An institutional stroke protocol will help facilitate timely imaging and treatment.
- In the presence of intracerebral hemorrhage, load with levetiracetam 30 to 40 mg/kg IV and consult neurosurgery urgently.
- For questions about thrombolysis therapy, consult 800-NO-CLOTS, a pediatric thromboembolic hotline staffed by Toronto Sick Kids.

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Acute Weakness

Introduction

Acute muscle weakness is the decreased ability to move muscles with or against resistance. It usually results from pathology anywhere in the neuromuscular system and may occur abruptly or evolve over the course of hours to days. Acute weakness can be life-threatening if it advances to include the respiratory muscles or is secondary to an intracranial process.

One of the most common causes of acute weakness in children is acute inflammatory demyelinating polyneuropathy, also known as Guillain-Barré syndrome (GBS). Acute COVID-19 disease has been linked to some cases of GBS.

Other common etiologies of acute weakness include viral myositis, intracranial tumor, seizure, medication side effect, toxin exposure, and conversion disorder. In addition, diseases that cause chronic weakness may develop acutely and must be considered in the differential diagnosis.

Clinical Presentation

History

Determine the timing and severity of the weakness and the presence of associated symptoms, including fever, rash, headache, double vision, altered mental status, changes in sensation, and bowel and bladder dysfunction. Other pertinent points include a history of trauma or travel, seizure, preceding infection, possible medication or toxin exposure, and family history of childhood weakness.

Physical Examination

The first priorities are circulation, airway, and breathing. After the patient has been stabilized, perform a thorough neuromuscular examination attempting to localize the affected portion of the neuromuscular system. Grade the muscle strength (grade 5, normal; grade 4, active movement against gravity and resistance; grade 3, active movement against gravity; grade 2, active movement with gravity eliminated; grade 1, flicker or trace of contraction; or grade 0, no contraction), and note the distribution of weakness. Assess mental status, pupillary response to light, cranial nerves, sensation, and reflexes.

Upper motor neuron lesions are caused by pathology of the cerebral cortex and spinal cord. These lesions typically present with acute onset of weakness that may be unilateral or bilateral. Other symptoms include increased muscle

tone, hyperreflexia, and encephalopathy. In the early phase, the patient may have hypotonia prior to the later development of spasticity. Mental status changes can be indicative of an intracranial process, while focal tenderness along the back is suggestive of a spinal cord lesion, focal inflammation, or infection.

Lower motor neuron lesions include disorders of the anterior horn cell, neuromuscular junction, muscle, and peripheral nerve. Symptoms depend on site of lesion and may include absent or diminished reflexes, hypotonia, muscle atrophy, and fasciculations. Primary disorders of the muscle typically present with a subacute or indolent course of muscle weakness, associated with muscle pain, swelling, or tenderness. Muscle atrophy may be a late finding. Evaluate the skin to look for the heliotrope rash of dermatomyositis, attached ticks, or signs of trauma.

Laboratory Workup

Obtain a complete blood cell count, C-reactive protein level, and/or erythrocyte sedimentation rate if there is concern for an infectious or inflammatory disease. Check a comprehensive metabolic panel, including calcium, magnesium, and phosphate levels. If there is proximal muscle weakness (myopathy) with muscle tenderness and/or a history of dark, tea-colored urine, obtain a creatinine kinase (CK) level (myositis) and perform a urinalysis (dipstick and microscopic analysis). Urine that is positive for blood on a dipstick but negative for red blood cells on microscopy is consistent with myoglobinuria and a diagnosis of rhabdomyolysis.

Perform a lumbar puncture if encephalitis, GBS, or multiple sclerosis (MS) is suspected. Obtain noncontrast computed tomography (CT) of the head if there is a concern for intracranial hypertension. Send the cerebrospinal fluid (CSF) for cell count and differential, total protein and glucose levels, bacterial cultures, viral polymerase chain reactions, and, if indicated, an autoimmune encephalitis panel and/or oligoclonal band evaluation (if MS is a concern). Order an electroencephalogram if seizure is suggested by the history or physical examination findings. An electromyogram nerve conduction may be required for diagnostic and prognostic evaluation of neuromuscular disorders and peripheral neuropathies (GBS).

Radiology Examinations

Emergent CT of the head is indicated for abrupt onset of weakness with deterioration of mental status, focal neurologic deficits, or preceding trauma, to look for acute intracranial hemorrhage or mass. In a clinically stable patient with a concern for an intracranial process, perform magnetic resonance (MR)

imaging of the brain to better assess the diagnostic detail of an intracranial lesion. If spinal cord pathology is suspected, perform MR imaging of the spine to evaluate the patient for trauma, infection, transverse myelitis, acute flaccid myelitis (AFM), or tumor.

Differential Diagnosis

Upper Motor Neuron Disorders

Pathology in the cerebral cortex presents with acute onset of (typically unilateral) weakness, headache, vomiting, seizure, and/or mental status changes. Persistence of these neurologic deficits is an indication for urgent evaluation to rule out an evolving process, such as stroke, intracranial abscess, tumor, and epidural hematoma. In some cases, spinal cord injury, spinal epidural hematoma, and other causes of spinal cord compression (tumor) may predominantly affect the upper motor neurons. The symptoms associated with this mixed injury may include unilateral or bilateral weakness, altered sensation below the level of the lesion, and bowel and/or bladder dysfunction. Focal back pain at the level of the lesion may also be present, and reflexes below the level of the lesion may be absent or diminished.

Lower Motor Neuron Disorders

Disorders of the anterior horn cell present with weakness, normal or decreased reflexes, and fasciculations, with later progression to muscle atrophy. The term *acute flaccid paralysis* has been used to describe this condition, with poliomyelitis being the classic disorder. In recent years, outbreaks have been seen of AFM, linked with enterovirus D68. This presents like other diseases of the anterior horn cells, with rapid onset focal limb weakness that may be asymmetric. Cases are most common in late summer or early fall and follow a biennial pattern. Typically, there is a viral illness about 1 week before the onset of the paralysis. Magnetic resonance imaging of the spine will show corresponding gray matter lesions at the level of the clinical deficit.

Similarly, diseases of the peripheral nerves cause diminished reflexes (bilateral or unilateral) and weakness, but paresthesia and/or dysesthesia may also be present. The classic presentation of GBS occurs 2 to 4 weeks after a benign febrile respiratory or gastrointestinal illness. Symptoms start with paresthesia of the distal extremities, followed by ascending symmetric paralysis (glove and stocking). A teenager may present with cranial neuropathies, including bulbar weakness, ophthalmoplegia, and facial paralysis (Miller Fisher variant). In addition, the cardiovascular system may be affected in the Miller Fisher variant, in which dysautonomia may be prominent. Neuropathic

pain and paresthesia range from absent to pronounced. There can also be associated autonomic dysfunction with changes in blood pressure, cardiac arrhythmias, and bowel and/or bladder dysfunction. In up to 20% of patients, paralysis will ascend to include the respiratory muscles, necessitating patient observation in a unit capable of assisting ventilation.

Bulbar dysfunction is consistent with peripheral nerve weakness and can include absent or diminished gag reflex, dysarthria, or dysphagia. This can be seen in conditions including GBS, botulism, myasthenia gravis, and AFM, among others.

Disorders of the neuromuscular junction cause generalized weakness and hypotonia. These include botulism, tick paralysis, myasthenia gravis, and organophosphate toxicity.

Primary Muscle Disorders

Disorders of the muscle, including myositis and rhabdomyolysis, are often associated with a slower onset of weakness, myalgias, and an increased CK level. Also consider a congenital myopathy, although they are rare.

Other Conditions

Suspect a conversion disorder when the acute weakness and physical examination findings are not consistent with an organic lesion. The neuroanatomic constellation of symptoms will be inconsistent and the remainder of the medical workup negative. A history of minor trauma or psychosocial stressors is common.

The differential diagnosis of acute weakness is summarized in Table 77–1.

Treatment

Pediatric neurology consultation is necessary for further evaluation and treatment of acute weakness. Localization of the lesion and narrowing of the differential diagnosis will guide further testing. Nerve conduction velocities, electromyography, and (rarely) muscle biopsy may be needed to assign the final diagnosis of conditions such as GBS, MS, myasthenia gravis, peripheral neuropathy, or muscular dystrophy, among others.

In some cases of acute weakness, immediate treatment is necessary, even if the diagnosis is not confirmed. Intravenous (IV) immune globulin (0.4 mg/kg/d for 5 days) is the first-line therapy for GBS and has been shown to improve recovery time. Plasma exchange is an alternative for refractory or recurrent symptoms.

Treat transverse myelitis, acute disseminated encephalomyelitis, and other demyelinating diseases with high-dose IV pulse methylprednisolone

Table 77–1. Differential Diagnosis of Acute Weakness	
Diagnosis	**Clinical Features**
Disorders of the Cerebral Cortex	
Acute disseminated encephalomyelitis	Acute encephalopathy, irritability, confusion Neurologic deficits with early deterioration, seizures, fever, headache, vomiting Possible meningismus
Acute intracranial hemorrhage Cerebrovascular accident	Abrupt onset Altered mental status, focal neurologic deficits Headache, nausea, vomiting, seizures
Encephalitis	Altered mental status, lethargy, personality change Fever, headache, nausea, vomiting Global weakness, focal neurologic deficits
Hemiplegic migraine Alternating hemiplegia of childhood	Unilateral weakness associated with headache Additional migraine aura (eg, visual, auditory) Personal or family history of migraines
Multiple sclerosis	Presents with encephalopathy (children $<$ 12) or sensory symptoms (children $\geq$ 12) Mono- or polyfocal motor, sensory, or visual deficits Frequent relapses after remission Oligoclonal bands present in CSF
Todd paralysis	Focal weakness after a seizure Rapid recovery of symptoms ($<$ 24 h) is typical
Transient ischemic attack	Unilateral weakness Duration $<$ 24 h
Tumor	Headache, abnormal gait, ataxia, behavior changes Nausea and vomiting (especially in the morning) Hyperreflexia, papilledema, seizures, upper motor weakness
Disorders of the Spinal Cord	
Anatomic abnormalities: atlantoaxial instability, Chiari malformation, tethered cord	Global motor and sensory deficits, gait abnormalities Progressive worsening of symptoms Bowel and/or bladder dysfunction
Discitis Epidural abscess	Fever, irritability, refusal to bear weight Focal back pain and associated weakness
Transverse myelitis	Rapid onset of motor, sensory and/or autonomic dysfunction; flaccidity followed by spasticity Bowel and/or bladder dysfunction Neck or back pain Often preceded by an illness (prior 5–28 d)
Traumatic injury: epidural hematoma, vertebral body compression fracture, dislocation, transection	Pain, weakness, paresthesia, bowel and bladder dysfunction Onset of symptoms following trauma
Tumor	Focal back pain, weakness, gait abnormality Loss of sensation, paresthesia, bowel and/or bladder dysfunction Scoliosis, spinal deformity

Continued

Table 77–1. Differential Diagnosis of Acute Weakness, continued

Diagnosis	Clinical Features
Disorders of the Anterior Horn Cell	
Paralytic poliovirus	Preceding fever, malaise, sore throat, diarrhea Focal flaccid paralysis (one or more muscle groups) Extremely rare in the United States
Acute flaccid myelitis	Preceding fever or respiratory symptoms Rapid-onset flaccid weakness; often asymmetric Summer and fall predominance Nonpolio enterovirus association
Spinal muscle atrophy	Progressive muscle weakness/atrophy Areflexia, tongue fasciculations Motor delay, cognition unaffected
Disorders of the Peripheral Nerves	
Acute inflammatory demyelinating polyradiculopathy (Guillain-Barré Syndrome)	Ascending weakness (usually symmetric) Diminished or absent reflexes, paresthesia Bowel and/or bladder dysfunction ↑ CSF protein with normal or mildly ↑ cell count
Acute intermittent porphyria	Abdominal pain, paresthesia, tachycardia Weakness progresses proximally to distally Red or brown urine
Toxins: heavy metals	History of exposure Weakness (often distal), paresthesia, altered reflexes
Disorders of the Neuromuscular Junction	
Botulism	*Patient < 6–12 months of age* Ingestion of spores in honey, dust, or soil Afebrile, poor feeding, constipation, lethargy, developmental regression *Patient > 6–12 months of age* Ingestion of foodborne toxin Afebrile, cranial nerve dysfunction, dysphagia, descending paralysis, normal sensorium
Myasthenia gravis	Ptosis, diplopia, extraocular muscle weakness Global, slowly progressive weakness; worsens with activity
Organophosphate toxicity	Salivation, lacrimation, urination, diarrhea, emesis Miosis, bradycardia, bronchospasm Bulbar, respiratory, and proximal muscle weakness
Tick paralysis	Ascending weakness, fatigue, paresthesia Areflexia, unsteady gait Tick found attached (often on the scalp)
Primary Muscle Disorders	
Inflammatory myopathies: dermatomyositis, polymyositis	Fever, fatigue, heliotrope rash (in dermatomyositis) Proximal symmetric muscle weakness ↑ CK level

Table 77–1. Differential Diagnosis of Acute Weakness, continued	
Diagnosis	**Clinical Features**
Congenital myopathies Metabolic myopathies Mitochondrial disease Muscular dystrophies	Slowly progressive weakness Muscle tenderness and wasting Patient may have hypertrophy in advanced stages ↑ CK level
Myotonic dystrophies Periodic paralysis	Episodic weakness, myotonia, painful or painless muscle stiffness Common triggers are cold, stress, or exercise
Pyomyositis	Fever, malaise Pain, cramping, weakness localized to affected muscles
Rhabdomyolysis	Myalgia, weakness, dark urine Urine + for hemoglobin/myoglobin without red blood cells Markedly ↑ CK level
Viral myositis	Preceding viral illness (commonly influenza B) Myalgia, muscle tenderness, dark urine, ↑ CK
Other Conditions	
Conversion disorder	Inconsistent neurologic examination findings (−) Medical workup findings (+) History of minor injury and/or emotional stress

Abbreviations: CK, creatinine kinase; CSF, cerebrospinal fluid.
+ indicates positive finding; − negative finding; ↑, increased.

(0.5–1 mg/kg/d; 1,000-mg/d maximum, for 3–5 days). Intravenous immune globulin and plasma exchange are second-line therapies in the setting of incomplete improvement or recurrence. Tick paralysis improves with tick removal alone.

Confirm the diagnosis of myasthenia gravis with fatigability testing or a Tensilon test prior to treating with cholinesterase inhibitors. Again, steroids, immune modulators, or IV treatments may be considered for refractory cases. Treat botulism with botulism immune globulin.

Urgent neurosurgical consultation is required when there is a concern for intracranial or spinal mass, infection, or hemorrhage. These lesions may require surgical decompression or evacuation early in the treatment course. In addition, consult pediatric oncology if a tumor is the source of weakness.

Respiratory compromise with progression to respiratory failure is a risk for many patients with acute weakness, especially in GBS where symptoms will progress for up to 4 weeks. Other patients at risk are those with intracranial processes, bulbar dysfunction, and other conditions that can involve the diaphragm or respiratory musculature. Closely follow the respiratory status by trending the oxygen saturation, respiratory effort, forced vital capacity, and negative inspiratory forces (NIF). A satisfactory NIF is greater than 30 cm H_2O with an oxygen saturation greater than 90%. Blood gas analysis can further aid in determination of respiratory function and the need for transfer to a unit

with capability to manage respiratory support equipment, including continuous positive airway pressure, bilevel positive airway pressure, or intubation with mechanical ventilation.

Intracranial or spinal abscess requires broad antibiotic coverage in addition to urgent neurosurgical evaluation. If meningitis or encephalitis is suspected, start empirical antivirals and/or antibiotics until cultures and viral study results are available to guide definitive treatment. Consult an infectious diseases specialist to guide testing, treatment, and reporting of these infectious etiologies.

Bowel and bladder dysfunction are frequently associated with acute weakness. Early in the hospitalization, institute a bowel regimen of daily stool softeners along with suppositories as needed. Monitor pre- and postvoid bladder volumes to evaluate for urinary retention. If the volumes are consistently greater than those predicted for age (normal bladder volume in oz = [patient's age in years] + 2), or postvoid volumes are elevated, consult urology to initiate an intermittent catheterization program, every 4 to 6 hours as needed.

Weakness limits mobility in many patients, therefore placing them at risk for deep vein thrombosis. See Chapter 46, Deep Venous Thrombosis, for the initiation of prophylaxis, if indicated.

Consult with rehabilitation services, including physical, occupational, and speech therapy, as soon as the patient is stable. Their input may also be necessary for discharge planning. In addition, diagnoses resulting in weakness can cause prolonged hospitalization and lead to lifelong mobility alterations. Involve psychology services as early in the course as feasible. If a conversion disorder is suspected, limit the medical workup, but psychological evaluation and treatment are essential for diagnosis and ongoing care.

Indications for Consultation

- **Neurology:** Acute weakness
- **Neurosurgery:** Tumor, abscess, or hemorrhage of the brain or spinal cord
- **Infectious diseases:** AFM, encephalitis, or spinal abscess
- **Physical medicine and rehabilitation with physical, occupational, and/or speech and swallow therapy:** Significant functional impairment

Disposition

- **Discharge criteria:** Dependent on the primary process, improvement or stabilization of weakness, with an adequate plan in place to meet functional needs
- **Intensive care unit transfer:** Rapid progression of weakness, respiratory compromise, worsening bulbar muscle weakness, or signs of increased intracranial pressure

Follow-up

- **Primary care:** 1 week
- **Neurology:** 2 to 4 weeks

Pearls and Pitfalls

- A thorough history and physical examination are essential to determining the location of the pathologic lesion.
- Prompt diagnosis of the etiology of weakness is critical, because treatments are specific and tailored to individual disease states.
- Perform emergent imaging if a spinal process (MR) or intracranial space occupying lesion (CT or MR) is suspected.
- Respiratory failure is an acute, life-threatening complication of many acute weakness states.

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CHAPTER 78

Altered Mental Status

Introduction

Altered mental status (AMS) is a derangement in consciousness and is defined as impaired arousal and awareness of one's self and environment. Alteration of level of consciousness begins with becoming unaware of self, followed by reduced awareness of the environment, and finally an inability to be aroused. Awareness is determined by the cerebral hemispheres, whereas arousal is controlled by the ascending reticular activating system (ARAS). Although derangements in either one or both systems may alter mental status, there is a spectrum of decreasing states of consciousness, ranging from confusion (loss of clear thinking) to coma (no response to pain and the eyes remain closed), with many intermediate levels of consciousness existing between these two.

The etiology of AMS can be either focal (mass, hemorrhage) or diffuse/systemic (infection, ingestion, intoxication, inborn error of metabolism, diabetic ketoacidosis [DKA]). Structural causes are associated with focal neurologic deficits due to the proximity of the ARAS to brainstem reflex pathways, whereas medical etiologies lead to global cerebral dysfunction and generally do not cause focal neurologic deficits.

Although there are numerous possible etiologies for AMS, a rapid thorough assessment of the patient's history and a physical examination are crucial for determining the appropriate initial interventions targeting the underlying cause. Persistent AMS is more worrisome than transient AMS (ie, seizure or syncope), as the former is associated with increased morbidity and mortality. An age-based approach is helpful for identifying the most common diagnoses.

Clinical Presentation

History

Ask about the onset of the change in consciousness (acute versus subacute), including the specific events and actions directly preceding the change in mental status. Also inquire about a history of recent illnesses, behavioral changes, and specific associated symptoms (eg, diplopia, dizziness, headache, seizure-like activity, weakness).

For an infant, determine whether there are symptoms suggestive of an inborn error of metabolism, such as poor feeding, lethargy, failure to thrive, and seizures. In an older child, a careful review of the patient's medical history

may yield clues, such as diabetes (DKA) and kidney (uremia) or liver disease (encephalopathy). Inquire about contact with sick persons, recent travel, immunization status, and any potential immunodeficiency. Key information to collect for both suspected accidental ingestion in toddlers and intentional overdose in adolescents includes a current medication list and the availability of medications in the home or environment. Also inquire about any recent history of trauma, particularly head trauma.

Altered mental status due to a thrombotic or ischemic stroke may occur in patients with sickle cell anemia or congenital heart disease. A patient with a seizure disorder can be postictal or have nonconvulsive status epilepticus (subclinical seizures) and present with AMS. Malfunction of a ventriculoperitoneal shunt (VPS) can present with acute headache and/or vomiting, whereas a patient with a brain tumor may complain of headaches and vomiting over weeks to months. Such tumors can cause mass effect leading to focal neurologic deficits (such as eye deviation, pupillary changes, and motor weakness) or hydrocephalus with increased intracranial pressure (ICP).

Physical Examination

Immediately assess the vital signs and circulation, airway, and breathing, and evaluate the patient for signs of trauma (ecchymoses, hematomas). Priorities on a focused physical examination include features that can help differentiate between focal and diffuse/systemic etiologies. Perform a thorough neurologic examination evaluating the pupillary response, fundi, cranial nerves, reflexes, upper and lower motor neuron functions, sensory responses, coordination, and gait. Specific findings associated with structural lesions include abnormal pupillary light reflexes (either asymmetrical or dilated pupils), abnormalities in extraocular movements, asymmetry of motor response, and decorticate or decerebrate posturing.

As a result of the relatively fixed volume within the skull, insults causing a mass effect can increase ICP, which is characterized by irritability, headache, vomiting, and sometimes a unilaterally dilated pupil suggesting uncal herniation. In addition, downward eye deviation ("setting sun"), papilledema, and cranial nerve palsies (particularly III, IV, and VI) may be seen. Cushing triad (hypertension, bradycardia, and irregular respirations) is a late sign of increased ICP and signifies impending herniation.

If the neurologic examination is nonfocal and structural lesions are not suspected, a more thorough physical examination may suggest the underlying medical etiology. Classic signs of infection include fever, nuchal rigidity, lymphadenopathy, impaired straight leg raising, and rash. For metabolic derangements, the focused physical examination varies with the specific organ system that is responsible. Liver disease may manifest with

hepatomegaly, ascites, and jaundice. Diabetic ketoacidosis may manifest with signs of dehydration, Kussmaul breathing, and fruity breath odor.

A patient with an ingestion or intoxication can present with varied symptoms and altered vital signs; thus, knowledge of common toxidromes (see Chapter 68, Toxic Exposures, Table 68–4) is essential for identification, intervention, and treatment.

Laboratory Workup

Initial laboratory tests to obtain include an immediate bedside serum glucose determination, complete blood cell count, serum electrolytes and calcium, liver function studies, and coagulation profile. Obtain a venous blood gas if the patient is breathing abnormally and/or a toxic ingestion is suspected. Send an ammonia level if the patient has known or possible liver disease or an inborn error of metabolism is suspected (hypoglycemia, failure to thrive, neurodevelopmental delay). If an intracranial infection is suspected in a patient with signs of elevated ICP, treat with appropriate antibiotics (see Chapter 66, Sepsis), and defer the lumbar puncture (LP) until the patient is clinically stable and preprocedure imaging obtained. Culture additional sites as indicated. Obtain serum and urine toxicology to guide management in a suspected ingestion or intoxication. A stool guaiac may be positive in cases of intussusception.

Radiology Examinations

If the patient is comatose, order head computed tomography (CT), without contrast, to immediately rule out a central nervous system bleed, mass lesion, or hydrocephalus. Also obtain a CT if there are signs or symptoms of elevated ICP, particularly if the patient requires an LP. Magnetic resonance (MR) imaging provides more structural detail than CT without exposing the child to ionizing radiation, although it may take more time to arrange and perform this test. Obtain MR imaging when the initial workup fails to identify the underlying diagnosis. Nevertheless, if indicated, do not delay antibiotic treatment while waiting for imaging.

Differential Diagnosis

Although there are many causes of AMS (Table 78–1), a focused history, physical examination, laboratory tests, and imaging will help narrow the differential diagnosis. Structural causes of AMS are often associated with focal neurologic findings, such as abnormal pupils, impaired extraocular movements, focal weakness, asymmetrical reflexes, and posturing. Medical etiologies cause global cerebral dysfunction and generally do not produce

Table 78–1. Differential Diagnosis of Altered Mental Status

Diagnosis	Clinical Features
Acute demyelinating encephalomyelitis	Recent infection or vaccination Fever, headache, vomiting Weakness, vision loss, discoordination
Autoimmune encephalitis	Viral prodrome Behavioral changes, sleep disturbances Seizures, abnormal movements
Brain tumor/increased ICP	Headache, vomiting, ataxia, gait disturbances Cushing triad: bradycardia, hypertension, Cheyne-Stokes breathing Asymmetric or dilated pupils, cranial nerve VI palsy
Central nervous system infection	Fever, photophobia, headache, vomiting Nuchal rigidity
Concussion/head trauma	(+) History Confusion, headache, memory loss Scalp/skull hematoma or ecchymoses
Confusional migraine	History of migraines Headache, confusion, aphasia
Diabetic ketoacidosis	Abdominal pain, vomiting, polyuria Fruity breath odor Kussmaul breathing Hyperglycemia and ketonuria
Hemorrhagic stroke	Headache, vomiting Signs of increased ICP Focal neurologic deficits
Hypertension	Headache
Hypoglycemia	Dizziness, tremor, diaphoresis ↓ Glucose
Hypotension	Dizziness Poor perfusion
Inborn errors of metabolism	Lethargy, poor feeding Seizures Hypoglycemia
Ingestion/intoxication	Confusion, slurred speech, hallucinations Hyperthermia, respiratory depression Seizures
Intussusception	Episodic abdominal pain, currant jelly stools
Ischemic stroke	Headache, vomiting, focal neurologic deficits Signs of increased ICP
Liver failure	Jaundice Easy bleeding Ascites
MIS-C	Fever, gastrointestinal symptoms Confusion, headache, irritability, lethargy History of suspected or documented SARS-CoV-2 infection

Table 78–1. Differential Diagnosis of Altered Mental Status, continued

Diagnosis	Clinical Features
Nonaccidental trauma	Story inconsistent with injuries History of prior fractures Fracture in nonmobile infant Retinal hemorrhages
Psychiatric conditions	Catatonia (can maintain posture) Echolalia Resists eye opening
Seizure	Shaking, twitching, eye rolling Incontinence
Sepsis	Fever, poor perfusion, widened pulse pressure Source of infection
Subarachnoid hemorrhage	Headache, photophobia, irritability Meningismus
Uremia	Anorexia, lethargy, fatigue
Venous thrombosis	Headache, seizures Signs of increased ICP
VPS malfunction	History of hydrocephalus and shunt Headache, vomiting Signs of increased ICP

Abbreviations: ICP, intracranial pressure; MIS-C, multisystem inflammatory syndrome in children; VPS, ventriculoperitoneal shunt.
+ indicates positive finding; ↓, decreased level.

focal neurologic deficits. In addition, a gradual change in mental status is more suggestive of a medical etiology, whereas an abrupt onset may indicate a structural lesion or seizure.

Altered mental status accompanied by fever, photophobia, headache, and vomiting suggests an infectious etiology, such as brain abscess, encephalitis, or meningitis. Acute onset of behavioral changes, seizures, and sleep disturbances is suspicious for autoimmune encephalitis, which has recently been recognized as a more prevalent cause of encephalitis. Consider multisystem inflammatory syndrome in children (MIS-C) in a patient with AMS and either recent infection with, or exposure to, SARS-CoV-2 (see Chapter 65, Multisystem Inflammatory Syndrome in Children [MIS-C]).

Intoxications and ingestions may present with similar symptoms, such as temperature derangements and vomiting. Maintain a high level of clinical suspicion, as often there is no reported history of ingestion. In addition to exogenous toxins, numerous metabolic derangements can result in AMS, including electrolyte imbalance, hypoxia, thyroid and adrenal disease, acid-base disturbance, and extremes of temperature.

Consider nonconvulsive status epilepticus, in which there are electrographic seizures without motor movements, in a patient who remains with AMS for more than 60 to 90 minutes after a seizure.

Any mechanism of injury that is inconsistent with the clinical findings or is unlikely, given the patient's developmental capability, raises the concern for nonaccidental trauma (see Chapter 69, Child Abuse: Physical Abuse and Neglect).

Intussusception (see Chapter 106, Acute Abdomen) is an unusual cause of AMS in a young infant who may also present with vomiting and guaiac-positive stools.

Treatment

Initial management of AMS involves addressing the circulation, airway, and breathing and restoring and ensuring stable respiratory and hemodynamic status. Continuously monitor the vital signs and provide oxygen by facemask or nonrebreather mask until normal oxygenation is documented. A patient with a Glasgow Coma Scale score below 8 may require intubation. Secure large-bore intravenous (IV) access for the administration of medications and isotonic fluids. Correct hypoglycemia (< 40 mg/dL [< 2.2 mmol/L]) with 5 mL/kg of D_{10} (0.5 mg/kg). Administer a 20 mL/kg bolus of isotonic fluid (0.9% sodium chloride or lactated Ringer solution) for hypotension, poor perfusion, or signs of dehydration. Monitor the clinical response and repeat as necessary. Identify and treat abnormalities in temperature, blood pressure, and electrolytes.

In a case of known or suspected trauma, stabilization of the C-spine is essential until a fracture can be ruled out. Assess the patient for other signs of injury and obtain imaging as indicated. If a head injury is suspected, obtain an emergent head CT and consult neurosurgery for any intracranial hemorrhage, as surgical intervention may be necessary.

Electively intubate a patient with increased ICP to protect the airway and allow hyperventilation to a $Paco_2$ of 35 to 40 mm Hg. Elevate the head of the bed to 45 degrees with the head maintained midline. Give mannitol (0.5–1 g/kg) or hypertonic (3%) saline (3–5 mL/kg) for treatment of suspected cerebral edema, and consult with a neurosurgeon.

Treat acute demyelinating encephalomyelitis with high-dose glucocorticoids. A typical course is 5 days of IV methylprednisolone (30 mg/kg/d, maximum 1,000 mg), followed by a 4- to 6-week oral prednisone taper.

There are specific antidotes for some ingestions or intoxications (see Chapter 68, Toxic Exposures, Table 68–5). Treat a suspected opiate intoxication with IV naloxone (0.1 mg/kg IV, 2 g maximum) and repeat every 2 to 3 minutes as needed. Note that the opiate antagonist has a shorter half-life

than the opiate, so multiple doses or a continuous infusion of naloxone may be required.

The management of seizures (see Chapter 82, Seizures) is discussed elsewhere.

Indications for Consultation

- **Neurology:** New-onset or focal seizures, focal neurologic deficits
- **Neurosurgery:** Head trauma, increased ICP, VPS malfunction, brain tumor, intracranial hemorrhage
- **Poison control:** Ingestion or overdose
- **Psychiatry:** Psychosis, conversion reaction
- **Surgery:** Intussusception

Disposition

- **Intensive care unit transfer:** AMS, unstable airway, intracranial bleed.
- **Discharge criteria:** The patient's mental status is at or near baseline, and the underlying cause has been addressed.
- **Subacute rehabilitation:** Once the mental status change plateaus or begins to improve.

Follow-up

- **Primary care:** 1 week
- **Neurology:** 1 week

Pearls and Pitfalls

- Lethargy may be the only presenting symptom in a child with intussusception.
- Consider child abuse in an infant with AMS, regardless of the presence or absence of bruising.
- Kernig and Brudzinski signs may be absent in a comatose patient with meningitis.
- Structural lesions such as hydrocephalus or bilateral subdural hematomas may cause a nonfocal examination.
- Acute onset of psychosis usually has an organic etiology, even with a history of psychiatric illness.

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CHAPTER 79

Cerebrospinal Fluid Shunt Complications

Introduction

The word *hydrocephalus* originates from the Greek for "water on the brain." Cerebrospinal fluid (CSF) is produced primarily in the choroid plexus in each pair of lateral ventricles and circulates through the third and then fourth ventricles to the arachnoid granulations, then to the dural sinus, and into the venous drainage system for reabsorption. Under typical conditions, daily production of CSF approximately equals absorption.

The most common mechanism of hydrocephalus is obstruction to CSF circulation (classified as noncommunicating hydrocephalus) with dilatation of the ventricular system proximal to the obstruction. Etiologies of hydrocephalus that result in obstruction include myelomeningocele, brain tumors, and intraventricular hemorrhage secondary to prematurity. Impaired absorption of CSF (classified as communicating hydrocephalus), secondary to meningitis, causes dilation of the entire ventricular system.

Once hydrocephalus is determined to be chronic, consult with a neurosurgeon to discuss CSF shunt placement or endoscopic third ventriculostomy. Cerebrospinal fluid shunts are named for the positions of the proximal and distal catheters. Proximal catheters are in the lateral, third, or fourth ventricles or in an intracranial cyst and exit the skull via a burr hole. Distal catheters are tunneled under the skin to their final location, which can be in the peritoneal space, right atrium, and pleural space, among others. Most commonly, ventriculoperitoneal shunts are placed.

Between the proximal and distal catheters is a one-way valve system that allows drainage of CSF at a predetermined pressure differential. Some valves have adjustable pressure settings, and these must be reset after any magnetic resonance (MR) imaging. All CSF shunts include an inline reservoir, which is located proximal to the valve and exterior to the skull to allow CSF withdrawal or medication infusion if necessary. Rarely, antisiphon devices are spliced inline to prevent overdrainage.

The most common acute complications of CSF shunts are shunt malfunctions and shunt infections. Cerebrospinal fluid shunt malfunction is most frequent and occurs in 40% of new or revised shunts within 2 years of placement, secondary to debris, fibrosis, choroid plexus, or parenchymal occlusion of the proximal catheter. Delayed malfunctions (> 2 years after

insertion) are frequently caused by obstruction, a break in the catheter, migration of the distal catheter, and, rarely, kinking or knotting. A CSF shunt infection is the second most frequent complication, most of which occur within 6 months of shunt surgery. The most common pathogens include *Staphylococcus epidermidis*, *Staphylococcus aureus*, and gram-negative bacilli.

A rare complication is slit-ventricle syndrome (small ventricles on brain images, with poor ventricular compliance). If CSF shunt malfunction then develops, the patient's intracranial pressure (ICP) can increase quickly and without radiologic evidence of ventricular expansion, making the diagnosis difficult.

Less acute complications of CSF shunts include an abdominal pseudocyst, which is a loculated fluid mass within the peritoneum around the catheter tip. It can appear with signs of shunt malfunction at presentation, along with decreased appetite, abdominal pain, tenderness, distention, mass, guarding, inguinal hernia, and intractable hiccups.

Cerebrospinal fluid overdrainage can also occur, generally within 1 month after either shunt insertion or revision. Symptoms include positional headaches and vomiting, which is worse when upright and improved when recumbent.

Clinical Presentation

History

With a CSF shunt malfunction, the symptoms are highly variable and age dependent. An infant usually presents with irritability, poor feeding, and lethargy, whereas an older child or adolescent will complain of persistent headache, nausea, vomiting, and blurred vision. In addition, the parent may suspect a malfunction because the symptoms are comparable to previous episodes. The presentation of a CSF shunt infection is similar to a shunt malfunction, with or without infectious symptoms, such as fever, wound erythema or exudate, abdominal pain, and peritonitis in the context of a recent revision (within 6 months).

Physical Examination

A patient with a CSF shunt malfunction may have altered mental status, irritability, nonerythematous swelling around the shunt tract, a bulging or full fontanel, increased head circumference, cranial nerve VI palsy, papilledema, and ataxia. Rarely, a patient will present with signs of severe increased ICP, including the sunset eye sign, hypertension, bradycardia, and irregular respirations. If the shunt is infected, there may be nonspecific signs of a shunt malfunction, fever, or cellulitis, signs of a wound infection around the shunt tract, or signs of peritonitis.

Laboratory Workup and Radiology Examinations

Shunt Malfunction

If a patient presents with signs and symptoms consistent with shunt malfunction, immediately obtain a shunt series and preferably perform fast MR imaging or low-dose computed tomography (CT) of the brain. A shunt series includes plain radiographs of the skull, neck, chest, and abdomen and will demonstrate disconnections, kinks, and migration of catheters. Proximal and distal catheters are radiopaque, whereas reservoirs and connectors can be radiolucent; therefore, the images must be reviewed carefully. Computed tomography or MR images of the brain will show the location of the proximal catheter tip and size of the ventricles. Comparison to a prior study is critical, but if these images are unavailable, evidence of transependymal flow and sulcal effacement are suggestive of malfunction. Order limited abdominal ultrasonography (US) if an abdominal CSF pseudocyst is suspected.

Cranial US is useful for a patient with an open anterior fontanelle.

Shunt Infection

If a patient presents with signs or symptoms of a shunt infection, immediately order a shunt series and fast MR imaging of the brain (or head CT or cranial US) to rule out coincident malfunction. Also obtain a complete blood cell count, blood and urine cultures, and/or viral studies, as indicated, to rule out other infectious etiologies. If these workup findings are negative and the patient is within 6 months of a previous shunt surgery or if a shunt infection is highly suspected, consult with a neurosurgeon to arrange a shunt tap or, in rare circumstances, a lumbar puncture. Send the CSF for Gram stain, culture, cell count, and assessment of glucose and protein levels, and measure the opening pressure, if possible.

Differential Diagnosis

The differential diagnosis of shunt complications is summarized in Table 79–1.

Treatment

Management of External Ventricular Drain

The external ventricular drain (EVD) has several components, including a sampling/access port, antireflux collection chamber, drainage bag, and pressure scale. It is the responsibility of the neurosurgeon to give instructions on the level at which the drain is to be set. The level of the ventricles must be estimated to create a zero-reference point; it is approximated at the midpoint of an

Table 79–1. Differential Diagnosis of Cerebrospinal Fluid Shunt Complications

Diagnosis	Clinical Features
CSF shunt infection	Shunt operation within the past 6 mo Purulent wound Erythema along the shunt tract
CSF shunt malfunction	Symptoms similar to those of previous malfunction Headache and vomiting without diarrhea Disconnection on the shunt series Increase in ventricle size on CT/MR images
Gastroenteritis	Contact with sick persons May have diarrhea
Meningitis	Meningismus, fever, decreased level of consciousness No change in ventricle size on CT/MR images
Urinary tract infection	No shunt operation within the past 6 mo Dysuria (+) Urinalysis
Viral syndrome	Contact with sick persons May have rhinorrhea, cough, conjunctivitis, pharyngitis

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; MR, magnetic resonance.
+ indicates positive finding.

imaginary line between the outer aspect of the child's eye and the external auditory meatus. The difference in height between the child's ventricles and the drip chamber creates both a pressure gradient and a safety valve. The height of the drip chamber equates to the pressure inside of the head or ICP. This pressure must be reached before any CSF will drain into the drip chamber.

When there are concerns about the EVD, ensure that the pressure scale on the intravenous (IV) pole is positioned with 0 cm being at the estimated zero point. Check that the pressure level arrow at the top of the drip chamber is at the prescribed height above or below the zero point/the ventricles and secure with the locking screw. When moving or repositioning the child, be sure to clamp, rezero, and unclamp the drain immediately.

Symptoms of underdrainage of CSF include those of increased ICP such as bulging of fontanelle in infants, headaches, vomiting, irritability, and lethargy. Symptoms of overdrainage of CSF include dipping of fontanelle in infants, headaches, irritability, pallor, and tachycardia.

Shunt Malfunction

For the rare patient who presents with signs of severe increased ICP, start emergent treatment, including elevating the bed to 30 degrees, intubating and hyperventilating to a P_{CO_2} level of 28 to 33 mm Hg, moderate hypothermia, and administering a bolus of either IV mannitol (0.5–1.0 g/kg) or 3% saline (5 mg/kg). If the patient is moribund, consult with a neurosurgeon to arrange

an emergency shunt tap or ventricular tap through the burr hole or open fontanelle, prior to urgent definitive shunt revision. For most other patients who are ambulatory and have headaches and vomiting over several days, urgent neurosurgery consultation is indicated to plan a shunt revision within 24 hours.

Shunt Infection

Urgent neurosurgery consultation is necessary. Surgical approaches to hardware removal vary, but most neurosurgeons will completely remove the shunt and place an EVD. However, with small ventricles or in a medically complex patient, the neurosurgeon may choose to externalize the distal end of the existing shunt, at the level of the clavicle or abdomen. Treat with IV vancomycin (20 mg/kg administered every 8 hours, 1-g maximum) and IV ceftriaxone (50 mg/kg administered every 12 hours, 2-g maximum). Tailor the antibiotic coverage once the culture and sensitivity results are available. Generally, the course of antibiotics is 7 to 21 days, with 14 days being typical, followed by shunt reinsertion.

Indications for Consultation

- **Infectious diseases:** CSF shunt infection
- **Neurosurgery:** Any suspicion for a CSF shunt malfunction or infection; emergent surgical management of increased ICP

Disposition

- **Intensive care unit transfer:** Severely increased ICP, meningitis, and/or sepsis; depending on the institution, externalized shunts and EVDs
- **Pediatric center with neurosurgical services:** Shunt complication is highly suspected and services are not available locally; preferably, transfer to the pediatric neurosurgical center actively following up the patient
- **Discharge criteria:** No further symptoms/signs of the acute complication and recovery from surgical treatment of the hydrocephalus (eg, repaired CSF shunt after malfunction, reinternalized CSF shunt after infection)

Follow-up

- **Primary care:** 1 to 2 weeks
- **Neurosurgery:** 2 to 4 weeks

Pearls and Pitfalls

- In general, CSF shunt malfunctions present in a consistent fashion for a given patient. Ask the family how the patient's shunt failure usually appears.

- In a symptomatic patient, an increase in ventricle size on brain images is the most specific finding for shunt malfunction.
- A shunt infection is unlikely if the patient has not undergone shunt surgery within the past 6 months and/or is presenting with diarrhea. Neurosurgery services will therefore be reluctant to tap the shunt in these circumstances.
- Tapping a shunt should only be done by someone familiar with the procedure.

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CHAPTER 80

Demyelinating Disorders

Introduction

Demyelinating disorders are characterized by the disruption of the myelin sheath that surrounds the nerve axons of the central and peripheral nervous system. The resulting interruption of nerve transmission produces a wide range of neurologic symptoms, depending on the specific location affected. Common symptoms include weakness, paresthesias, ataxia, vision loss or visual disturbance, and bowel and bladder dysfunction.

Demyelinating disorders may arise from infectious, postinfectious, metabolic, and hereditary etiologies. Acquired demyelinating diseases typically develop acutely over days to weeks while hereditary disorders have a chronic onset.

Multiple sclerosis (MS) is the most common pediatric demyelinating disorder. Other inflammatory demyelinating conditions include optic neuritis, transverse myelitis, neuromyelitis optica spectrum disorders (NMOSDs), acute disseminated encephalomyelitis (ADEM), and Guillain-Barré syndrome (GBS).

Some demyelinating conditions resolve completely with treatment and are unlikely to recur. Others, including MS and NMOSD, are characterized by recurrent or progressive disease with an accumulation of persistent neurologic deficits over time. Fulminant presentations can be life-threatening in cases of severe autonomic dysfunction or acute respiratory failure due to weakness of the respiratory muscles.

Clinical Presentation

History

Determine the location, duration, and progression of any weakness or paresthesias (numbness, tingling, or burning). Ask about difficulty speaking, eating, or walking; clumsiness; headache; nausea; vomiting; intractable hiccups; urinary retention; and constipation. Inquire about vision changes, including vision loss, blurred or double vision, and change in color perception. A patient with optic neuritis may have vision changes plus pain with eye movement. A patient with transverse myelitis may have back pain, although severe, unremitting back pain that wakes a patient at night is also concerning for a spinal cord tumor. Reports of confusion, agitation, or lethargy are consistent with encephalopathy, a hallmark of ADEM.

Review the past medical history, including any recent infections or vaccinations, potential for immunosuppression, and any previous episodes of neurologic symptoms. Confirm that the patient has no recent trauma. Ask about fever, which can occur in ADEM. Elicit any history of rash, joint disease, or joint swelling.

Assess the family history for any neurologic diseases, especially in a patient with a chronic onset and slow progression of symptoms, developmental delay, or history of learning difficulties or behavior problems.

Physical Examination

First, note the patient's vital signs and assess their airway, breathing, and circulation. Perform a full neurologic examination, assessing mental status, visual acuity, visual fields, cranial nerves, motor strength, sensation, reflexes, coordination, and gait. Measure the maximum inspiratory pressure, when available, if there is concern for weakness involving the respiratory muscles.

Decreased visual acuity and a relative afferent pupillary defect are consistent with optic neuritis. Symmetric lower extremity weakness suggests transverse myelitis or GBS. These can be distinguished by the presence of a sensory level or bladder/bowel involvement in the case of transverse myelitis, and diminished or absent lower extremity reflexes and/or autonomic signs and symptoms in the case of GBS. Note that lower extremity weakness plus spasticity is more likely due to a spinal cord tumor or other cause of cord compression than demyelination. Some hereditary sensory motor demyelinating disorders are associated with various features, such as muscle atrophy and foot deformities (pes cavus, hammertoes) in Charcot-Marie-Tooth disease.

Laboratory Workup

If a demyelinating disorder is suspected, obtain a complete blood count and differential, complete metabolic panel, C-reactive protein level, and an erythrocyte sedimentation rate. Perform a lumbar puncture and send cerebrospinal fluid (CSF) for any suspected acute demyelinating disorder. Send CSF for cell count, differential, protein, glucose, Gram stain, culture, oligoclonal bands, and immunoglobulin G index. Oligoclonal bands are rare in patients with NMOSD but present in more than 90% of patients with MS. Albuminocytologic dissociation (elevated protein in the absence of pleocytosis) is a classic finding in GBS after the first week of illness.

If a patient is found to have central demyelinating lesions on imaging, send myelin oligodendrocyte glycoprotein antibodies, as well as aquaporin-4 antibodies (AQP4-Ab), which are highly suggestive of NMOSD.

There is a significant overlap in the symptomatology of ADEM and infectious meningitis or encephalitis. Send blood and CSF cultures, as well as CSF polymerase chain reaction (PCR) testing for herpes simplex virus, varicella zoster virus, enterovirus, mycoplasma, Epstein-Barr virus, cytomegalovirus, and rubella. Obtain further infectious workup in a case of transverse myelitis, as idiopathic transverse myelitis and direct infectious myelitis can be difficult to distinguish based on clinical presentation and CSF findings alone. In addition to the aforementioned studies, obtain a respiratory viral panel and send CSF viral culture and PCR for parvovirus; human herpesvirus 6 and 7; influenza; hepatitis A, B, and C; human T-lymphotropic virus; *Bartonella; Borrelia;* and tuberculosis.

Radiology Examinations

Neuroimaging is the mainstay of the diagnostic workup for demyelinating disorders, as well as the primary means of monitoring treatment response. If central nervous system (CNS) involvement is suspected, obtain magnetic resonance (MR) imaging, with and without contrast, of the brain and orbits. If clinically indicated by the presence of lower extremity weakness, spasticity, back pain, or bowel and bladder dysfunction, include the cervical, thoracic, and lumbar spine. A patient with clinical signs of only optic neuritis or transverse myelitis may prove to have asymptomatic brain lesions, helping to make the diagnosis of MS or NMOSD. Order emergent computed tomography of the head if at any point the patient has an acute change in mental status.

In a patient with suspected GBS, MR imaging of the lumbar spine may show enhancement of the spinal nerve roots and cauda equina, though this is not a specific finding. Although the diagnosis is usually determined clinically, electromyography (EMG) is the most sensitive and specific test for GBS. In a patient with chronic onset of lower extremity weakness, the nerve conduction studies portion of EMG can help distinguish chronic inflammatory demyelinating polyneuropathy (CIDP) from a hereditary peripheral sensory motor neuropathy.

Differential Diagnosis

Inflammatory

Always consider a demyelinating disorder for any patient presenting with a neurologic deficit but particularly in a case where the deficits are multifocal, sudden or subacute in onset, or waxing and waning.

Multiple sclerosis is the most common pediatric demyelinating disease, typically with onset in adolescence and following a relapsing-remitting course.

Symptoms can include vision loss, diplopia, weakness, paresthesias, ataxia, or urinary symptoms. A key diagnostic feature of MS is the dissemination in space and time of demyelinating CNS lesions, although the very first episode is often monofocal, making it difficult to distinguish a first attack of MS from ADEM or other inflammatory demyelinating disorders.

Optic neuritis and transverse myelitis can both present idiopathically or in conjunction with a multifocal inflammatory demyelinating disorder like MS, NMOSD, or ADEM. In optic neuritis, inflammation of the optic nerve leads to decreased visual acuity, abnormal color vision, visual field deficits, and sometimes pain with eye movement. In transverse myelitis, inflammation of the spinal cord causes acute or subacute onset of bilateral symmetric or asymmetric sensory or motor deficits with a defined sensory level. Symptoms include bowel and bladder dysfunction and sometimes back pain. Most patients who are treated for optic neuritis or transverse myelitis in isolation (ie, those patients without evidence of additional demyelinating CNS lesions) will not have a recurrence.

Neuromyelitis optica spectrum disorder is now recognized as a separate clinical entity from MS, though it is often only distinguishable from MS by the presence of AQP4-Ab. Optic neuritis associated with NMOSD is often bilateral at presentation or rapidly progresses from unilateral to bilateral. Transverse myelitis in NMOSD is likely to have complete, rather than partial, spinal cord involvement at the affected level and is more likely to be longitudinally extensive. Brainstem involvement can lead to area postrema syndrome, with intractable nausea, vomiting, or hiccups that last more than 48 hours, or to acute neurogenic respiratory failure. Complications include posterior reversible encephalopathy syndrome and fulminant cerebral demyelination with edema and risk of herniation.

Acute disseminated encephalomyelitis is typically monophasic, with acute multifocal neurologic deficits including encephalopathy. It usually occurs within 3 weeks of a viral infection, although it also has been associated with vaccinations and drug exposures. A patient younger than 10 years with CNS demyelination is much more likely to have ADEM than MS. Common symptoms include weakness, ataxia, headache, fever, meningismus, and altered mental status. The patient may also have dysarthria, cranial nerve palsies, seizures, and neurogenic respiratory failure. Acute hemorrhagic leukoencephalitis, thought to be a hyperacute variant of ADEM, is rare and usually fatal, progressing to coma and death over 2 to 3 days.

Myelin oligodendrocyte glycoprotein antibodies have been identified in a variety of demyelinating diseases, including ADEM and NMOSD. Their full

clinical significance, including diagnostic and prognostic value, is unclear, but they seem to predict a non-MS outcome.

The classical presentation of GBS is a symmetrical ascending paralysis with diminished or absent reflexes and hypotonia. Symptoms peak over 2 to 4 weeks and, in severe cases, can include neurogenic respiratory failure and autonomic dysfunction with cardiac dysrhythmias and hypotension. A triad of acute ophthalmoplegia, areflexia, and ataxia with or without distal weakness is seen in the Miller Fisher variant of GBS. A preceding infection can often be identified.

Viral

Progressive multifocal leukoencephalopathy (PML) presents with subacute onset of neurologic deficits and multifocal white matter lesions on MR imaging of the brain. It is caused by reactivation of the John Cunningham virus in a patient with impaired cell-mediated immunity.

Metabolic

Osmotic demyelination syndrome (previously *central pontine myelinolysis*) is caused by the overly rapid correction of hyponatremia. The patient will have an acute onset of confusion, bulbar symptoms, weakness, movement disorders, seizures, and lethargy, potentially progressing to coma.

Hereditary

Chronic onset and family history of neurologic symptoms suggest a hereditary demyelinating disorder. Leukodystrophies are caused by genetic defects in the synthesis or maintenance of the myelin sheath and include adrenoleukodystrophy, metachromatic leukodystrophy, and Krabbe disease. Charcot-Marie-Tooth disease is the most common of the hereditary motor-sensory neuropathies and is caused by a genetic mutation that impairs myelin function.

Treatment

Closely monitor patients' hemodynamic and respiratory status and bulbar function, and note any acute change in mental status. Transfer a patient with developing neurogenic respiratory failure or severe autonomic dysfunction to an intensive care unit (ICU).

Consult a neurologist to discuss treatment decisions for a patient with a demyelinating disorder. The first-line treatment for all CNS inflammatory demyelinating conditions is a high-dose steroid pulse. Give intravenous (IV) methylprednisolone 30 mg/kg/d (maximum 1,000 mg/d) for 5 days, followed

by an oral prednisone (start at 1–2 mg/kg/d) taper over 4 to 6 weeks for a patient with residual symptoms. Intravenous immunoglobulin (IVIG) is also the first-line treatment for CIDP.

Second-line therapy for ADEM is IVIG at a dose of 2 g/kg divided over 2 to 5 days. Although IVIG is sometimes used for optic neuritis, transverse myelitis, and NMOSD, there is no strong evidence supporting its use.

Arrange for plasma exchange (PLEX) in cases of fulminant or steroid-refractory MS, NMOSD, ADEM, and transverse myelitis. It is sometimes used in cases of optic neuritis, but evidence of benefit is limited. A complete treatment course is 5 to 7 rounds administered every other day. Long-term immunomodulatory therapy is beneficial for patients with MS and NMOSD to prevent future attacks.

There is no role for steroids in the treatment of GBS. Standard treatment is IVIG (as above) or PLEX if the presentation is severe with progressive weakness, bulbar weakness, inability to walk, or worsening respiratory status.

In a case of PML, remission can be achieved if normal immune function is restored, for example, by the treatment of AIDS or the withdrawal of immunosuppressive medications.

The symptoms of osmotic demyelination syndrome are frequently irreversible. Treatment is mostly supportive, but there is increasing evidence that relowering the plasma sodium, even after symptoms develop, is beneficial.

Treatment for hereditary demyelinating disorders is supportive. The patient may benefit from physical and occupational therapy and genetic counseling.

Indications for Consultation

- **Neurology:** Suspected demyelinating disorder
- **Palliative care:** Poor prognosis with expected continued progression of neurologic disease and functional impairment
- **Physical, occupational, and/or speech therapy:** Significant functional impairment
- **Physical medicine and rehabilitation:** Significant functional impairment

Disposition

- **ICU transfer:** Severe autonomic dysfunction (bradycardia, dysrhythmia, hypotension, severe hypertension), acute neurogenic respiratory failure, rapidly progressive weakness, bulbar palsy, flaccid quadriparesis, acute change in mental status
- **Discharge criteria:** Hemodynamic stability, neurologic symptoms are improved or no longer progressing, all necessary inpatient treatment has been completed, and the patient's functional needs can be met in the home setting

- **Subacute rehabilitation:** Patients with significant persistent neurologic deficits who will benefit from aggressive inpatient physical, occupational, and/or speech therapy

Follow-up

- **Neurology:** 1 to 2 weeks
- **Physical, occupational, and/or speech therapy:** Frequency depends on severity of patient's functional impairment

Pearls and Pitfalls

- The symptoms of acute demyelinating disorders overlap with those of emergent conditions such as ischemic stroke, intracranial hemorrhage, encephalitis, and spinal cord compression. Obtain neuroimaging urgently, if not done prior to admission.
- Severe presentations of demyelinating conditions can be life-threatening. Monitor closely for the development of autonomic dysfunction and neurogenic respiratory failure.
- A high-dose steroid pulse is the first-line treatment for all CNS inflammatory demyelinating conditions, but not GBS.

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CHAPTER 81

Headache

Introduction

Headache is a common reason for children to seek medical care, although the evaluation and management rarely require hospitalization. Admission is indicated when a headache is associated with altered mental status/level of consciousness, seizures, or an abnormal neurologic examination finding. Examples include severe migraine or migraine variants, headaches secondary to intracranial infection (encephalitis, meningitis), and increased intracranial pressure (ICP) secondary to mass effect, trauma, hemorrhage, or thrombosis.

Clinical Presentation

History

Obtain a thorough history, including the onset of the headache (including any aura) and its intensity, frequency, location/focality, and associated symptoms, such as fever, nausea, vomiting, visual changes, photophobia, seizures, and neck stiffness. Headaches that are worse in the morning and improve as the day progresses, or are aggravated by coughing or straining, could be due to increased ICP. Inquire about medication use, possible toxin exposure, and significant medical problems (ventriculoperitoneal shunt, immunodeficiency or immunosuppression, coagulopathy). A positive family history of migraine headaches is helpful in narrowing the differential. Obtain a menstrual history because of the possible association of menses with migraines. Finally, perform a thorough psychosocial assessment, including a substance use history.

Physical Examination

Priorities in the physical examination include vital signs (hypertension alone or as part of Cushing triad [hypertension, bradycardia, and irregular respiration]), growth parameters, pupillary response and extraocular movements, and neurocutaneous findings, such as hamartomas, neurofibromas, café au lait macules, or hemangiomas. Perform a funduscopic examination to look for the absence of venous pulsations and blurring of the disk margins and a comprehensive neurologic examination to look for signs of increased ICP, focal neurologic findings, and nuchal rigidity. If none of these signs is present, the likelihood of a secondary headache related to significant central nervous system (CNS) pathology is quite low.

Laboratory Workup and Radiology Examinations

If the clinical presentation is suspicious for a primary CNS condition, obtain a complete blood cell count, erythrocyte sedimentation rate, and/or C-reactive protein level to screen for an infectious or inflammatory process. If meningitis is a concern, obtain a blood culture and perform a lumbar puncture (LP) to obtain cerebrospinal fluid for Gram stain and culture, cell count, and protein and glucose levels. Always measure the opening pressure when an LP is performed during the evaluation of a headache. In general, if signs of increased ICP are absent, head computed tomography (CT) is not necessary prior to the LP. If an obstructive process causing increased ICP is suspected, delay the LP, regardless of the CT results. However, an LP can be both diagnostic and therapeutic of idiopathic intracranial hypertension (pseudotumor cerebri).

If a focal neurologic deficit exists, neuroimaging is usually indicated to rule out secondary intracranial causes of headache. Because there is no consensus over the routine use of CT and/or magnetic resonance (MR) imaging for headache, undertake a careful analysis of the benefits and probable yield prior to exposing the patient to the risks associated with each (radiation, contrast material, sedation, anesthesia). Computed tomography is indicated if acute bleeding or thrombosis is suspected, but perform MR imaging if there is concern about an intracranial mass, parenchymal lesion, or inflammatory condition. Magnetic resonance venography may be helpful if there is concern for idiopathic intracranial hypertension or venous sinus thrombosis.

Differential Diagnosis

The priority is to rule out an intracranial mass lesion, hemorrhage, thrombosis, and meningitis/encephalitis (Table 81–1).

A positive family history of headache in a first- or second-degree relative is suggestive of a primary headache, whereas recurrent, chronic, severe, progressive, or unconventional headaches are more likely with a secondary etiology. Headaches that raise a concern for primary CNS pathology include those that wake a child from sleep, are worse in the morning or improve over the course of the day, or are worse when recumbent or with a Valsalva maneuver. Sudden onset of severe headache (the so-called thunderclap headache) demands urgent evaluation to rule out subarachnoid hemorrhage or venous sinus thrombosis.

Treatment

Treat a migraine with triptans (serotonin receptor agonists), such as sumatriptan (5 mg intranasally, 25 mg orally, or 0.1 mg/kg per dose intradermally) and repeat in 2 hours, if necessary. A migraine cocktail, consisting of a

Table 81–1. Differential Diagnosis of Headaches

Diagnosis	Clinical Features
Central nervous system infection (meningitis)	Fever, altered mental status Nuchal rigidity, photophobia (+) Kernig and/or Brudzinski signs Patient may have petechiae and/or purpura
Idiopathic intracranial hypertension (pseudotumor cerebri)	Patient overweight/obese Visual disturbances Papilledema
Inflammatory conditions	Fever, malaise, myalgia, fatigue, weight loss Rash/skin changes Arthralgia/arthritis
Intracranial mass	Headache awakens the patient at night, is worse in the morning Abnormal neurologic examination finding Signs of ↑ intracranial pressure (Cushing triad)
Migraine headaches	(+) Family history Multiple previous episodes Nausea and/or vomiting Phonophobia, photophobia Possible pattern, such as menses related
Non–central nervous system infection	Patient may have an upper respiratory infection, pharyngitis, or facial pain Fatigue, myalgia, abdominal pain
Posttraumatic origin	Antecedent history of trauma (acute or chronic)
Vascular origin	Abnormal headache character Focal neurologic findings, especially cranial nerve deficits
Viral meningitis	Fever Headache with or without photophobia Patient may not have meningeal signs

+ indicates a positive finding; ↑, increased.

combination of ketorolac (0.5 mg/kg; 15-mg maximum if the patient weighs < 50 kg; 30-mg maximum if the patient weighs > 50 kg), an antiemetic (prochlorperazine 0.10–0.15 mg/kg, 10-mg maximum), an antihistamine (diphenhydramine 0.5 mg/kg, 25- to 50-mg maximum), and intravenous fluids, may be effective if sumatriptan therapy fails. Consult a pediatric neurologist for status migrainosus or migraine variants.

Treat the underlying cause of a secondary headache. For a headache associated with a systemic infection or inflammatory condition, administer acetaminophen (10–15 mg/kg per dose every 4–6 hours) or ibuprofen (5–10 mg/kg every 6 hours). See Chapter 66, Sepsis, for the treatment of suspected meningitis.

Venous sinus thrombosis often requires anticoagulation therapy (see Chapter 46, Deep Venous Thrombosis) with low–molecular weight heparin

(enoxaparin, 1 mg/kg every 12 hours), unless significant bleeding has occurred, in addition to treatment of the cause of the thrombosis. Obtain emergent consultation with a pediatric neurosurgeon for intracranial bleeding and treat with platelets, fresh frozen plasma, cryoprecipitate, and/or other clotting factors, as indicated for an underlying coagulopathy.

Diagnostic and therapeutic LP is often adequate in the acute setting of idiopathic intracranial hypertension, but long-term treatment requires identification of the underlying cause. A headache secondary to viral meningitis (enterovirus) is often relieved by the LP.

Indications for Consultation

- **Infectious diseases:** Unusual organism causing a systemic or CNS infection
- **Neurology:** Status migrainosus, migraine variants, seizure
- **Neurosurgery:** Intracranial hemorrhage, intracranial mass, increased ICP
- **Ophthalmology:** Possible papilledema or assessment of eye involvement in systemic illness, especially inflammatory conditions
- **Rheumatology:** Systemic inflammatory conditions affecting the CNS

Disposition

- **Intensive care unit transfer:** Signs of impending herniation/increased ICP, intracranial bleeding, hemodynamic instability associated with systemic illness/infection
- **Discharge criteria:** Baseline mental status and neurologic examination findings

Follow-up

- **Primary care:** 4 to 7 days
- **Subspecialists involved in care during hospitalization:** 1 week

Pearls and Pitfalls

- Risk factors for a serious cause of a headache include a new headache in a preschool-aged patient, occipital headache, inability to characterize the quality of headache, atypical headache pattern, and abnormal neurologic findings.

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CHAPTER 82

Seizures

Introduction

Approximately 5% of children will have a seizure by 16 years of age. The goals of the initial evaluation are to recognize whether the seizure has stopped or if there is concern for status epilepticus, identify potential treatable causes, decide whether to start seizure medications, and determine when the patient can be discharged or if further diagnostic evaluation and management are indicated.

Generally, the patient and family want to know why the seizure occurred, what tests are necessary, if medication is required, and if a seizure will happen again.

Clinical Presentation

History

The context in which the seizure occurs is crucial and guides management. Ask about recent illnesses, head trauma, and systemic infections. Determine if the child is appropriately vaccinated, potentially immunocompromised, taking medications (especially antiepileptic drugs [AED]), or at risk for a toxic/metabolic etiology. Note the child's baseline neurodevelopmental status and whether there have been abnormal neurologic examination findings, a history of neurologic impairment, or a developmental delay. Ask about a family history of febrile seizures or epilepsy.

Physical Examination

Obtain the patient's vital signs and address the airway and breathing, if needed. Pay close attention to any airway obstruction caused by the postictal state or medications used to stop the seizure activity.

Evaluate the patient for ongoing seizure activity. Clonic jerks or tonic stiffening of the trunk or limbs may be present. Subtler signs of ongoing seizure include tachycardia; dilated, poorly reactive pupils; sustained eye deviation; oral or hand automatisms; and increased salivation. Look for evidence of focality, including pupillary asymmetry, lateralized facial or limb weakness, and alterations in tone or reflexes. Note worrisome signs that could indicate increased intracranial pressure (ICP), such as sustained hypertension or the presence of bradycardia.

Perform a thorough neurologic examination. In addition to recognizing persistent seizures, look for evidence of underlying structural, vascular, infectious, or neoplastic processes. Check for upper motor neuron

signs, such as arm drift, asymmetrical differences in limb tone, movement and reflexes, up-going toes (Babinski sign), or finger flexor reflex (Hoffman reflex; flexion of distal thumb when the third or fourth fingernail is tapped). Assess the patient for the Chvostek sign (hypocalcemia). Perform a funduscopic examination to look for signs of increased ICP, such as absent venous pulsations and papilledema. Check the skin for signs of a neurocutaneous disorder, such as neurofibromatosis (café au lait spots), Sturge-Weber disease (port wine stain), and tuberous sclerosis (ash leaf spots).

Differential Diagnosis

Differentiation of a seizure from nonepileptiform events can be difficult in a young child. The history often provides adequate details to detect characteristics of the nonepileptiform events described in Table 82–1. Otherwise, direct observation or video recording of the events allows the most accurate assessment. Episodes that can be extinguished with a change in position or immobilization of extremities are unlikely to be epileptiform. Atypical movements during sleep in an infant are most often benign sleep myoclonus.

There are 4 categories to consider when evaluating the patient with seizures: a provoked seizure (eg, electrolyte abnormalities, ingestion), acute symptomatic process (eg, stroke or encephalitis), remote symptomatic cause (preexisting structural brain abnormality), or idiopathic.

Table 82–1. Differential Diagnosis of Seizures

Diagnosis	Clinical Features
Benign sleep myoclonus	Migrating, multifocal repetitive limb jerks during sleep Jerks extinguished when aroused
Breath-holding spell	Occurs when child is upset or after occipital head trauma Two types: pallid or cyanotic
Migraine	Patient may have an aura Associated with headache, nausea, photophobia
Reflux (Sandifer syndrome)	History of spitting up Generalized stiffening and opisthotonic posturing Occurs within 30 min of a feeding
Shuddering spell	Often occurs with excitement, urination, or feeding; no associated regression or encephalopathy (helps to distinguish it from infantile spasms)
Syncope	Episodes occur when standing or overheated Preceded by nausea and/or darkening of vision with light-headedness No postictal period

Laboratory Workup

Febrile Seizure

An electroencephalogram (EEG), lumbar puncture (LP), and neuroimaging are not indicated for a patient with a simple febrile seizure (generalized seizure lasting < 15 minutes and not recurring within 24 hours) and a normal, nonfocal neurologic examination. Complex febrile seizures have focal onset, last over 15 minutes, or recur within 24 hours. A patient with central nervous system inflammation or infection does not have simple seizures. An LP and neuroimaging are indicated if the history and/or examination findings are suggestive of meningitis or encephalitis.

Other indications for an LP are a sick-appearing infant 6 to 12 months of age who is immunocompromised, fully unimmunized, or not completely immunized for *Haemophilus influenzae* type b (Hib) or *Streptococcus pneumoniae*. In addition, have a low threshold for performing an LP in a patient who has had recent antibiotic exposure that may affect the physical examination, so that classic meningeal signs are not evident. Other tests will be dictated by the probable source of the fever.

Afebrile Seizure

Neonatal seizures, defined as seizures in the first month after birth, are a distinct entity that require a high index of suspicion for infectious and metabolic disorders. Obtain a complete blood cell count (CBC), serum glucose level, chemistry values, and ammonia level. Observe an afebrile, well-appearing infant 1 to 6 months of age for 24 hours. Also, consider an inborn error of metabolism in a young infant with altered mental status or metabolic acidosis. In an older infant or child, the history and physical examination guide the choices for laboratory testing, especially if there is a prior illness, concern about an ingestion, or dehydration. Otherwise, routine laboratory testing is of limited value in the alert, well-appearing patient or a child with known epilepsy who has a breakthrough seizure. However, if the patient has had a first afebrile seizure, obtain a calcium level at a minimum. Add a complete set of electrolytes to help identify potential causes of a provoked seizure if the patient is in status epilepticus or has a history of poor oral intake or excessive gastrointestinal losses. Chemistry values are also helpful if the patient has a chronic encephalopathy, is receiving gastrostomy tube feedings, or has neurologic examination findings that have changed from baseline.

Obtain serum AED levels for a patient with suspected overdose or nonadherence with the prescribed AED regimen, as well as those with difficult-to-control epilepsy.

If the patient is not awakening as expected after a seizure or has subtle, rhythmic oral or eye movements, obtain an EEG to evaluate for persistent electrographic seizures (subclinical status epilepticus). Also order an EEG if infantile spasms are a concern, as prompt initiation of therapy can improve the outcome. Although brief afebrile seizures are an indication for a follow-up outpatient EEG, do not order one for a patient with a simple febrile seizure.

Status Epilepticus

The most common cause of status epilepticus is low AED level(s) in a patient with known epilepsy, although acute symptomatic processes account for approximately 20% of cases. Obtain a bedside glucose level, CBC, and complete metabolic profile. Perform an LP and treat appropriately if meningitis is a concern. See Chapter 68, Toxic Exposures, if an ingestion is a possibility.

Radiology Examinations

Although computed tomography (CT) is usually more available, magnetic resonance (MR) imaging is the preferred modality because it is more sensitive for parenchymal abnormalities. This is especially true for a patient who presents with status epilepticus without preexisting epilepsy or has a change in seizure morphologic appearance from their previous pattern.

Obtain neuroimaging of the head if the patient has a prolonged postictal state, a focal neurologic examination finding, history of anticoagulation therapy, altered mental status, persistent vomiting or headache, or a history of cancer. Noncontrast CT is the study of choice also if there has been significant trauma with a concern for an intracranial hemorrhage. Contrast is indicated if there is concern for intracranial infection or mass. However, the yield of actionable neuroimaging findings in a child with a generalized seizure and nonfocal examination is extremely low. Consult with a pediatric neurologist to determine if urgent MR imaging is necessary during the acute inpatient stay.

Treatment

First-Time Seizure—Febrile

A simple febrile seizure does not require daily seizure medication or abortive treatment with rectal diazepam. This is also generally true for a patient with complex febrile seizures. However, because a child with febrile status epilepticus has a higher chance that future seizures will progress to status epilepticus, have the neurologist discuss the use of rectal diazepam with the parents.

First-Time Seizure—Afebrile

In general, the definition of epilepsy is 2 unprovoked seizures separated by 24 hours. This is based on the risk of a second unprovoked seizure, which is approximately 1 in 3. Therefore, most children do not require an AED after a single unprovoked seizure. Potential exceptions include the presence of preexisting structural brain abnormalities, such as stroke or cortical dysplasia. In such a patient, the risk of recurrent seizure may be as high as 70%. Additionally, if an EEG was obtained, a pattern suggestive of epilepsy may warrant starting an AED after consultation with a pediatric neurologist. Seizure counseling also includes discussions regarding safety, a seizure action plan, potential medication side effects, and approximate duration of medication therapy.

A patient who presented with afebrile status epilepticus is at increased risk for subsequent status epilepticus. Discuss whether to prescribe an AED with a pediatric neurologist.

Status Epilepticus—Febrile and Afebrile

Status epilepticus is a neurologic emergency that requires immediate treatment, with the hospitalist simultaneously evaluating the patient for potential causes. Address circulation, airway, and breathing and obtain intravenous (IV) access, a bedside glucose level, a comprehensive metabolic panel, and a CBC. Perform an LP and neuroimaging (if indicated), but the patient must be stable enough for the procedures.

Emergent first-line therapy is IV lorazepam 0.1 mg/kg (maximum, 4 mg per dose) or diazepam 0.2 mg/kg (maximum, 12 mg per dose). Repeat if the seizure activity persists after 5 minutes. If IV access is not available, administer rectal diazepam, 0.5 mg/kg if 6 months to 11 years of age or 0.2 mg/kg if older than 12 years (20-mg maximum); or midazolam (intranasal 0.2 mg/kg; intramuscular 5 mg if the patient weighs 13–40 kg or 10 mg if the patient weighs more than 40 kg).

If the seizures persist, deliver a loading dose of IV fosphenytoin, 20 to 30 mg phenytoin equivalents per kg, administered slowly over 10 to 15 minutes (1.5 mg fosphenytoin sodium is equivalent to 1 mg phenytoin sodium and is referred to as *1 mg phenytoin sodium equivalents*; maximum, 1.4 g per dose). Intravenous phenytoin is an alternative (20–30 mg/kg administered slowly over 20–30 minutes).

If the patient has refractory seizures, consult with a pediatric neurologist. Options include a loading dose of a second control medication or transfer to an intensive care unit (ICU) for initiation of a pharmacologic coma. Second medication options include IV levetiracetam (30–60 mg/kg),

IV valproic acid (20–40 mg/kg; contraindicated if the patient has thrombocytopenia or a possible metabolic disease), or IV phenobarbital (20 mg/kg; maximum, 1 g per dose; monitor the patient for respiratory depression and hypotension).

Indications for Consultation

- **Neurology:** Focal neurologic findings, persistent altered mental status, status epilepticus, febrile seizure in an infant younger than 6 months, afebrile seizure in a patient younger than 24 months, concern for infantile spasms, recurrent seizures
- **Neurosurgery:** Signs of increased ICP or abnormal head imaging findings

Disposition

- **ICU transfer:** Status epilepticus, respiratory depression secondary to AEDs, persistent altered mental status
- **Video EEG monitoring unit:** Concern for nonepileptic disorder mimicking seizures, ruling out subclinical seizures, capturing events that have not been witnessed by medical providers
- **Discharge criteria:** Baseline neurologic examination findings

Follow-up

- **Primary care:** 2 to 3 days
- **Neurology:** 1 to 2 weeks

Pearls and Pitfalls

- Rapidly consider all of the possible treatable causes of seizure.
- Excessive benzodiazepine use can cause respiratory failure.

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Newborn Care

CHAPTER 83

Breastfeeding

Introduction

The pediatric hospitalist can impact population health by counseling mothers on the benefits of breastfeeding, facilitating successful breastfeeding in the newborn period, protecting breastfeeding during hospital admission of mothers or infants, and establishing hospital breastfeeding policies that protect and empower the nursing dyad.

Establishing Breastfeeding

Promote breastfeeding by encouraging immediate skin-to-skin contact upon delivery, with the initial infant assessment occurring on the mother's abdomen. Routine neonatal care such as initial weight, vitamin K, and erythromycin can be provided while skin-to-skin or delayed until after the initial breastfeeding session. Even after cesarean sections or multiple births, in the absence of complications, the infant can be delivered onto the mother's chest. Minimize any medically necessary separation of infant and mother.

After an initial alert period of approximately 2 hours, most neonates transition to a somnolent period, often spanning their first night. Initial sleep stretches can last up to 4 to 6 hours, during which the infant has difficulty latching when awakened. In a term infant who is appropriate for gestational age (GA), with no risk factors or signs of hypoglycemia, encourage the mother to offer the breast at any awakening and at diaper changes, and to provide mild stimulation if the infant has not fed for 4 hours.

Following this period of sleep, infants typically begin cluster feeding, classically during the second night after birth, feeding at 30- to 60-minute intervals for stretches of several hours. This feeding pattern can lead to maternal anxiety regarding whether the colostrum is sufficient for the infant, so that unnecessary nonmedical supplementation may occur. Encourage the mother to anticipate cluster feeding and its resultant feelings, and stress that frequent latching is what will result in increased milk production over the next several days.

Milk supply does not "come in" all at once but increases over time, coming to volume typically around day 3 to 5. This can be accompanied by a sense of fullness, breast engorgement, and breast edema. However, the incidence of problematic engorgement is reduced by frequent, effective feeding. Treat engorgement and edema with therapeutic breast massage and reverse pressure softening. In reverse pressure softening, gentle positive pressure is applied to

the areola at the base of the nipple to facilitate latching and subsequent breast emptying either by infant or pump.

In-person feeding assessment and assistance with latching and positioning are essential and are best learned at the bedside from an experienced lactation professional. While sustained pain during feeding is often a sign of poor latch, short-lived pain with initial latch (< 60 seconds) is commonplace during the first weeks of breastfeeding. Nevertheless, evaluate any report of pain. If the infant is not latching regularly by 24 hours after birth, instruct the mother to pump for 15 minutes, every 2 to 3 hours, to mimic breastfeeding patterns. Hand expression is often more efficient at removing colostrum in the first days, while bilateral pumping provides the necessary nipple stimulation for hormonal signaling.

Improve the milk supply by recommending hand expression, aiming for 5 sessions per day, but advise 8 sessions per day if the infant is not latching. Establishing a full milk supply and ongoing production depend on the release of prolactin and oxytocin secondary to nipple stimulation, and the decrease in feedback inhibitor of lactation through the frequent removal of milk from the breast. Therefore, if an infant is unable to nurse effectively, protect the milk supply by providing the mother with a pump and instructions to empty regularly. Not emptying for more than 4 to 6 hours from the last feed increases the maternal risk of clogged ducts, mastitis, and reduced milk volumes.

The At-Risk Nursing Dyad

Pay special attention to nursing dyads at risk of premature breastfeeding cessation. Risk groups include late preterm or early term infants, low–birth weight (BW) infants, multiple gestation infants, infants of diabetic mothers, infants separated from their mothers, infants born via C-section, and infants born to mothers with a history of breast surgery or premature breastfeeding cessation with a previous child. The following proactive measures will reduce the risk of lactation failure in these dyads:

- Prioritize skin-to-skin contact in the first hour after birth and as much as possible during the next 24 hours.
- Teach the mother to hand express onto a plastic spoon every 2 to 3 hours, or after each nursing, and feed this to the infant.
- Initiate pumping at least 8 times per 24 hours by day 2, if latch is suboptimal or the infant is small or premature. Use a bilateral, hospital-grade breast pump, and permit no more than 5 hours to elapse without pumping overnight. If mother and infant are separated, initiate pumping within 6 hours of birth.

- Avoid supplementation without a medical indication, unless the infant was born at < 38 weeks' GA or < 2.72 kg (< 6 lb) (see the Supplementation section).
- Avoid pacifiers until breastfeeding is well established.
- Use nipple shields for infants who are not latching despite assistance, but do not recommend them routinely.

Supplementation

Early supplementation with formula reduces the length and rate of exclusive breastfeeding. Therefore, recognize the conditions that truly require supplementation, advise how to supplement without unnecessarily disrupting breastfeeding, and learn when to counsel against supplementation. Possible indications for supplementation include weight loss, hypoglycemia, hyperbilirubinemia, and lack of maternal milk production. Do not recommend supplementation for cluster feeding, maternal "recovery" (rooming out of newborn to promote maternal sleep), or mothers who plan to feed a combination of human milk and formula. Resist the temptation to reflexively supplement or advise pumping and bottle feeding for the goal of being to be able to measure intake. Note that exclusive pumping reduces the duration of breastfeeding and the likelihood of reaching the mother's breastfeeding goals.

Newborns lose weight due to fluid shifts, diuresis, and the passage of meconium. If the weight loss exceeds 7% of body weight, perform a physical examination of the newborn and mother, complete a feeding assessment, and plot the weight on a weight loss nomogram (https://www.newbornweight.org/), although this does not provide a definitive indication for supplementation. For an infant born at less than 38 weeks' GA or less than 2.72 kg (< 6 lb) BW, use a lower threshold to initiate supplementation.

Asymptomatic hypoglycemia (see Chapter 85, Hypoglycemia of the Newborn) requires supplementation, but maternal-expressed colostrum is preferred if an adequate amount can be obtained using hand expression. In the absence of maternal colostrum, use 40% glucose gel.

Hyperbilirubinemia in the breastfeeding infant during the first 7 to 10 days after birth may be due to breastfeeding jaundice, in which there is suboptimal intake of milk as evidenced by weight loss and low urine and stool output. If phototherapy is indicated (see Chapter 88, Neonatal Hyperbilirubinemia), short interruptions (< 30 minutes) in treatment to breastfeed do not reduce its effectiveness. However, expressed milk or formula supplementation may be used to reduce the intestinal reabsorption of bilirubin and rapidly lower serum bilirubin in an infant who is not responding appropriately to phototherapy.

During the second and third weeks after birth, the infant may develop human milk jaundice, despite feeding well and being well hydrated. In this case, bilirubin levels will slowly decline over time even in the presence of continued breastfeeding, and interruption of breastfeeding is not usually required.

Supplementation is also necessary if the mother is known to have inadequate milk supply (such as with insufficient glandular tissue, often evidenced by tubular breasts and no breast changes during pregnancy) or has to temporarily stop breastfeeding due to separation or medical problems.

If supplementation is necessary, advise the mother to express milk using a hospital-grade, bilateral pump every time the infant is supplemented. At a minimum, this is 8 times in 24 hours if the infant is not feeding at the breast. The practice of first feeding at the breast, then supplementing by bottle and pumping, is referred to as "triple feeds" and is a temporary intervention intended to ensure infant nutrition while improving maternal milk supply. It requires ample support for the mother but requires close follow-up and a defined end point.

To determine the supplementation volume, consider the physiological stomach size and typical volume of colostrum ingested by breastfeeding infants, rather than the larger volume taken by formula-fed infants. If supplementation is given after a feeding at the breast, use 5 mL every 2 to 3 hours in an infant greater than 37 weeks' GA and greater than 2.72 kg ($>$ 6 lb) BW, and 5, 10, and 15 mL every 2 to 3 hours on days 1, 2, and 3, respectively, in an infant who is late preterm or less than 2.72 kg ($<$ 6 lb) BW. If an infant is not latching to the breast, supplementation volumes depend on infant cues (rooting lip smacking, fist sucking, acting fussy or restless), with typical intake amounts as follows: 2 to 10 mL/feed on day 1, 5 to 15 mL/feed on day 2, 15 to 30 mL/feed on day 3, and 30 to 60 mL/feed on days 4 and 5.

Provide supplemental feeds in a manner that avoids artificial nipples and fast flow rates. Options include supplementation at the breast using a supplemental nursing system, cup feeding, spoon feeding, finger feeding, and syringe feeding. If the infant will be receiving a bottle feed, use a very slow flow nipple and paced feeding.

In addition to protecting the maternal milk supply by ensuring frequent effective emptying of the breast and stimulation with an electric breast pump, keep the baby familiar with the breast by providing frequent skin-to-skin contact and attempting latch during various states of hunger and alertness. Continued follow-up with a lactation professional is essential to facilitate the transition to feeding at the breast, which will improve the duration and exclusivity of breastfeeding.

Breastfeeding Considerations Beyond the Neonatal Period

Admission of a breastfeeding patient is an opportunity to support the breastfeeding relationship. Minimize the amount of time the infant is kept from feeding secondary to medical reasons and permit breastfeeding up until 4 hours prior to anesthesia. However, provide an electric breast pump and pumping instructions to empty at regular intervals, including at least once overnight, to mothers of infants who are not feeding effectively. Acute gastroenteritis does not necessitate pausing breastfeeding. Also, the infant can nurse as desired while receiving nasogastric or intravenous rehydration.

If intake is a concern, such as in the setting of poor weight gain, quantify a breastfeeding session by comparing a weight obtained on a lactation scale (accurate to < 5 g) before and after a feed, under identical circumstances (weigh with diaper and clothes on, do not change diaper or clothes between weights). Take care to differentiate perceived low supply from true low supply. Physiological oversupply, which is common in early lactation, downregulates to match infant demand around 6 weeks postpartum. At this point, breasts feel softer and less full and are less likely to leak. At the same time, the infant is becoming developmentally more alert and fussier, so that the mother may interpret these changes as indicative of insufficient supply. When supplementation is unnecessarily introduced, the infant empties the breast less frequently, causing downregulation and turning perceived into true low supply.

Contraindications

There are few absolute contraindications to breastfeeding: human immunodeficiency virus and human T-lymphotropic virus infection in countries where safe human milk alternatives are readily available, active tuberculosis while contagious, active herpes simplex virus lesions on the nipple (breastfeeding from the unaffected breast is not contraindicated), ongoing substance abuse (cocaine and amphetamines pose the highest risk), the mother receiving chemotherapy, and infantile galactosemia.

Maternal varicella-zoster and cytomegalovirus seropositivity in a premature or immunodeficient infant may require risk counseling or special management of breastfeeding.

The following are not contraindications to breastfeeding: hepatitis B, hepatitis C, prescribed opioid use, moderate alcohol intake, and maternal exposure to x-rays and computed tomography scans.

While human milk is not a likely source of COVID-19 transmission, advise a mother with suspected or confirmed acute COVID-19 disease to practice

hand hygiene prior to touching her infant or expressing milk, wear a mask when within 6 feet of the baby and when expressing milk, and sanitize all pumping equipment. No special precautions, such as masks, are necessary when both members of the nursing dyad are confirmed positive for COVID-19.

There are misconceptions regarding breastfeeding after maternal exposure to radiation or anesthetic agents. There is no need to discard milk ("pump and dump") after contrast imaging studies. Radionuclides used in thyroid imaging are an exception and require varying lengths of breastfeeding cessation. Similarly, anesthesia usually does not require any pause in breastfeeding, once a mother is awake enough to safely hold her infant. Exceptions are meperidine, ketamine, and high-dose morphine.

To limit potential risk to the infant, advise a breastfeeding mother not to use marijuana or marijuana-containing products in any form, including those containing cannabidiol. In addition to the known dangers of secondhand smoke, smoking tobacco may also decrease milk production. The safety of various drugs and toxins can be checked on the Drugs and Lactation Database (https://www.ncbi.nlm.nih.gov/books/NBK501922/).

Indications for Consultation

- **Lactation consultant and/or breastfeeding specialist:** Painful, shallow, or traumatic latch; concerns regarding infant's ability to transfer at the breast; insufficient milk supply
- **Speech therapist:** Disorganized suck patterns, poor transfer at breast despite adequate latch and milk supply

Pearls and Pitfalls

- Address breastfeeding problems by feeding the infant to ensure hydration and nutrition, protecting the milk supply by emptying the breast at least 8 times per day with a bilateral electric breast pump, and maintaining the infant's familiarity with the breast through skin-to-skin contact and regular latch attempts.
- Avoid separation of the nursing dyad, and provide immediate education regarding pumping and/or hand expression when separation or feeding cessation occurs.
- Use a weight loss nomogram to compute neonatal weight loss percentiles to prevent unnecessary supplementation.
- Counsel the mother against supplementing in the early neonatal period, unless medically indicated.

- Teach the mother to hand-express colostrum 5 times a day for the first 3 days after birth to encourage ample milk supply.
- Mothers rarely need to discard milk after anesthesia and radiological procedures.

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CHAPTER 84

Early-Onset Sepsis

Introduction

Early-onset sepsis (EOS) is an infection acquired via vertical transmission from mother to neonate within the first 72 hours after birth. In contrast, late-onset sepsis is an infection that occurs more than 72 hours after birth. The most common organisms causing EOS are group B *Streptococcus* (GBS) and *Escherichia coli*, which are implicated in up to 70% of cases. Early-onset sepsis from GBS has decreased dramatically since the widespread use of intrapartum GBS prophylaxis, although the prevalence of late-onset GBS has not been affected. Other pathogens to consider include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus* species, *Enterobacter* species, influenza, and *Listeria monocytogenes*. Polymicrobial infections are rare.

Clinical Presentation

History

Neonatal risk factors for EOS include prematurity, low birth weight, low Apgar scores, and the presence of congenital anomalies. Maternal factors include intra-amniotic infections (IAIs), peripartum fever, prolonged rupture of membranes (> 18 hours), GBS colonization, previous infant with invasive GBS disease, lack of prenatal care, and substance use. An IAI is defined as maternal fever of greater than 38 °C (> 100.4 °F) and at least 2 of the following: maternal leukocytosis (> 15,000 cells/ mm^3 [$> 15 \times 10^9$/L]), maternal tachycardia (> 100 beats/min), fetal tachycardia (> 160 beats/min), and uterine tenderness or foul-smelling amniotic fluid. However, IAI may still occur if maternal fever is the only abnormality.

The infant may have vomiting, diarrhea, feeding intolerance, and decreased wet diapers. However, the infant may appear well if identified solely by risk factors.

Determine if maternal GBS screening was performed, the results, and treatment, if any. Intrapartum prophylaxis for GBS with penicillin, ampicillin, or cefazolin given more than 4 hours prior to delivery is preferred, although prophylaxis given more than 2 hours prior to delivery is 89% effective in preventing GBS EOS. Erythromycin or clindamycin is adequate prophylaxis only if the GBS is susceptible upon culture.

Physical Examination

The initial physical examination of a neonate with sepsis can be normal. Evaluate the vital signs for temperature instability, tachycardia/bradycardia, tachypnea, desaturations, and hypotension. Other relevant examination findings include lethargy, irritability, pallor, cyanosis, mottling, jaundice, abnormal tone, delayed capillary refill, apnea, grunting, and retractions.

Laboratory

The neonatal early-onset sepsis risk calculator, developed by Kaiser Permanente (https://neonatalsepsiscalculator.kaiserpermanente.org/), is a useful tool for evaluating the risk of EOS in late preterm (> 34 weeks' gestation) and full-term infants. This combines both perinatal risk factors and physical examination findings in the first 6 to 12 hours after birth to determine the risk of EOS per 1,000 births. Perinatal risk factors are the local incidence of early-onset disease (if unknown, suggested ranges are available), gestational age (weeks and days), highest maternal antepartum temperature, rupture of membranes (hours), and maternal GBS status (negative, positive, unknown) and type/duration of intrapartum antibiotics. The results and subsequent guidance about antibiotic treatment are then stratified by the infant's clinical status (well appearing, equivocal, clinical illness; see Table 84–1). The use of the calculator has decreased empiric antibiotic treatment and unnecessary blood cultures.

If EOS is a concern, the priority laboratory test is a blood culture obtained prior to the first dose of antibiotics. Most positive results will occur in the first 24 hours. The diagnosis of EOS cannot be established using laboratory tests alone, given their poor positive predictive values. However, multiple normal results of C-reactive protein (CRP; < 1 mg/dL [< 10 mg/L]) and procalcitonin (PCT; < 1 ng/mL) have high negative predictive values for EOS. A complete blood cell count (CBC), with manual differential, is useful if collected during the first 4 to 12 hours after birth. An elevated immature to total neutrophil ratio (I/T ratio; > 0.2) and a low absolute neutrophil count (ANC; < 1,500/mcL [$< 1.5 \times 10^9$/L]) may suggest infection.

Indications for a lumbar puncture (LP) include an infant who is at high risk of EOS and is critically ill, has apnea or seizures suggestive of meningitis, or has a positive blood culture (obtained previously). Other indications for an LP include laboratory data indicative of sepsis and a lack of response to antimicrobial therapy. However, do not delay initiating antibiotic therapy if the LP cannot be performed promptly. The spinal fluid culture may be falsely negative if the patient received antibiotics prior to the LP, in which case it is important to evaluate the cerebrospinal fluid (CSF) for pleocytosis and elevated protein or low glucose levels, which suggest meningitis. As many as

Table 84–1. Kaiser Permanente Sepsis Calculator Classification of Clinical Presentation

Clinical Assessment	Description
Clinical illness	Apgar score < 5 at 5 min Hemodynamic instability requiring vasoactive drugs Neonatal encephalopathy or perinatal depression Persistent need for nasal continuous positive airway pressure, high-flow nasal cannula, or mechanical ventilation[a] Seizure Supplemental O_2 needed for > 2 h to maintain O_2 saturation > 90%[a]
Equivocal	Persistent physiologic abnormality lasting for > 4 h • Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O_2 • Tachycardia (HR > 160 beats/min) • Tachypnea (RR > 60 respirations/min) • Temperature instability (> 38 °C [100.4 °F] or < 36.4 °C [97.5 °F]) Two or more physiologic abnormalities lasting for ≥ 2 h[b] • Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O_2 • Tachycardia (HR > 160 beats/min) • Tachypnea (RR > 60 respirations/min) • Temperature instability (> 38 °C [100.4 °F] or < 36.4 °C [97.5 °F])
Well appearing	No persistent physiologic abnormalities

Abbreviations: HR, heart rate; RR, respiratory rate.

[a] Outside of the delivery room.

[b] Abnormality can be intermittent.

Adapted from Neonatal early-onset sepsis calculator. Kaiser Permanente Research. Accessed April 10, 2022. https://neonatalsepsiscalculator.kaiserpermanente.org/InfectionProbabilityCalculator.aspx.

20% to 30% of neonates with a positive blood culture will have meningitis, but the blood culture can be negative in an infant with meningitis.

Order a chest radiograph if the infant has respiratory symptoms, such as tachypnea, grunting, nasal flaring, or rales.

Treatment

After obtaining the appropriate cultures, start empiric antibiotics (see Table 84–2), targeted at GBS and *E coli*, on an ill-appearing neonate and if recommended by the early-onset sepsis risk calculator. Extended-spectrum β-lactamase–producing organisms are rare in EOS; therefore, empiric broad coverage is not necessary. In a term neonate who is critically ill, or if there is concern for gram-negative rod meningitis, add a broad-spectrum antibiotic, such as a third-generation cephalosporin (ceftazidime), and transfer the infant to the neonatal intensive care unit (NICU). Do not routinely give a third-generation cephalosporin because of an increased risk of opportunistic infection and potential for antimicrobial resistance. In addition, ceftriaxone is

Table 84–2. Empiric Antibiotics for Early-Onset Sepsis		
Ampicillin IV, IM	**Weight < 2,000 g**	**Weight ≥ 2,000 g**
	50 mg/kg/d administered in doses divided every 12 h Meningitis: 100 mg/kg/d administered in doses divided every 12 h	75 mg/kg/d administered in doses divided every 8 h Meningitis: 150 mg/kg/d administered in doses divided every 8 h
Gentamicin IV, IM	**> 35 wk PMA, ≤ 7 d**	**≥ 35 wk PMA, ≤ 7 d**
	4 mg/kg every 24 h	4 mg/kg every 24 h
Ceftazidime IV, IM	**≤ 7 d**	**≤ 7 d**
	100 mg/kg/d administered in doses divided every 12 h	100–150 mg/kg/d administered in doses divided 8–12 h
Vancomycin IV	**≤ 7 d**	**≤ 7 d**
	10–15 mg/kg/dose administered every 12–18 h	10–15 mg/kg/dose administered every 8–12h

Abbreviations: IM, intramuscular; IV, intravenous; PMA, postmenstrual age.

contraindicated because it may increase the risk of kernicterus. Add vancomycin if there is a concern for *S aureus* or coagulase negative *Staphylococcus*.

Cultures obtained after antibiotics have been given are more likely to be sterile. In this scenario, a CBC and inflammatory markers may help determine need for ongoing antibiotic therapy.

If EOS is confirmed via a positive blood culture, perform an LP to assess for meningitis, if not already completed, and obtain repeat blood cultures to document sterility. In general, treat bacteremia without a focus for 10 days, uncomplicated meningitis due to GBS for 14 days minimum, and gram-negative rod meningitis for 21 days. Otherwise, discontinue antibiotics once the blood culture (and spinal fluid, if obtained) is negative for 36 to 48 hours. Do not necessarily continue antibiotics solely based on laboratory abnormalities (elevated CRP, PCT, I/T ratio, or low ANC).

Indications for Consultation

- **Infectious diseases:** Positive blood or CSF culture, lack of clinical improvement despite culture-specific antibiotics, atypical organism identified

Disposition

- **NICU:** Hemodynamic instability, meningitis, respiratory distress with increasing oxygen support, apnea, feeding intolerance, seizures, lethargy
- **Discharge home:** Cultures negative for at least 36 to 48 hours, or if antibiotics not started, after an appropriate period of observation (about 48 hours); ensure that the vital signs are stable and the infant is feeding, stooling, and voiding normally

Follow-up

- **Primary care physician:** 1 to 2 days

Pearls and Pitfalls

- A neonate may be well appearing despite having EOS.
- Consider alternative diagnoses if the cultures are negative at 36 to 48 hours but the infant is not improving despite receiving antibiotics.
- Laboratory tests are insufficient for establishing a diagnosis of EOS.

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CHAPTER 85

Hypoglycemia of the Newborn

Introduction

Neonatal hypoglycemia is commonly screened for, identified, and treated in the newborn period. There is a lack of consensus on the numeric definition of hypoglycemia in infants younger than 48 hours. This is a result of the normal fluctuation of blood glucose values following birth and the unknown (and likely variable) threshold or duration at which long-term neurologic injury may occur due to hypoglycemia. Though the exact glucose value to diagnose hypoglycemia by hour of life is debatable, prevention of hypoglycemia remains a focus in newborns to avoid adverse outcomes.

It takes 4 to 6 hours after birth for neonatal hepatic processes to begin providing glucose and up to 48 hours to maintain a glucose level greater than 70 mg/dL (> 3.9 mmol/L). As a result, normal, healthy newborns experience decreasing blood glucose levels with a transient nadir between 1 and 3 hours after birth that is not considered pathologic. Under normal circumstances, initiation of feeding is a limited source of substrate in the early hours after birth and thus not the primary driver of achieving normoglycemia for most newborns during this time period.

Risk factors that are known at birth are used to screen for asymptomatic neonatal hypoglycemia. These include born either small or large for gestational age, infants of diabetic mothers, late preterm infants, maternal β-blocker exposure, and/or evidence of asphyxia or birth trauma. When related to specific pregnancy or newborn factors, hypoglycemia is typically a transient problem that resolves in the early days after birth and can be ameliorated by increased attention to exogenous glucose intake. Thus, it is important to distinguish asymptomatic neonatal hypoglycemia detected on screening from symptomatic hypoglycemia or hypoglycemia of the newborn that is not due to a known risk factor, including sepsis, cold stress, or other maternal or newborn factors.

Clinical Presentation

History

Review the birth history (trauma, asphyxia), birth weight percentile, gestational age, and pregnancy history (maternal diabetes, medications [β-blockers, corticosteroids, terbutaline]). Ask if there is any family history of unexplained infant death, hyperinsulinism, or genetic or metabolic disorders. Obtain a thorough history of intake and output including what and how well

the infant is feeding, frequency of stool and urine output, and general activity level, tone, and interest in feeding.

Physical Examination

Most newborns with hypoglycemia are asymptomatic and do not have abnormal examination findings. However, signs of hypoglycemia include hypothermia, lethargy, hypotonia, and jitteriness, although these are not specific. Severe hypoglycemia can present with bradycardia, feeding difficulty or poor suck, tachycardia, seizures, or coma. Other disorders that may cause secondary hypoglycemia do not typically present with physical examination findings in the first days after birth.

Laboratory Workup

Point-of-care blood glucose measurements are often obtained in infants who are asymptomatic but determined to be at risk for neonatal hypoglycemia, typically by a protocol in that nursery. Although laboratory-analyzed glucose values are considered the gold standard, point-of-care machines are readily available with immediate results and no need for extreme precision. However, there is variance in the reliability of point-of-care values, so warm the newborn's heel pretest and ensure adequate machine calibration. If an infant is being screened for asymptomatic hypoglycemia, typically a minimum of 2 normal blood glucose measurements is necessary to discontinue the screening (varies by local protocol). It is uncommon for infants with known risk factors for neonatal hypoglycemia to require further laboratory or diagnostic evaluation after the first days after birth.

If an infant without risk factors has symptomatic hypoglycemia, confirmed by serum blood testing, obtain a complete blood cell count (CBC) with differential and blood cultures for infection/sepsis. Hypoglycemia that is severe, refractory, or persistent or occurs outside of the first 48 hours after birth is cause for concern. Order a critical sample, including a serum glucose, CBC, insulin, C-peptide, cortisol, growth hormone, urine organic acids, chemistry profile, liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels), ammonia, lactate, and urinalysis to evaluate for possible underlying etiologies including sepsis and metabolic and endocrine disorders. The critical sample should be followed by glucagon stimulation testing.

Differential Diagnosis

Asymptomatic neonatal hypoglycemia detected due to risk factor screening is the most common etiology of neonatal hypoglycemia. This type of hypoglycemia typically resolves in the early days after birth with appropriate exogenous glucose supplementation.

For a symptomatic infant without risk factors or those with hypoglycemia more than 48 hours after birth, congenital hyperinsulinism is the most common etiology. Inborn errors of metabolism, particularly glycogen storage diseases, defects in gluconeogenesis, and fatty acid oxidation defects, more commonly present after 1 month of postnatal life. A myriad of processes, both acquired (eg, sepsis, respiratory distress) and congenital (eg, other inborn errors of metabolism, cardiac anomalies), can result in secondary hypoglycemia in the newborn.

Treatment

The management of a hypoglycemic newborn depends on the underlying cause. If the infant is symptomatic, treat until their glucose is corrected to an acceptable range (goal of 60 mg/dL [3.3 mmol/L]; 70 mg/dL [3.9 mmol/L] at 48 hours after birth).

A newborn with asymptomatic hypoglycemia who was screened due to maternal, birth, or infant growth factors can be treated and observed for resolution. Treatment options include oral glucose dextrose gel (40%, absorbed systemically), feeding, or intravenous (IV) dextrose administration. Directly following delivery, maintain the infant skin-to-skin contact for at least the first hour or until successful breastfeeding has occurred, whichever comes first. Initiate the first feed by 1 hour after birth, although some newborns may need up to 2 hours after birth. Obtain the first glucose measurement at 90 to 120 minutes after birth.

Generally, treatment algorithms are divided into less than or more than 4 hours after birth. In the 4 hours directly after delivery, lower glucose levels are tolerated as the infant transitions to postnatal life. Be sure to feed the newborn at least every 2 to 3 hours, and ideally obtain all screening glucose measurements preprandially, but do not adjust the feeding schedule to facilitate testing. Measurements following glucose or feeding interventions are not considered a valid measurement of glucose homeostasis, but document that the glucose values increased to the normal range with feeding or intervention.

Less Than 4 Hours After Delivery

When hypoglycemia is detected (blood glucose < 41 mg/dL [< 2.3 mmol/L]), administer dextrose gel (40% dextrose gel, 0.5 mL/kg) in the buccal mucosa followed immediately by an adequate feed. An adequate feed is defined for breastfeeding infants as a good breastfeeding attempt. For a bottle-fed infant or breastfeeding infant with poor latch, feed expressed colostrum, donor breast milk, or formula. Give 2 to 10 mL/kg in the first 24 hours after birth and

5 to 15 mL/kg at 24 to 48 hours after birth. Recheck the glucose after 1 hour, and if it remains less than 41 mg/dL (< 2.3 mmol/L), repeat the gel administration, feed, and recheck after 1 hour. If at any point during this 4-hour period the glucose is greater than 40 mg/dL (> 2.2 mmol/L), allow the infant to feed as normal, without dextrose gel administration, and obtain routine preprandial glucose measurements.

More Than 4 Hours After Delivery

Hypoglycemia in this period is defined as a glucose level less than 45 mg/dL (< 2.5 mmol/L). Use the same treatment approach as for infants younger than 4 hours, aside from a higher glucose level goal. From 4 to 48 hours after birth, glucose readings greater than 45 mg/dL (> 2.5 mmol/L) do not require intervention. After 48 hours, 60 mg/dL or greater (≥ 3.3 mmol/L) is considered a normal blood glucose level.

Once a newborn has 3 consecutive preprandial blood glucose measurements at a normal level (> 41 mg/dL [> 2.3 mmol/L] less than 4 hours after birth; > 46 mg/dL [> 2.6 mmol/L] more than 4 hours after birth), regular blood glucose monitoring is no longer required. Of note, glucose measurements following intervention with dextrose gel/feeding (usually 1 hour post-intervention) do not reflect unassisted glucose homeostasis. Do not include them as an adequate glucose measurement for determining when to discontinue screening. Additionally, if a breastfed newborn requires supplementation during regular feedings to achieve euglycemia, continue supplementation until maternal breast milk supply is established.

At any time, if a newborn is not responding to intervention (1 hour post-intervention glucose measurement has not improved), has a very low blood glucose measurement (< 25 mg/dL [< 1.4 mmol/L] at 0 to 4 hours after birth; < 35 mg/dL [< 1.9 mmol/L] at 4 to 24 hours after birth), or requires more than 3 to 4 doses of dextrose, transfer the patient to the neonatal intensive care unit (NICU) or level 2 nursery for continuous IV dextrose infusion, and obtain a critical sample.

Indications for Consultation

- **Neonatology:** Persistent hypoglycemia, suspected sepsis, severe symptoms (lethargy, bradycardia, inability to feed)
- **Pediatric endocrinology:** Suspected hyperinsulinism, blood glucose less than 60 mg/dL (< 3.3 mmol/L) after 48 hours after birth
- **Pediatric genetics/metabolism:** Abnormal physical findings (macroglossia, midline defects, abnormal facies), blood gas, or lactate level in the setting of hypoglycemia

Disposition

- **Level 2 nursery/NICU transfer:** Need for IV dextrose infusion and further evaluation/monitoring
- **Return to routine baby care:** Infant can maintain euglycemia on regular newborn feeding
- **Discharge:** Asymptomatic and able to maintain normal glucose on oral feeds

Follow-up

- **Primary care:** Within 24 to 48 hours

Pearls and Pitfalls

- Avoid cold stress: place infant skin-to-skin with the mother or a warm caregiver, increase room temperature, delay bathing, use warmer bed.
- Continue supplementation once required for euglycemia until maternal breast milk supply is established.
- Adequately warm an infant's heel prior to all glucose checks.
- Routinely calibrate the glucometer.

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CHAPTER 86

Late Preterm Infants

Introduction

The definition of an infant born late preterm (LPT) is one who was born between 34 0/7 weeks' and 36 6/7 weeks' gestation. These infants have classically been viewed as just "smaller" versions of their term counterparts, so that the associated morbidities were often overlooked. However, there is now an awareness of the physiologic and metabolic immaturity of this population. They are at increased risk for early-onset sepsis, respiratory distress, jaundice, and feeding difficulties.

Clinical Presentation

History

Obtain a full prenatal history and review the mother's chart. Note the mother's age, prenatal laboratory results, preexisting health conditions (eg, inheritable genetic conditions, preexisting diabetes, chronic hypertension), pregnancy complications, results of any genetic screening (noninvasive prenatal testing, serum integrated screen, chorionic villus sampling, amniocentesis), fetal survey results, medication use, and social history, including drug/substance use and smoking. Similarly, note information about the delivery, including the infant's gestational age (GA) at delivery (and the modality by which the pregnancy was dated), the mode of delivery (vaginal versus C-section), presentation, length of time from rupture of membranes to delivery, whether or not the amniotic fluid was clear, the assigned Apgar scores, and what resuscitation was required.

Physical Examination

Perform a thorough examination, paying close attention to signs of the common morbidities associated with being an infant born LPT. Priorities include the vital signs, presence of a murmur, quality of the peripheral pulses and perfusion, and signs of respiratory distress (grunting, nasal flaring, cyanosis). Note any dysmorphic features. On neurological examination, assess the overall tone (can be mildly decreased in the infant born LPT) and the standard newborn reflexes. Look for signs of hypoglycemia, including jitteriness/tremors, diaphoresis, irritability, and tachypnea.

If the infant appears younger than the given GA or if the GA is unknown, use the Ballard or Dubowitz scoring systems to estimate the infant's GA. Plot

the growth parameters, including weight, length, and head circumference, on the appropriate growth chart for preterm infants.

Laboratory Workup

Check the blood glucose 30 minutes after the infant's first feed, or sooner if they are symptomatic, and regularly repeat over at least the first 24 hours, until 3 subsequent preprandial values are greater than 45 mg/dL (> 2.5 mmol/L). Measure the bilirubin level before discharge, but obtain it earlier if clinically indicated. A transcutaneous bilirubin can suffice, unless the level is close to the phototherapy threshold (see Chapter 88, Neonatal Hyperbilirubinemia). The same newborn screening tests that are performed on a full-term newborn are also necessary for an infant born LPT, including a state newborn screen, a critical congenital heart defect screen, and a hearing screen. Obtain the state newborn screen after the infant born LPT is feeding well, which is often at 36 to 48 hours, rather than the traditional 24 hours in a full-term newborn.

Differential Diagnosis and Treatment

Respiratory Distress

Late preterm infants are at risk of respiratory distress due to immature lung development, decreased surfactant, neurological immaturity and breathing control, and decreased muscle tone. This distress can manifest in many different ways depending on the primary pathology.

Respiratory Distress Syndrome

Although respiratory distress syndrome (RDS) is less common in the infant born LPT than those born at younger GAs, it does occur, and more commonly in males. It manifests in the first few minutes to hours after birth, with increased work of breathing (grunting, nasal flaring, retractions) in addition to hypoxia and decreased aeration on auscultation. Chest radiographs reveal low lung volumes, diffuse granular ("ground glass") opacities, and air bronchograms. If the infant has persistent tachypnea, increased work of breathing, an oxygen requirement, or a chest radiograph concerning for RDS, transfer them to a neonatal intensive care unit (NICU) for consideration of surfactant administration and positive pressure ventilation. Do not feed an infant with respiratory distress. Place an intravenous (IV) line and start dextrose-containing fluids.

Transient Tachypnea of the Newborn

Transient tachypnea of the newborn (TTN) is the most common cause of respiratory distress in the infant born LPT. It is the result of delayed clearance of fetal alveolar fluid and presents with respiratory distress, most commonly

tachypnea, usually within the first few hours after birth. More significant TTN can lead to hypoxia and signs of increased work of breathing, including grunting, nasal flaring, and retractions. The condition is usually benign and self-limited, with resolution of symptoms in the first 12 to 24 hours after birth, although it can persist up to 72 hours. Obtain a chest radiograph to help differentiate between TTN and RDS. The chest radiograph in a patient with TTN will show interstitial edema and fluid in the right horizontal fissure. Provide respiratory support with oxygen by nasal cannula, but if the infant does not improve, transfer to the NICU for noninvasive (ie, high-flow nasal cannula, continuous positive pressure, or noninvasive positive pressure ventilation) or mechanical ventilation. An infant born LPT with mild tachypnea may still be able to feed, but if there is persistent or severe tachypnea, stop the oral feeds, place IV, and hydrate with a dextrose-containing IV fluid.

Apnea of Prematurity

Apnea of prematurity is usually characterized by respiratory pauses for 20 seconds or longer, or a shorter episode that is accompanied by hypoxemia and/or bradycardia. The risk of apnea of prematurity decreases with increasing GA, with 100% of infants born prior to 28 weeks' gestation being affected down to 20% of those born at 34 weeks' gestation. Therefore, admit an infant less than 35 weeks GA to the NICU for continuous cardiorespiratory monitoring. Also admit to the NICU an infant 35 weeks or greater GA if there any clinical concerns for apnea of prematurity. Prior to discharge, arrange for a car seat challenge to assess for apnea, bradycardia, or desaturation.

Early-Onset Sepsis

Perform risk stratification for neonatal sepsis using the Kaiser Neonatal Early-Onset Sepsis Calculator (https://neonatalsepsiscalculator.kaiserpermanente.org/). Maternal risk factors for early-onset sepsis include positive or unknown maternal group B *Streptococcus* status without adequate antenatal antibiotic prophylaxis, antepartum maternal temperature greater than or equal to 38 °C (≥ 100.4 °F), and rupture of membranes for more than 18 hours. Infant risk factors include tachypnea, tachycardia, temperature instability, or respiratory distress lasting over 4 hours, or 2 of the previously mentioned findings lasting for over 2 hours. See Chapter 84, Early-Onset Sepsis, for specific treatment.

Feeding Difficulties and Weight Loss

The infant born LPT is at risk of feeding difficulties and poor milk transfer due to poor suck and swallow coordination, inadequate latch, poor tone, and decreased stamina. There are also many maternal risk factors for delayed or

insufficient lactogenesis that are more common in LPT infants, including gestational hypertension and preeclampsia, gestational diabetes, multiple gestation, cesarean delivery, and chorioamnionitis. Postpartum, an infant born LPT may require more medical interventions and is often subjected to increased evaluation and testing, which can delay skin-to-skin and breastfeeding initiation.

When clinically possible, facilitate early and prolonged skin-to-skin time, which can help stabilize the infant's temperature, heart rate, respiratory status, and blood glucose. Continued rooming-in and frequent skin-to-skin time continue to be beneficial throughout the infant's nursery stay.

Because the infant born LPT often has difficulty with milk transfer, the mother is at risk for low milk supply due to inadequate stimulation. Also, an infant born LPT is often sleepier than full-term infants, and extra care is needed to ensure 8 to 12 feeds per day, even when it means waking the baby to do so. Facilitate establishing the milk supply with frequent access to breastfeeding and, when the infant's latch appears suboptimal or there is concern for poor milk transfer, hand expression and/or pumping (see Chapter 83, Breastfeeding). Milk expressed by hand or with a pump can then be fed to the infant after attempting to feed at the breast. Involve a lactation consultant early if there are any difficulties.

Milk transfer can be assessed with pre- and postfeed weights. However, an infant born LPT may require supplementation with 5 to 10 mL of either expressed breast milk, donor breast milk, or formula after each breastfeeding session, starting on day 1 after birth. Increase to 10 to 30 mL on day 2 after birth and continue until the breastfeeding is well established. This may involve a supplemental nursing system, syringe feeding, cup feeding, or bottle feeding, depending on the clinical scenario and maternal preference. When supplementation is required, ensure that the mother is pumping at least 6 times daily to establish and maintain her supply.

Hypoglycemia

The infant born LPT is at a significantly increased risk for hypoglycemia. As noted previously, follow the glucose levels closely over at least the first 24 hours after birth. Dextrose gel 40% is a safe and effective adjunct to breastfeeding and formula feeding for newborns with hypoglycemia (see Chapter 85, Hypoglycemia of the Newborn), and it will often obviate the need for IV dextrose in the infant born LPT.

Hypothermia

Late preterm infants are at risk of hypothermia due to decreased brown and white fat as well as increased heat loss secondary to a higher surface-area-to-mass ratio.

The goal is an axillary temperature between 36.5 and 37.5 °C (97.7–99.5 °F). If the temperature is not in this range, confirm with a rectal temperature.

Dry the infant immediately following delivery and then place them skin-to-skin with the mother, as their clinical status allows. When not skin-to-skin, keep the infant double swaddled in a room with an appropriate ambient temperature. Delay the initial bath for the first 12 to 24 hours, until adequate thermoregulation and euglycemia have been documented. If hypothermia is confirmed, immediately place the infant on a radiant warmer and check the blood glucose. If temperature support is required repeatedly, transfer the infant to the NICU for thermoregulation in an isolette and evaluation for any contributing factors other than prematurity.

Hyperbilirubinemia

An infant born LPT has an increased risk of hyperbilirubinemia requiring phototherapy due to an immature hepatic bilirubin conjugation pathway. As noted above, use the appropriate nomogram to assess the infant's bilirubin. The infant born LPT requires close outpatient follow-up to assess the need for repeat bilirubin checks, as their bilirubin levels peak later (usually between days 5 and 7) and remain elevated longer than those in full-term infants (see Chapter 88, Neonatal Hyperbilirubinemia).

Indications for Consultation

- **Neonatology:** Prematurity less than 35 weeks GA; respiratory distress requiring supplemental oxygen or positive pressure; need for continuous IV fluids due to respiratory distress or persistently low glucose; any concern for apnea or bradycardia; persistent hypothermia requiring an isolette

Disposition

- **NICU:** For therapies beyond the scope of practice in the newborn nursery (see above)
- **Discharge:** Tolerating oral feeds without excessive weight loss and with good urine and stool output, able to maintain stable temperature without support, no concerns for apnea of prematurity, passed critical congenital heart disease screening and car seat testing

Follow-Up

- **Primary care:** 24 to 48 hours after discharge
- **Early intervention:** As recommended by your state's early intervention criteria

Pearls and Pitfalls

- An infant born LPT can appear more mature than they are ("great pretenders").
- Bilirubin levels peak later and remain elevated longer in the infant born LPT.
- Mothers of infants born LPT experience significantly greater levels of emotional distress than those of full-term babies, and this can last for months postpartum.

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CHAPTER 87

Neonatal Abstinence (Withdrawal) Syndrome

Introduction

Neonatal abstinence syndrome (NAS) is a withdrawal syndrome experienced by newborns after in utero exposure to any substance that can cause physiologic dependence. Neonatal opioid withdrawal syndrome (NOWS) specifically refers to the symptoms experienced as a result of exposure to opioids, including heroin, codeine, oxycodone, methadone, and buprenorphine. NOWS is most common, but a number of substances can cause NAS (antidepressants, barbiturates, nicotine, gabapentin), and polypharmacy is unfortunately common.

Clinical Presentation

History

Assess whether the newborn has had gastrointestinal (feeding difficulties, vomiting, diarrhea), central nervous system (tremors, seizures, increased muscle tone, hyperactive Moro reflex), or autonomic (fever, nasal congestion, sweating, yawning, sneezing) signs or symptoms. This information may come from the parents or the nursery staff, or it may be available upon review of the chart of a baby being observed for NAS/NOWS due to known maternal substance use.

Ask the mother about her pregnancy and any complications, as well as the use of prescription (especially opioids) and nonprescription medications, nicotine, cannabinoids, alcohol, and illicit substances with a validated screening tool such as the 4Ps for adults or CRAFFT for adolescents. Review the prenatal record, and note whether any toxicology testing was performed or if the mother is engaged in a prescribed pain management plan or a medication-assisted treatment (MAT) program for opioid use disorder. If engaged in a MAT program, ask about adherence to the regimen, progress, and any relapses during the pregnancy.

The parents may be concerned about the implications of disclosing illicit substance use. Pose these questions in a nonjudgmental way, with an emphasis on gathering history to help the baby. The nursery social work team may be expert at performing such an interview.

Physical Examination

Review the vital signs, looking for fever and tachypnea. Plot the length, weight, and head circumference on standard growth curves to assess for measurements that are low for gestational age. On examination, look for tremors, excessive fussiness, increased tone, a hyperactive Moro reflex, skin excoriations, and diaper rash (from excessive stooling). If possible, observe a feeding to determine whether the newborn is able to feed effectively for age or is poorly coordinated or frantic while feeding.

Laboratory Workup

Labor and delivery units and newborn nurseries have standardized polices for obtaining toxicology testing on mothers and newborns. These may include criteria such as a history of substance use during the pregnancy, unexpected preterm labor, placental abruption, late entry to prenatal care, or unexplained gaps in prenatal care. Inform the mother whenever a toxicology test on the baby is going to be sent. In addition, in some centers informed consent is required. To prevent confusion about results, ensure that the specimen is obtained before any narcotic medication is given. Also inform the parents if toxicology testing on the newborn is being ordered. Ideally, obtain a urine specimen from the newborn as soon as possible after birth. For both types of testing, confirm any unexpected results, if indicated, with the laboratory.

When evaluating an infant with symptoms consistent with NAS/NOWS, assess for other etiologies and obtain glucose and electrolyte levels, a magnesium level (if the mother received this during labor), a complete blood cell count, and blood cultures if sepsis is a concern.

Differential Diagnosis

Depending on the clinical scenario, the differential diagnosis of NAS/NOWS may include hypermagnesemia, hyperthyroidism, hypocalcemia, hypoglycemia, hypoxic-ischemic encephalopathy, and sepsis (Table 87–1).

Evaluation of Severity of Withdrawal

There are multiple tools available for the evaluation of NAS/NOWS. The Finnegan Neonatal Abstinence Scoring System and MOTHER score (modified Finnegan score) have been widely used, although the subjective nature of the evaluation of some of the signs and symptoms of withdrawal can lead to poor reliability.

Eat, Sleep, Console is a newer tool to assess the function of infants with NAS/NOWS. Assessment includes whether the infant can eat appropriately,

Table 87–1. Differential Diagnosis of Neonatal Abstinence Syndrome	
Diagnosis	**Clinical Features**
Hypermagnesemia	Mother treated with magnesium during labor
Hyperthyroidism	Maternal history of hyperthyroidism Infant fever
Hypocalcemia	History of intrauterine growth restriction or asphyxia Maternal diabetes
Hypoglycemia	Large for gestational age Maternal diabetes Polycythemia Prematurity
Hypoxic-ischemic encephalopathy	History of asphyxia Low Apgar score
Sepsis	Maternal fever or chorioamnionitis Prolonged rupture of membranes Infant fever

sleep undisturbed for 1 hour, and console within 10 minutes. Choose a tool that is standardized by your institution.

Treatment

Nonpharmacologic Care

Nonpharmacologic care is the initial treatment for NAS/NOWS and is associated with decreased symptoms, need for pharmacologic care, and length of stay. Facilitate rooming-in and skin-to-skin time with the parents, and provide swaddling, pacifier use, and a low-stimulation environment. When appropriate, breastfeeding is part of this care plan as well. It offers the advantage of potentially lessening withdrawal symptoms. Buprenorphine and methadone are not contraindications to breastfeeding.

Pharmacologic Care

Morphine

Pharmacologic care is needed if nonpharmacologic care has not successfully treated the withdrawal symptoms. Morphine is the first-line medical therapy for both opioid and benzodiazepine withdrawal. Start with doses on an as-needed basis (0.05 mg/kg as a starting dose). If the newborn needs frequent as-needed doses, initiate scheduled dosing, usually every 3 hours. The morphine dose can be increased until the symptoms are controlled or the maximum dose of 1 mg/kg/d is reached.

Once the symptoms are controlled, taper the dose every 12 to 24 hours, as long as the withdrawal symptoms remain controlled.

Other Medications

A newborn who has been exposed to multiple substances in utero is at increased risk for continuing to have severe symptoms of withdrawal despite receiving a maximal dose of morphine. Oral clonidine is a second-line agent (< 7 days of age: 4–6 mcg/kg/d divided into doses administered every 4–6 hours; > 7 days of age: 6–8 mcg/kg/d, divided into doses administered every 4–6 hours; 12-mcg/kg/d maximum for both age groups). Taper the clonidine (decrease by 25% every 3–4 days by increasing the dosing interval) after the morphine has been discontinued. Phenobarbital is an alternative (load with 20 mg/kg, then 5 mg/kg/d either as a single dose or divided into doses administered every 12 hours; taper after all other medications have been discontinued by 25% once or twice a week).

Indications for Consultation

- **Neonatology:** For severe withdrawal symptoms, particularly if there is scheduled opioid dosing, a second medication is needed, or supportive care such as tube feeding is needed.
- **Social work and local child protective services (CPS):** In most communities, both prescribed and illicit use of opioid medication often results in a referral to local CPS, who can work with the family to coordinate postdischarge services for both the mother and the newborn.
- **Lactation consultation:** Mother/infant dyads with exposure to opioids may have challenges with breastfeeding initiation related to the symptomatology of NOWS. Hospital lactation support is essential to help mothers latch the baby properly, learn how to soothe the baby while skin-to-skin, and promote attachment.

Disposition

- **Neonatal intensive care unit:** As per institutional policy
- **Discharge:** No significant signs of withdrawal for 24 to 48 hours; feeding adequately with either weight gain or age-appropriate weight loss; consolable by caregivers; follow-up arranged with the primary care physician, subspecialists, or community services

Follow-up

- **Primary care:** Within 1 to 2 days of discharge.
- **Visiting nurse:** Within 1 to 2 days of the primary care visit. A visiting nurse can perform weight checks and also be a resource for the mother to evaluate newborn safety and support safe sleep initiatives and breastfeeding.

- **Early intervention:** Regardless of whether the newborn received pharmacologic care, refer to an early intervention program.

Pearls and Pitfalls

- If possible, allow the mother to stay with the baby while being observed, or treated for, NAS/NOWS to promote bonding and participate in the nonpharmacologic care. If the mother cannot be present, volunteers in a "cuddler" program can help support the infant.
- Women and neonates affected by substance use disorder benefit from a multidisciplinary team approach to care.
- Use a standardized tool to evaluate symptoms and guide the management of infants with NAS/NOWS.
- Nonpharmacologic care is the first line of treatment.
- Decreased exclusivity and continuation of breastfeeding are common in the NOWS population. Continued lactation support after discharge is important in the form of support groups, lactation expertise, and social support for the families.
- Encourage and support breastfeeding for a mother who is engaged in a MAT program with buprenorphine or methadone, if they are adherent with their treatment plan and HIV-negative.
- Coordinate care with appropriate in-hospital and community services to facilitate a smooth discharge for at-risk families.
- A phenobarbital taper can be completed as an outpatient.

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CHAPTER 88

Neonatal Hyperbilirubinemia

Introduction

Jaundice is a common, and generally benign, finding in the neonatal period. Hyperbilirubinemia can lead to neurotoxicity, and it can be an early sign of liver disease, so careful screening and treatment for jaundice is an essential part of routine newborn care. Most cases of jaundice are due to unconjugated (indirect) hyperbilirubinemia, resulting from an imbalance between production and metabolism and excretion of bilirubin. Common conditions that worsen the imbalance include physiological jaundice, breastfeeding jaundice, human-milk jaundice, and ongoing hemolysis caused by ABO incompatibility, glucose-6-phosphatase dehydrogenase (G6PD) deficiency, and other hereditary hemolytic disorders.

Jaundice due to conjugated (direct) hyperbilirubinemia is much less common and far more likely to indicate significant pathology. Conjugated hyperbilirubinemia generally results from a specific defect in bilirubin excretion, and it is critical to identify because early intervention can reduce long-term morbidity and mortality.

Clinical Presentation

History

Jaundice in the first 24 hours after birth is a red flag, because it is never physiological and is usually caused by hemolysis. Other concerning signs include lethargy, high-pitched cry, vomiting, and poor feeding, which can indicate acute bilirubin encephalopathy. Opisthotonus and seizures occur with extremely high bilirubin levels. Although jaundice that persists beyond 3 weeks of age usually reflects human-milk jaundice, it also raises a concern for biliary atresia or neonatal hepatitis.

Obtain intake and output histories, including frequency, amount, and source of nutrition, and composition of any formula. Ask about dark urine or clay-colored stools. Review the maternal and birth history (including fetal ultrasonography [US] results and any genetic testing), look for evidence of a congenital viral infection, and determine the percentage of weight loss, if any. Ask about family history of jaundice or parental consanguinity. Check the newborn screening results, if available.

Physical Examination

Obtain the vital signs and growth parameters, and assess the infant for signs of dehydration. Measure the size of the liver and spleen and palpate for

abdominal masses and ascites. Document the level of jaundice and the presence of bruising or cephalohematomas. Note dysmorphic features that can be associated with syndromes, such as triangular facies in Alagille syndrome, macroglossia in hypothyroidism, and microcephaly in congenital cytomegalovirus (CMV).

Laboratory Workup

Obtain total serum bilirubin (TSB). If elevated, also order a direct bilirubin level, a complete blood cell count (CBC) with differential and smear, and reticulocyte count, along with a blood type and direct antibody test (Coombs test), if the previous results are unavailable. Transcutaneous bilirubin (TcB) is an acceptable screening test, but obtain a venous or capillary TSB if the infant is more than mildly jaundiced or has an elevated TcB. Estimates based on examination findings alone are not accurate. If the TSB level is 25 mg/dL (427.6 mcmol/L) or greater, or over 20 mg/dL [342.1 mcmol/L] in a sick or preterm infant, send blood for type and crossmatch and an albumin level. Calculate the ratio of TSB to albumin, which is one criterion for determining the need for an exchange transfusion, because bilirubin that is unbound to albumin more readily crosses the blood-brain barrier.

If the history and physical examination findings suggest sepsis, obtain blood, urine, and cerebrospinal fluid samples for culture and full analysis. New-onset jaundice after 2 weeks of age can be the presenting sign of a urinary tract infection (UTI), especially in a patient with galactosemia.

Obtain a quantitative G6PD level, if suggested by the patient's ethnic or geographic origin (African, Mediterranean, Middle Eastern, Southeast Asian), or if the patient has a poor response to phototherapy or has evidence of ongoing hemolysis (decreasing hemoglobin or hematocrit and increasing aspartate aminotransferase [AST] and lactate dehydrogenase [LDH] levels). A G6PD screening test can be positive during an acute hemolytic episode, so it is important to order a quantitative (not a qualitative) G6PD assay.

If the infant has conjugated (direct) hyperbilirubinemia, consult a gastroenterologist to determine the appropriate testing, which may include obtaining blood for culture and CBC; albumin, AST, serum glutamic pyruvic transaminase, alkaline phosphatase, and glucose levels; prothrombin time, partial thromboplastin time, and hepatitis serologies; as well as urine for bacterial and CMV culture, urinalysis, and reducing substances. If clinically suspected, repeat testing for galactosemia and hypothyroidism, because these require urgent management to prevent serious sequelae. If the results are negative for sepsis, UTI, or other specific disease, perform an abdominal US and obtain an α1-antitrypsin level.

Differential Diagnosis

The differential diagnosis of unconjugated hyperbilirubinemia is summarized in Table 88–1, and the differential diagnosis of conjugated hyperbilirubinemia is presented in Table 88–2.

Table 88–1. Differential Diagnosis of Unconjugated Hyperbilirubinemia

Diagnosis	Clinical Features
Common Diagnoses	
Human-milk jaundice	Presents after 7 d and may last for weeks ↑TSB < 0.5 mg/dL/h (< 8.6 mcmol/L/h) TSB usually does not reach phototherapy levels
Dehydration/breastfeeding jaundice	Often due to poor feeding Poor weight gain < 3–4 stools/d and < 6–7 wet diapers/d
Physiological origin	Presents at 24–72 h and resolves by 10 d (−) Coombs test
Less Common Diagnoses	
ABO/Rh incompatibility	Can present in first 24 h after birth (+) Coombs test ↓ Hemoglobin level compared to level in the newborn nursery
G6PD deficiency	African, Mediterranean, Middle Eastern, or Southeast Asian background Poor response to phototherapy Abnormal quantitative G6PD enzyme assay
Hypothyroidism	Delayed stool production after birth Macroglossia, large fontanelles May have conjugated hyperbilirubinemia
Infection/sepsis	Vomiting, lethargy, temperature instability Suspect urinary tract infection if onset after 2 wk May have conjugated hyperbilirubinemia
Rare Diagnoses	
Crigler-Najjar syndrome	Presents at 1–3 d after birth TSB > 15 mg/dL (> 256.6 mcmol/L) Type I responds to phenobarbital treatment
Other hemolytic disorders	Can present in first 24 h after birth (−) Coombs test Peripheral smear: abnormally shaped red blood cells
Polycythemia	Plethora, lethargy/irritability, jitteriness Hematocrit level > 65%
Sequestered blood	Cephalohematoma, bruising, central nervous system hemorrhage

Abbreviations: G6PD, glucose-6-phosphate dehydrogenase; TSB, total serum bilirubin.
+ indicates positive finding; -, negative finding; ↑, elevated level; ↓, decreased level.

Table 88–2. Differential Diagnosis of Conjugated Hyperbilirubinemia

Diagnosis	Clinical Features
Common Diagnoses	
Biliary atresia	Presents in the first 2 mo after birth More common in preterm infants 3:2 female preponderance Hepatosplenomegaly (may not be present early in the course)
Idiopathic neonatal hepatitis	Recovery without intervention (most cases) Diagnosis usually requires liver biopsy
TPN cholestasis	Usually after 2 wk of TPN Reverses when TPN stops
UTI/sepsis	Vomiting, lethargy, temperature instability May also have unconjugated hyperbilirubinemia
Less Common Diagnoses	
α1-Antitrypsin deficiency	(+) Family history Liver biopsy: (+) periodic acid–Schiff stain granules
Alagille syndrome	Facies: broad forehead, deep-set eyes, pointed chin Congenital heart disease, butterfly vertebrae Liver biopsy: paucity of small bile ducts
Choledochal cyst	May have a palpable right upper quadrant mass Can present in the neonatal period, or later
Congenital infection	CMV; other toxoplasmosis, other agents, rubella, cytomegalovirus, herpes simplex; HIV; parvovirus B19, hepatitis B virus; hepatitis C virus Intrauterine growth restriction Hepatosplenomegaly, thrombocytopenia, rash Abnormal funduscopic or slit-lamp examination findings
Cystic fibrosis	May have (+) family history Delayed stool production, meconium ileus Abnormal newborn screen results, (+) sweat test
Galactosemia	Poor growth, hypotonia, cataracts, liver dysfunction *Escherichia coli* sepsis or UTI Abnormal newborn screen results, quantitative gut-associated lymphoid tissue test (+) Urine-reducing substances
Gallstones/biliary sludge	May have history of TPN, hemolysis, or fasting (+) Ultrasonography
Hypothyroidism	Delayed stool passage after birth, lethargy, hoarse cry Macroglossia, large fontanelles, poor growth May also have unconjugated hyperbilirubinemia
Panhypopituitarism	Normal growth parameters, micropenis Lethargy, hypotension, temperature instability Hypoglycemia, electrolyte disturbances
Tyrosinemia	Failure to thrive, vomiting, diarrhea, bleeding, hepatomegaly Cabbage-like odor Abnormal newborn screen results and/or plasma amino acid and urine organic acid analysis findings

Abbreviations: CMV, cytomegalovirus; TPN, total parenteral nutrition; UTI, urinary tract infection.
+ indicates positive finding.

Treatment

Unconjugated Hyperbilirubinemia

For an infant 35 weeks or older, check Bilitool (www.bilitool.org/), which is consistent with American Academy of Pediatrics (AAP) guidelines, for risk zone assessment (≥ 38 weeks) and treatment recommendations with intensive phototherapy. Have the following information available when entering the site: date and time of birth, date and time of blood sampling (or the infant's age in hours), and total bilirubin level. Recommendations for intensive phototherapy (more than double bank) will depend on TSB level, gestational age, rate of bilirubin rise, and risk factors for hyperbilirubinemia and neurotoxicity. Modern biliblankets can be used in addition to standard phototherapy. They permit continuous treatment while a caregiver holds and feeds the baby. Risk factors for severe hyperbilirubinemia are summarized in Box 88–1.

Monitor the response to therapy by retesting the TSB level in 2 to 12 hours, depending on the infant's age and prior levels. Transcutaneous bilirubin measurements on exposed (uncovered) skin are unreliable once treatment is initiated. Discontinue phototherapy when the TSB level decreases to less than 13 to 14 mg/dL (222.4–239.5 mcmol/L). A rebound bilirubin test is not routinely indicated, except for an infant with a positive Coombs test and signs of ongoing hemolysis. To determine the risk of rebound, use the Rebound Hyperbilirubinemia Calculator (https://jscalc.io/calc/68NNiFfS7iTMZhZY).

The criteria for exchange transfusion are TSB level above exchange transfusion thresholds, bilirubin rate of increase greater than 0.5 mg/dL/h (> 8.6 mcmol/L/h) despite intensive phototherapy, or clinical symptoms of acute bilirubin encephalopathy, regardless of bilirubin level. Intravenous immunoglobulin (0.5–1.0 g/kg) is a safe and effective adjunctive therapy.

Encourage more frequent feeding (every 2–3 hours) with breastfeeding, mother's expressed milk, donor human milk, or milk-based formula. Do not

Box 88–1. Important Risk Factors for Severe Hyperbilirubinemia

Predischarge TSB or TcB measurement in the high-risk zone (≥ 38 weeks)
Younger gestational age (35–37 weeks)
Cephalohematoma/bruising
Jaundice in the first 24 hours after birth
Exclusive breastfeeding, especially with poor latch and/or excessive weight loss
Previous sibling with jaundice
Isoimmune or other hemolytic disease
East Asian race

Abbreviations: TcB, transcutaneous bilirubin; TSB, total serum bilirubin.
Adapted from the American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics.* 2004;114(1):297–316.

administer intravenous hydration unless the infant is severely dehydrated or unable to tolerate oral feedings.

If jaundice is caused by an acute illness (UTI, sepsis, hypothyroidism), treat the underlying cause.

Conjugated Hyperbilirubinemia

If there is evidence of biliary obstruction, consult a gastroenterologist and/or a pediatric surgeon. Urgent workup and management are necessary to avoid morbidity and mortality from metabolic conditions such as inborn errors and surgical conditions such as biliary atresia. Treatment options include the Kasai procedure (for biliary atresia), liver transplantation (for tyrosinemia or late biliary atresia), choledochal cyst excision, cholecystectomy, and bile duct resection.

Ensure adequate nutritional support and medical management of any underlying disorders. Consult a geneticist and an experienced nutritionist for dietary guidelines for liver and metabolic diseases.

Indications for Consultation

- **Gastroenterology:** Conjugated hyperbilirubinemia
- **Geneticist:** Suspected metabolic disease
- **Lactation consultant:** All infants undergoing phototherapy or with concern for hyperbilirubinemia
- **Pediatric surgery:** Suspected extrinsic/biliary obstruction

Disposition

- **Intensive care unit transfer:** Need for exchange transfusion
- **Discharge criteria (unconjugated hyperbilirubinemia):** TSB level less than 13 to 14 mg/dL (222.4–239.5 mcmol/L), good oral intake with adequate urine output and stool production patterns

Follow-up

- **Primary care:** Within 24 hours, for a follow-up bilirubin level evaluation

Pearls and Pitfalls

- Some infants with cholestatic jaundice exposed to phototherapy may develop a dark, grayish-brown discoloration of the skin, serum, and urine (bronze baby syndrome).
- Chronic bilirubin encephalopathy (kernicterus) is characterized by severe athetoid cerebral palsy, paralysis of upward gaze, hearing loss, and intellectual impairment.

- Universal predischarge bilirubin screening may be performed by using TSB or TcB measurements. However, obtain a TSB level if the TcB value indicates high-intermediate or high risk according to the AAP guidelines or Bilitool, because TcB values tend to lead to underestimation of TSB values, and risk zones, at higher levels. In addition, TcB values are not useful after phototherapy.
- Clinical assessment of jaundice is inaccurate, and TcB measurements may be less useful in darker-skinned infants.
- Blue LED lights are most effective at lowering TSB level. At these wavelengths (450–475 nm), light penetrates the skin and is maximally absorbed by bilirubin.
- Breastfeeding jaundice and human-milk jaundice are *not* contraindications to continuing breastfeeding, even if other fluid supplementation is needed.
- Phototherapy is only indicated for indirect, not direct, hyperbilirubinemia.
- An elevated direct bilirubin is never normal.

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Nutrition

CHAPTER 89

Fluids and Electrolytes

Introduction

Volume depletion (dehydration) and electrolyte disturbances are common in hospitalized children. While most instances are relatively mild, in severe cases they can result in shock, seizures, coma, and death. Hypovolemia can occur with an increased, normal, or decreased serum sodium (Na^+) level (hypertonic, isotonic, or hypotonic hypovolemia), and abnormalities in serum Na^+ level can be seen in patients without hypovolemia (eg, syndrome of inappropriate antidiuretic hormone secretion [SIADH]).

Clinical Presentation: Dehydration

History

Assess the patient's intake (volume and specific fluid) and losses (vomitus, stool, urine). Usually there is a history of emesis, diarrhea, decreased oral intake and urinary output, malaise, or central nervous system (CNS) depression. High fever, high-pitched cry, and irritability can occur with hypernatremic dehydration.

Physical Examination

Evaluate the child's general appearance and look for signs of dehydration, including sunken eyes, dry mucous membranes, and absence of tears. Tachycardia (pulse > 95th percentile for age) and orthostatic pulse changes are early signs of hypovolemia. However, fever can be a confounder because it increases the heart rate by about 10 beats/min for each degree above 37 °C (98.6 °F). Overt hypotension is a late finding in hypovolemic shock, and its absence does not exclude the diagnosis of significant hypovolemia. Check the capillary refill by raising the extremity to be tested slightly above the heart and briefly pressing the nail bed on a finger or toe to compress the underlying capillaries (blanching). Observe as the skin returns to a normal color once the pressure is released. Moderate to severe dehydration and most types of shock cause a sluggish or prolonged capillary refill time greater than 2 seconds, although this can also occur as a consequence of simple exposure to a cold external environment.

Laboratory Workup

There is no need for laboratory testing for mild dehydration. For moderate or severe dehydration, obtain a set of electrolyte levels, if not previously done, as well as a urinalysis. The serum Na^+ level is not a reflection of volume status

and must be interpreted in the context of whether the patient is hypovolemic, euvolemic, or hypervolemic. Investigate causes of an abnormal glucose level, acidosis, and increased anion gap (normal < 12 mEq/L [< 12 mmol/L]). Assess the urine for ketone bodies, which are products of fatty acid oxidation during fasting or hypoglycemia.

$$\text{Anion gap} = [Na^+ - (\text{chloride} + \text{bicarbonate})]$$

Suspect acute kidney injury (AKI) if the patient is oliguric despite no clinical signs of dehydration, inappropriately polyuric, or has a blood urea nitrogen/creatinine ratio that is disproportionately high or continues to increase despite proper management. The obligatory urine output is 1 mL/kg/h for a child and 0.5 mL/kg/h for an adolescent.

Suspect SIADH (postoperative, pulmonary or CNS disease, malignancies, medications) if the patient presents with hyponatremia and inappropriately high urine osmolality, without clinical signs of dehydration. If AKI or SIADH is suspected, calculate the serum/urine ratios and the fractional excretion of Na^+ (FE_{Na}), which will generally be less than 1% in a patient with normal renal function, greater than 1% in a patient with renal disease, and less than 1% to 2% in a patient with SIADH, depending on Na^+ intake (Table 89–1):

$$FE_{Na} = (\text{urine } Na^+ \times \text{plasma creatinine})/(\text{plasma } Na^+ \times \text{urine creatinine}) \times 100$$

When the plasma osmolality is low, suggesting SIADH, use the urine/serum osmolality ratios as shown in Table 89–1. Repeat the electrolyte assessments 4 to 6 hours later if the patient is not improving or has significant abnormalities in the serum Na^+ or potassium (K^+) levels, severe acidosis, or signs of possible renal dysfunction. If the child has persistent ongoing losses and is primarily or

Table 89–1. Laboratory Values in Oliguria

	Prerenal	Renal	SIADH
Urine			
Sodium level (mEq/L)	< 20	> 40	> 40
Specific gravity	> 1.020	~1.010	> 1.020
Osmolality (mOsm/kg)	> 500	< 350	> 500
Urine/Serum Ratios			
Urine/serum osmolality	> 1.3	< 1.3	> 2
Urine/serum urea level	> 20	< 10	> 15
Urine/serum creatinine level	> 40	< 20	> 30
FE_{Na} (%)	< 1	> 2	< 1–2

Abbreviations: FE_{Na}, fractional excretion of sodium; SIADH, syndrome of inappropriate antidiuretic hormone secretion.
To convert milliequivalents per liter to millimoles per liter for sodium level, multiply by 1.0. To convert milliosmoles per kilogram to millimoles per kilogram for osmolality, multiply by 1.0.

exclusively receiving intravenous (IV) fluids, check the electrolyte levels daily for the first 2 to 3 days, then as warranted by the clinical condition. The causes of Na^+ and K^+ level abnormalities are summarized in Table 89–2.

Treatment: Fluid and Electrolyte Therapy

Calculate a patient's fluid and electrolyte requirements based on the clinical presentation and underlying diagnosis. Take into consideration the severity of illness, as well as the basal metabolic needs, initial hydration and electrolyte status (deficits), and ongoing losses. Acute changes in body weight reflect fluid losses. For example, a 20-kg patient who is 10% dehydrated has lost 2 kg, equal to 2 L of fluid. Markedly decreased urinary output implies greater than 10% dehydration.

Maintenance therapy is required to preserve intravascular volume in a euvolemic, otherwise healthy patient who does not have any abnormal deficits or ongoing losses, such as an infant with pre- or postoperative status. Add glucose, Na^+, and K^+ (only if the patient is voiding, without hyperkalemia) requirements to prevent iatrogenic hypoglycemia, hyponatremia, and/or

Table 89–2. Causes of Sodium and Potassium Level Abnormalities

Diagnosis	Causes
Hyponatremia	
Pseudo/fictitious	Hyperlipidemia, hyperproteinemia, hemolysis
Factitious	Hyperglycemia (diabetic ketoacidosis) Na^+ level ↓ 1.6 mEq/L (1.6 mmol/L) for each ↑ 100 mg/dL (5.55 mmol/L) of glucose
Euvolemic	Syndrome of inappropriate antidiuretic hormone secretion (CNS or pulmonary disease, medications, postoperative, malignancy)
Hypovolemic	Burns, dietary, cerebral salt wasting, gastrointestinal losses, iatrogenic
Hypervolemic	Cardiac impairment, edema, renal disease (nephrotic syndrome), iatrogenic origin, liver failure
Hypernatremia	
With ↓ total body Na^+ level	Diarrhea, renal disease, sweat
With normal total body Na^+ level	Diabetes insipidus (central, nephrogenic), heat
With ↑ total body Na^+ level	Hyperaldosteronism, iatrogenic, renal disease
Hypokalemia	
	Dietary issues (chronically ill), gastrointestinal losses, medications (β-agonists, diuretics), renal disease
Hyperkalemia	
	Acidosis, Addison disease, congenital adrenal hyperplasia, iatrogenic origin, medications, renal disease, rhabdomyolysis

Abbreviations: CNS, central nervous system; Na^+, serum sodium level.
↓ indicates decreased level; ↑, increased level.

hypokalemia. Overnight maintenance IV fluid is typically not needed in a euvolemic older child without ongoing losses who is receiving nothing by mouth for next-day surgery. However, avoid prolonged fasting prior to surgery.

Maintenance Fluid

Use the Holliday-Segar method (Table 89–3) for a patient weighing more than 3.5 kg. If the child is obese, use the ideal body weight or the 50th percentile weight for the child's height. These calculations are for an otherwise healthy child. For a patient who is ill or dehydrated, adjust the fluids to reflect the volume deficit, maintenance requirements, and clinical course (eg, changes in oral intake, urine output, ongoing losses). Use 5% dextrose to minimize catabolism, because this will provide 2 to 4 mg/kg/min of glucose infusion, equivalent to the liver glucose production rate.

Maintenance Electrolytes

Replace the daily Na^+ and K^+ losses in the sweat, urine, and stool. Use a solution that is at a minimum 0.45 normal saline (NS) and has 1 to 2 mEq/kg/d (1–2 mmol/kg/d) of K^+ (generally, 20 mEq/L [20 mmol/L] of K^+ will suffice). Defer administering K^+ if the patient has hyperkalemia, marked oliguria/anuria, or suspected renal insufficiency. Avoid concentrations of K^+ greater than 20 mEq/L (> 20 mmol/L) in a peripheral IV catheter to prevent phlebitis.

If a patient will be receiving nothing by mouth and receiving IV maintenance fluids for more than 48 hours, use an isotonic solution (NS, lactated Ringer [LR] solution). This will prevent iatrogenic hyponatremia. Normal saline can also be used as the initial IV maintenance fluid.

Volume Depletion

Calculate the fluid deficit and add that volume (as NS) to the daily maintenance fluids to be infused over 24 hours. However, correct significant volume depletion with urgent bolus infusions of NS.

Ongoing Losses

Always consider ongoing losses of both volume and Na^+ (emesis Na^+ level: 60–155 mEq/L [60–155 mmol/L]; diarrhea Na^+ level: 40–120 mEq/L

Table 89–3. Holliday-Segar Method

Body Weight	Water (mL/kg per 24 h)
First 10 kg of body weight	100
Second 10 kg of body weight	50
Each additional kilogram (> 20 kg)	20

[40–120 mmol/L]; third-spacing Na^+ level: 140 mEq/L [140 mmol/L]). Measure volume losses and assess replacement needs every 4 hours.

Severe Hyponatremia With Seizures (Na^+ Level < 120 mEq/L [< 120 mmol/L])

Use 3% sodium chloride (513 mEq/L [513 mmol/L]) through a central venous line until the seizures stop (1.2 mL/kg will increase serum Na^+ levels about 1 mEq/L [1 mmol/L]). Administer the sodium chloride slowly if only a peripheral IV catheter is available.

For nonemergent correction, increase the serum Na^+ level by no more than 0.5 mEq/L/h (0.5 mmol/L/h) to prevent central pontine myelinolysis.

Hypernatremia (Na^+ Level > 145 mEq/L [> 145 mmol/L])

$$\text{Free water deficit} = 4\ \text{mL/kg} \times \text{weight} \times (Na^+_{\text{plasma}} - Na^+_{\text{desired}})$$

Decrease the serum Na^+ level by no more than 0.5 mEq/L/h (0.5 mmol/L/h) to prevent cerebral edema.

Hypokalemia (K^+ Level < 3 mEq/L [< 3 mmol/L])

To properly interpret the serum K^+ level, consider the effect of blood pH level on the intracellular-extracellular movement of K^+. A decrease of 0.1 in blood pH level increases the serum K^+ level by approximately 1 mEq/L (1 mmol/L), while an increase of 0.1 in blood pH level decreases the serum K^+ level by approximately 1 mEq/L (1 mmol/L). In addition, note that only 2% of the total body K^+ (TBK) level is found in plasma, with most being in the intracellular space. Each 1-mEq/L (1-mmol/L) decrease in serum K^+ level represents a decrease in TBK level of approximately 12%. Therefore, in general, hypokalemia implies marked TBK depletion.

Symptoms of moderate hypokalemia include muscular weakness, myalgia, gastroparesis, and muscle cramps. Severe hypokalemia leads to depressed muscle function, flaccid paralysis, diminished reflexes, respiratory depression, and, potentially, rhabdomyolysis. Severe hypokalemia is characterized by electrocardiogram (ECG) abnormalities, such as a prominent U wave after the T wave, ST segment depression, and atrioventricular conduction abnormalities.

Whenever possible, correct a K^+ deficiency enterally, because this is much safer. Mild hypokalemia will usually resolve with oral repletion. However, severe symptomatic hypokalemia requires IV K^+ correction with 0.5 mEq/kg (0.5 mmol/kg) per dose (20-mEq [20-mmol] maximum). A rapid infusion of K^+ is rarely needed and requires close monitoring, preferably in an intensive care unit (ICU). Correct a significant K^+ deficit slowly over 3 to 5 days with an IV solution containing 30 to 40 mEq/L (30–40 mmol/L)

of potassium chloride or potassium acetate (if the patient is acidotic). Do not exceed an infusion rate of 0.5 mEq/kg/h (0.5 mmol/kg/h) or 4 to 5 mEq/kg/d (4–5 mmol/kg/d) and do not use a K^+ concentration greater than 40 mEq/L (> 40 mmol/L) through a peripheral IV catheter because it can cause acute phlebitis.

Hyperkalemia (K^+ Level > 6 mEq/L [> 6 mmol/L])

Recheck the electrolyte levels to confirm the K^+ level, check the bicarbonate level to assess for acidosis (which causes a K^+ shift into the extracellular fluid), look for hemolysis of the sample (spurious hyperkalemia), and obtain an ECG. If there are findings consistent with hyperkalemia (peaked T waves, shortening of the QT interval, prolonged PR interval, widened QRS complex) or if the K^+ level is greater than 7 mEq/L (> 7 mmol/L), initiate treatment, preferably in an ICU. First, administer 10% calcium gluconate to protect the myocardium: 1 mL/kg = 100 mg/kg per dose over 5 to 10 minutes (500-mg/kg/d maximum), and repeat in 6 hours, if necessary. Discontinue the administration of exogenous K^+ and use therapeutic agents that can transiently redistribute K^+: 25% dextrose (2 mL/kg over 30 minutes and repeat every 30 minutes), along with regular insulin (1 U/kg/h), as well as nebulized albuterol. To enhance K^+ excretion, use a loop diuretic (IV furosemide 1–2 mg/kg every 6 hours) and polystyrene sulfonate (1 g/kg). Dialysis is indicated for life-threatening hyperkalemia.

Ongoing Losses

Gastrointestinal (emesis, diarrhea, ileus, third-spacing), renal, and insensible water losses affect fluid maintenance requirements. Assess ongoing losses frequently, because they may change rapidly (Table 89–4).

Table 89–4. Changes in Maintenance Fluid Requirements

Condition	Increase	Decrease
Activity (eg, seizures)	30%	NA
Anuria/oliguria	NA	50%
Diabetes insipidus	≥ 200%–400%	NA
Diarrhea	≥ 10%–50%	NA
Humidified oxygen	NA	25%–40%
Hyperventilation	50%–65%	NA
Polyuria (eg, diabetic ketoacidosis)	100%	NA
Sweat	5%–50%	NA
Temperature	12% per degree Celsius > 37 °C	12% per degree Celsius < 37 °C

Abbreviation: NA, not applicable.

Resuscitation Fluids Practical Guidelines

What follows is a safe, simplified method to minimize common iatrogenic fluid and electrolyte disturbances. However, this plan is not a substitute for clinical judgment and assessing and reassessing the status of the patient.

Start Fluid Resuscitation With an Isotonic Solution (NS or LR)

1. Administer 20-mL/kg IV boluses over 15 to 20 minutes.
2. Reassess and repeat boluses as needed, up to 60 mL/kg in 60 minutes. Always consider possible life-threatening conditions that require a different approach, especially if more than 80 mL/kg is needed. These include sepsis (fever and hypotension), congestive heart failure (CHF) or myocarditis (respiratory distress, gallop rhythm, hepatomegaly), intracranial hypertension (history of hydrocephalus; bradycardia, altered mental status), and adrenal crisis (unresponsive shock). When CHF or myocarditis is a concern, administer multiple small boluses of 10 mL/kg rather than larger boluses, and monitor the response closely to avoid fluid overload. Follow the changes in pulse, blood pressure, urine output, and pulmonary auscultation, and change the fluid management as necessary.
3. If the patient is in shock, rapidly secure intraosseous access if IV access appears suboptimal.

Subsequent Fluid and Electrolyte Therapy

1. Calculate the maintenance (Holliday-Segar method) and deficit fluid volumes (as detailed earlier) while monitoring ongoing losses.
   a. Isonatremic/hyponatremic dehydration: Use 5% dextrose one-half NS or NS with 20-mEq/L (20-mmol/L) potassium chloride. This will provide additional sodium chloride to slowly compensate for the deficit, as well as the K^+ and glucose requirements (2–4 mg/kg/min).
   b. Hypernatremic dehydration: Use 5% dextrose one-quarter to one-half NS with 20-mEq/L (20-mmol/L) potassium chloride over *48 hours.*
   c. Confirm that the patient has voided before adding K^+ to the IV fluids.
   d. Resume oral feeding as early as possible. Allow breastfeeding ad lib, if clinically stable.
   e. Monitor the patient's pulse, blood pressure, and urine output.
2. If the patient is stable and well hydrated (postrehydration, nothing by mouth).
   a. Weight less than 10 kg: 5% dextrose one-quarter NS with 20-mEq/L (20-mmol/L) potassium chloride.
   b. Weight greater than 10 kg: 5% dextrose one-half NS or 5% dextrose NS with 20-mEq/L (20-mmol/L) potassium chloride.

Indications for Consultation

- **Endocrinology:** Possible adrenal crisis or urine output greater than 5 mL/kg/h (diabetes insipidus)
- **Metabolism:** Laboratory findings suggestive of a metabolic disorder (severe acidosis, unexplained increased anion gap, and/or hypoketotic hypoglycemia)
- **Nephrology:** Anuria or signs of renal disease (increased creatinine level), severe hypo- or hypernatremia or hypo- or hyperkalemia

Disposition

- **ICU transfer:** Shock not responding to resuscitation fluids, AKI, hyperkalemia requiring IV medications, severe hypokalemia, severe hypo- or hypernatremia
- **Discharge criteria:** Patient back to premorbid weight, tolerating maintenance oral fluids, with adequate urine output ($\geq$ 1 mL/kg/h)

Follow-up

- **Primary care:** 1 to 3 days

Pearls and Pitfalls

- To avoid fluid overload, use the patient's ideal body weight or the 50th percentile weight for height for an obese patient.
- Assume greater than 10% dehydration if the patient is anuric/oliguric or has hypernatremic dehydration.
- As a result of reperfusion, severe metabolic acidosis can worsen immediately after rehydration.
- In the context of oliguria, FE_{Na} less than 1% suggests prerenal azotemia, rather than intrarenal injury/acute tubular necrosis.
- Proteinuria and glucosuria can increase the urine specific gravity and thereby mask a renal concentrating defect.
- Always consider the possibility of acute adrenal insufficiency in a hypotensive, unresponsive patient with hyponatremia and/or hyperkalemia.
- Monitor ongoing losses and add them to maintenance and replacement fluids. These can be significant, especially with secretory diarrhea.
- While albuterol can temporarily lower the serum K^+ level, it does not cause systemic loss. There is no need to correct such a low K^+, unless there are ECG changes or another cause for hypokalemia is suspected.

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Obesity

Introduction

Nearly 1 in 5 American children have obesity. This national epidemic, reflecting the effects of social inequities, has disproportionately affected Hispanic, non-Hispanic Black, native Hawaiian, and Pacific Islander children, and those in under-resourced communities. Severe, or class II and class III obesity, is associated with a higher incidence of cardiovascular disease (CVD), type 2 diabetes mellitus (T2DM; see Chapter 26, Diabetes Insipidus), depressive symptoms, and anxiety, all of which are likely to persist into adulthood.

Most obesity results from excessive caloric intake compared to energy expenditure. Endocrinologic causes (hypothyroidism, Cushing syndrome) will usually have certain specific symptoms at the time of presentation. Medications can cause weight gain as well, such as steroid hormones, psychotropic agents, and antiepileptics. There are some rare syndromic causes of obesity, such as Prader-Willi syndrome, Bardet-Biedl syndrome, and McCune-Albright syndrome, which are associated with some combination of short stature, hypogonadism, developmental delay, and dysmorphic features.

Definition

For children 2 years of age and older, calculate the patient's age- and sex-specific body mass index (BMI) as follows:

$$\text{BMI} = (\text{mass in kilograms})/(\text{height in meters})$$

A patient with an age- and sex-specific BMI at or above the 95th percentile has obesity. Class II severe obesity includes patients at or above 120% of the 95th percentile; class III severe obesity is defined by a BMI at or above 140% of the 95th percentile.

Clinical Presentation

History

Ask about diet, physical activity, sleep history, early growth trajectory, any diabetes symptoms, and development, as well as menstrual history in females. Review the family history for obesity, T2DM, thromboembolic events, hypertension, and dyslipidemias. Assess the patient for psychological comorbidities (depression, bullying, anxiety, disordered eating) and social determinants of health that may increase the difficulty of maintaining a healthy diet or routine

physical activity. Review past and current medications, as well any prior or ongoing attempts at weight management.

Physical Examination

Priorities include the BMI, blood pressure, Tanner stage, and skin inspection for acanthosis nigricans (associated with hyperinsulinemia and diabetes), abdominal striae, and intertrigo. While hirsutism and acne are relatively common in female adolescents with obesity or overweight (BMI at or above the 85th percentile, yet below the 95th percentile), the presence of these signs suggests the possibility of polycystic ovary syndrome (PCOS). Perform a musculoskeletal examination to look for a limp, hip and/or knee pain, and pes planus.

Comorbidities

As with adults, there are significant comorbidities associated with childhood obesity that may affect inpatient management.

Endocrine

Insulin Resistance/Type 2 Diabetes

Obesity leads to insulin resistance and abnormal glucose tolerance, which are common precursors to T2DM. Institute screening at 10 years of age for any child with overweight who has 2 or more of the following risk factors: family history positive for T2DM (first- or second-degree relative); or physical findings or signs of insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, PCOS). For such patients, obtain a hemoglobin A1c (HbA_{1c}) level (a level of > 5.7% is prediabetic), although a fasting blood glucose level greater than 100 mg/dL (> 5.55 mmol/L) may also be used. The HbA_{1c} level is preferred for an inpatient, since acute illness, intravenous fluids, and corticosteroid use can all affect blood glucose levels.

Metabolic Syndrome

Metabolic syndrome is a complex disorder defined by a cluster of interconnected risk factors that increase the likelihood of developing CVD and T2DM. While metabolic syndrome is well defined in adults, its identification in childhood and adolescence remains somewhat controversial. Adult criteria include increased fasting plasma glucose level greater than 100 mg/dL (> 5.55 mmol/L), central (abdominal) obesity, increased triglyceride levels at or above 150 mg/dL (≥ 1.7 mmol/L), decreased high-density lipoprotein (HDL) cholesterol level (< 40 mg/dL [< 1.04 mmol/L] in males; < 50 mg/dL [< 1.3 mmol/L] in females), and blood pressure of 130/85 mm Hg or greater. Early

identification of these risk factors is important because they tend to track relatively well throughout adulthood and suggest an increased risk of CVD and T2DM.

Polycystic Ovary Syndrome

Clinical history and laboratory findings include menstrual irregularity, hirsutism, acne, and increased insulin levels. However, oligomenorrhea independent of PCOS is common in the first 2 years after menarche, and there are other conditions that may mimic PCOS. If PCOS is suspected, obtain a free testosterone level and luteinizing and follicle-stimulating hormone levels, as well as an early morning 17-OH progesterone level. Depending on the clinical picture, a total testosterone, dehydroepiandrosterone sulfate, sex hormone–binding globulin, prolactin, and/or free thyroxine and thyroid-stimulating hormone levels may be indicated to exclude other conditions. Do not obtain sonographic evaluation of the ovaries for a patient who is younger than 17 years, as there is a high prevalence of large, multicystic ovaries in this age group.

Cardiovascular

Hypertension

A child with obesity has a 4-fold greater risk of increased systolic blood pressure and a 2-fold greater risk of increased diastolic blood pressure. Persistent increased blood pressure is an indication for renal and cardiac assessment. Be aware that falsely increased blood pressure readings may occur in a patient with obesity if an undersized cuff is used.

Dyslipidemia

In general, children and adolescents with obesity are more likely to have increased levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol, and reduced levels of HDL cholesterol. If feasible, obtain a fasting lipid profile in a patient older than 2 years with a BMI in the 85th percentile or above, if not performed previously.

Respiratory

Almost half of all children with obesity can develop obstructive sleep apnea (OSA) and chronic hypoxemia, which may contribute to insulin resistance and low-level inflammation, independent of BMI. Nocturnal polysomnography is the standard test for diagnosing OSA. In addition to OSA, obesity hypoventilation syndrome (Pickwickian syndrome), when both awake and asleep, may occur in individuals who have severe obesity. There is also an association between obesity and asthma. Consult with a pediatric pulmonologist if the patient has dyspnea, as pulmonary function testing may be needed

to distinguish among obstructive lung disease, restrictive lung disease, and poor conditioning.

Neurologic

A child who has obesity is at risk for developing idiopathic increased intracranial pressure and pseudotumor cerebri, which may present as severe headache and transient visual disturbances, associated with papilledema on examination. Cerebrospinal fluid cell count and chemistry values will be normal, but the opening pressure will be elevated. The brain parenchyma and ventricles appear normal on neuroimaging, but there may be optic nerve tortuosity, flattening of the posterior globe, an empty sella, or transverse venous sinus stenosis.

Gastrointestinal

Nonalcoholic Fatty Liver Disease

Up to 10% of children with overweight have histologic evidence of hepatic steatosis, which may progress to steatohepatitis and, eventually, cirrhosis. Males are at higher risk of nonalcoholic fatty liver disease (NAFLD). Though alanine transaminase (ALT) and aspartate aminotransferase levels are often increased, they have low sensitivity and specificity for detection of NAFLD. An ALT level increased 2 times the upper limit of normal, as well as a value greater than 100 U/L ($>$ 1.67 mckat/L), are indications for consultation with a pediatric gastroenterologist. A fatty liver can also be an incidental finding on abdominal imaging obtained for indications other than NAFLD.

Gallstones

As many as 2% of adolescents with obesity may develop gallstones. The risk is greatest in older teens, females, individuals with severe obesity, and patients using oral contraception.

Musculoskeletal

Blount Disease

Blount disease is characterized by abnormal growth of the proximal tibial physis and is more common in males, occurring in up to 3% of obese preadolescent boys. It presents with progressive bowing (genu varum), gait disturbance, and arthritis.

Slipped Capital Femoral Epiphysis

Premenarchal girls or Tanner stage 3 boys with obesity are at increased risk for slipped capital femoral epiphysis (SCFE), which requires immediate surgical correction. Consider an SCFE in any patient with overweight who presents with limp, hip pain, or referred knee pain (commonly medial).

Fractures

Children with obesity may be at increased risk of fractures due to the combination of poor diet (vitamin D deficiency), sedentary lifestyle, greater force generated on impact, and a greater propensity to falls. A patient with obesity is more likely to require surgical correction as opposed to casting to attain adequate healing.

Considerations Specific to Obesity in the Inpatient Setting

Obesity is associated with inflammation, weakened immune response, and increased length of stay after surgery. Obesity is a risk factor for higher mortality in children with critical illness, oncologic diagnoses, and transplants. Patients with obesity are at specific risk for encountering difficulties with airways and anesthesia, as well as developing venous thromboembolism. In addition, obesity is a leading risk factor for severe disease in acute COVID-19 disease, leading to increased hospitalization, intensive care unit admission, ventilator support, and death.

Airway

A patient who has obesity is at increased risk for airway obstruction after administration of general anesthesia. Previously undetected hypopnea or OSA may manifest, and incomplete ventilation during or after anesthesia may lead to ventilation/perfusion mismatch, hypoxemia, and hypercapnia. Although oximetry may be useful, a formal nocturnal polysomnography evaluation and consultation with a pulmonologist or otolaryngologist may be necessary. Patients with extreme obesity are also at risk for obesity hypoventilation syndrome, in which the normal central response to hypercapnia is blunted, significantly increasing postanesthetic complications.

Infection

A child with obesity may be at increased risk for postinfectious complications as a result of the underlying metabolic derangement and the relatively avascular condition of adipose tissue. Give careful attention to skin hygiene and the potential presence of candidal infection (intertrigo).

Venous Thromboembolism

Venous thromboembolism is increasing among pediatric patients, although there is currently no universally accepted screening tool. Risk factors include BMI greater than 30, surgery or trauma, smoking, prolonged immobility or length of stay ($\geq$3 days), malignancy, respiratory disease, inflammatory bowel disease, hypercoagulable states (use of oral contraceptives, acute COVID-19

disease), current or previous indwelling central venous catheter, history of thrombotic events, family history of hypercoagulability or thrombosis (eg, factor V Leiden), osteomyelitis, and staphylococcal infections. See Chapter 46, Deep Venous Thrombosis, for determining when to screen or administer prophylaxis.

Pharmacologic

The pharmacodynamics of a particular drug can be altered by physiologic changes associated with obesity, such as increased circulating blood volume, reduced tissue perfusion, alterations in liver and kidney function, and changes to the gut microbiome. Most pediatric medications are dosed on the basis of body weight, so that some children with obesity seem to require more than an adult dose of a particular drug. In such cases, consultation with a clinical pharmacist may be helpful, but in general, do not exceed the maximum daily adult dose of any medication.

Ergonomics

Standard-sized hospital equipment (eg, blood pressure cuffs, wheelchairs, scales) may be inadequate to meet the needs of a patient with severe obesity. Infrequently, such patients may be unable to undergo procedures such as magnetic resonance imaging (due to weight or size limits) or echocardiography (due to excessive subcutaneous fat). Imaging modalities such as ultrasonography for appendicitis may also be more difficult to perform, which may then increase the need for abdominal computed tomography and the associated radiation exposure.

Approach to the Hospitalized Child With Overweight or Obesity

Management of acute illness often takes precedence over treating obesity. However, always consider the comorbidities and potential complications associated with obesity.

An important first step is to calculate the BMI, enter it into the patient's chart, and document whether the child has overweight or obesity. Hospitalization for an acute illness may provide a "teachable moment" or motivation for a family or patient to consider lifestyle modification, particularly if the child is hospitalized for an obesity-related complication.

Obesity is emotionally charged. Approaching the child and family in a nonjudgmental and empathetic manner can often begin a constructive discussion. Simply asking for the family or patient's permission to discuss weight (a prime tenet of motivational interviewing) may offer a more patient-centered approach and facilitate assistance with nutrition and exercise counseling. Consultation with a registered dietitian or physical therapist may be more

accessible in the inpatient setting for some families and patients, particularly at tertiary centers. At discharge, there may also be opportunities to refer a patient to a pediatric weight management program, if available.

Adolescent bariatric surgery is becoming more available and has generally been shown to be well tolerated and effective. However, challenges related to access and insurance coverage remain. Although weight-loss medications continue to be introduced and prescribed for adults, only orlistat has been approved by the US Food and Drug Administration for use in adolescents, and despite its relative safety, its minimal effectiveness and substantial side effects (steatorrhea) have generally limited its use.

Ample evidence exists that many health care professionals may be biased against patients with overweight. Individuals with obesity report feeling stigmatized in health care settings, which can amplify vulnerability to depression and low self-esteem and dampen motivation to change. Refer to the patient using person-first language, "child with obesity" instead of the "obese child." Unkind or insensitive comments made by hospital staff in the hospital environment and during procedures can affect the experience of the individual in the hospital setting. Having correct instruments and equipment is vital, while focusing on the patient, rather than the obesity, will ensure a more positive interaction.

Options for the Patient With Severe Obesity

Modalities available for this population include low-calorie diets, typically administered in liquid form, and bariatric interventions (eg, gastric bypass, laparoscopic gastric banding). Refer the patient to an obesity center.

Indications for Consultation

- **Cardiology or nephrology:** Severe hypertension
- **Endocrinology:** PCOS, diabetes
- **Gastroenterology/liver:** Dyslipidemia, NAFLD
- **Neurology:** Increased intracranial pressure
- **Orthopedics:** Blount disease, SCFE
- **Psychiatry:** Disordered eating, depression, suicide
- **Pulmonology:** OSA, obesity hypoventilation syndrome, severe restrictive lung disease
- **Surgery:** Gallstones

Pearls and Pitfalls

- Do not visually categorize a patient as having overweight or obesity without calculating the BMI.

- Do not overlook the opportunity to address lifestyle changes while the patient is admitted.
- Refer to the patient using person-first language ("the child with obesity").
- Children with overweight and obesity have the same acute nutrition needs as normal weight children. They should not be subject to longer periods of nothing by mouth due to their weight status.

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Ophthalmology

CHAPTER 91

Ocular Trauma

Introduction

Ocular trauma is the leading cause of noncongenital unilateral vision loss in children. Traumatic injury to the eye is classified as either open or closed globe. Open-globe injury refers to full-thickness injury to the cornea, sclera, or both. Open-globe injury can be further classified as laceration (penetrating, perforating, or intraocular foreign body) or rupture. The closed-globe category consists of contusion or lamellar (partial thickness) laceration

Ocular injuries that require urgent care include ocular burns, an open globe, traumatic optic neuropathy, extraocular muscle entrapment (secondary to orbital fracture), rhegmatogenous retinal detachment (traumatic tear), and retrobulbar hemorrhage.

In terms of chemical injuries, acids cause coagulation necrosis, resulting in corneal scarring and ulceration. Alkalis, which tend to be more severe injuries, lead to saponification of phospholipid layers, epithelial cell death, and caustic penetration of the cornea.

Clinical Presentation

History

With the exception of chemical injuries, where immediate treatment is the priority, obtain a detailed account of the trauma, including time, location (periorbital, head), mechanism of injury, extent (force of impact and how many times it occurred), and whether eye protection was in place. Also screen for other associated injuries. Determine the patient's visual function prior to injury and inquire about prior head, periorbital, and ocular trauma or surgery, as well as contact lens use. For chemical injuries, it is critically important to determine the nature of the chemical causing the injury.

Assess the pain level and qualifiers, changes in vision (decreased acuity, flashes, floaters, curtain), diplopia (monocular or binocular, variation with gaze), foreign body sensation, tearing, and photophobia.

Document the patient's current medication list and past medical history, with special attention paid to history of hemoglobinopathies, bleeding disorders, anticoagulation medications, vaccination status, and last meal (in the case of emergent surgical intervention).

Physical Examination

Ocular trauma has a highly variable presentation and requires a comprehensive examination. Start with visual acuity, followed by general inspection, noting any injury to the eyelids or orbit, as well as the presence of asymmetry or strabismus, proptosis, or a foreign body. Evert the eyelids prior to examination. Note ecchymoses and edema of periorbital soft tissues, subcutaneous emphysema, palpable step-off along the orbital rim, enophthalmos/hypoglobus, foreign body, or lacerations of the globe or periorbital tissues. For lacerations external to the globe, assess whether there is lid margin or canalicular (medial to the puncta) involvement or violation of the septum (prolapsed orbital fat).

Examine the pupil, looking for asymmetry or an irregular shape suggestive of globe rupture, or an afferent pupillary defect via the swinging light test, indicating significant retinal or optic nerve pathology. Check the extraocular movements, examine the anterior chamber (to look for blood), and, if a ruptured globe is not suspected, perform a fluorescein test to look for corneal abrasions. If multiple linear abrasions are noted, evert the eyelids to check for a foreign body, although a topical anesthetic may be necessary. If the patient cannot cooperate for a comprehensive examination, arrange for it be performed with anesthesia.

One of the few true ocular emergencies is an open globe. This is a potentially sight-threatening and organ-threatening injury. However, at examination, a full-thickness violation of either the sclera or cornea is not always evident. Signs of a potential open globe include prolapse of uveal tissue, severe subconjunctival hemorrhage, deep or shallow anterior chamber, hyphema, peaked or irregular pupil, laceration of the cornea or sclera, and an intraocular foreign body. If the clinical picture is suspicious for an open globe, cover it with an eye shield (not an eyepatch) but *do not* place pressure on the globe during examination, check ocular pressure or motility, or dilate the pupil.

The patient may present with a white-eyed orbital "blowout" fracture, in which the eye is relatively well appearing and without obvious hemorrhage. Watch for symptoms of nausea, vomiting, and bradycardia, which may indicate the oculocardiac reflex, a sign of orbital injury. Incomplete fractures of the orbit are common in children because of increased elasticity of the bones. Orbital roof fractures may result in cerebral edema and optic nerve compression and often present with diplopia on upward gaze. Orbital floor fractures can create a trapdoor phenomenon, in which the bone bends and then retracts, entrapping and incarcerating soft tissue within the maxillary sinus, causing decreased range of motion and diplopia. Restriction in extraocular movements secondary to tissue entrapment is an urgent condition. Arrange for surgical correction within 48 hours to prevent ischemia and fibrosis.

Arrange for a slit-lamp and dilated funduscopic examination to assess the anterior and posterior segments. This can be essential for diagnosing a variety of closed-globe injuries, including corneal abrasion, traumatic iritis, hyphema, commotio retinae, choroidal rupture, nonaccidental trauma, vitreous hemorrhage, and retinal detachment.

Laboratory Workup

If clinically indicated, screen the patient with a hyphema for sickle cell disease, which increases the risk of complications of hyphema, such as increased intraocular pressure, nonclearing hyphema, and corneal blood staining.

Radiology Examinations

The imaging of choice for acute ocular trauma and foreign bodies is unenhanced axial and coronal computed tomography (CT) of the face and orbits, with 1- to 2-mm sections. Computed tomography is helpful for assessing an open globe, traumatic optic neuropathy, entrapment secondary to orbital fracture, and retrobulbar hemorrhage. Computed tomography can also demonstrate the integrity and shape of the globe and the presence and location of intraocular foreign bodies. Magnetic resonance imaging provides the best visualization of orbital soft tissues but is contraindicated if a metallic retained foreign body is suspected. Magnetic resonance imaging may be helpful in the case of nonmetallic foreign body, once metallic exposure has been ruled out. Bedside ultrasonography is becoming more available and may be helpful if the patient cannot undergo other radiologic examinations.

Differential Diagnosis

The differential diagnosis of ocular trauma is summarized in Table 91–1.

Treatment

In general, consult an ophthalmologist for any ocular trauma, except for a superficial corneal abrasion with no concern for herpes simplex infection.

If there is an ocular burn, or any chemical exposure, immediately irrigate the eye(s) for 30 minutes, using normal saline or lactated Ringer solution, with or without a Morgan lens. Obtain a pH level of the tears 5 to 10 minutes after the irrigation and discontinue it once the pH level returns to the physiologic range (7.3–7.7). Recheck the pH in 10 minutes and, if it is not neutral, perform another 30 minutes of irrigation. If topical anesthesia is needed, administer 1 to 2 drops of proparacaine 0.5%. If the chemical substance is

Table 91–1. Differential Diagnosis of Ocular Trauma

Diagnosis	Clinical Features
Corneal abrasion	Pain, tearing, photophobia (+) Fluorescein test
Hyphema	Decreased visual acuity Pain with pupillary constriction
Ocular burn	Corneal perforation Decreased visual acuity
Open globe	Irregularly shaped or peaked pupil Uveal tissue prolapse Patient may have associated hyphema
Orbital fracture	Patient may have limitation of upward gaze and/or diplopia Numbness of cheek, upper lip, teeth (floor fracture) Numbness of scalp and forehead (roof fracture) Oculocardiac reflex
Retinal detachment, lens dislocation	Floaters, flashes of light, photophobia Blurred vision
Retrobulbar hemorrhage	Proptosis Afferent pupillary reflex defect
Traumatic iritis	Photophobia, tearing, blurry vision Aqueous flare and inflammatory cells on slit-lamp examination

+ indicates a positive finding.

known, contact the local poison control center, which will have a data sheet to help with management. Once the pH has returned to normal range, order antipseudomonal eye drops, such as ofloxacin 0.3%, ciprofloxacin 0.3%, or moxifloxacin 0.5% (1–2 drops every 2 hours while awake, for each), and preservative-free artificial tears (1–2 drops every 2–4 hours while awake). Daily ophthalmology follow-up is necessary, as subsequent surgical management may be indicated.

If the clinical picture is suspicious for an open globe, consult an ophthalmologist and place a protective Fox eye shield *(do not patch or apply pressure)* over the eye. Raise the head of the bed to 30 degrees, give the child nothing by mouth, administer an antiemetic (ondansetron 0.1 mg/kg per dose as needed every 6 hours; maximum, 8 mg per dose) and intravenous (IV) analgesia (morphine; see Chapter 103, Pain Management), and update the patient's tetanus status. Perform orbital CT to rule out an intraocular foreign body. Administer IV antibiotics, either vancomycin (15 mg/kg every 6 hours; maximum, 1.5 g per dose) *or* linezolid (30 mg/kg/d divided into doses administered every 8 hours; 1,200 mg/d maximum) *and* ceftazidime (50 mg/kg every 8 hours; maximum, 2 g per dose), for antimicrobial coverage of *Bacillus,* coagulase-negative *Staphylococcus, Staphylococcus aureus*, *Streptococcus,* and gram-negative bacteria.

Entrapment secondary to orbital fracture requires urgent surgery within 48 hours to avoid ischemia and fibrosis. Other indications for orbital fracture repair include enophthalmos greater than 2 mm, greater than 50% floor fracture, and functional diplopia secondary to restriction with positive forced duction test findings.

Retrobulbar hemorrhage requires emergent intervention within 60 to 120 minutes if it causes changes in vision or pupils or increased intraocular pressure. Consult an ophthalmologist about performing lateral canthotomy and inferior cantholysis.

Consult an ophthalmologist for recommendations of medical management of both traumatic iritis and hyphema. A patient with hyphema will need close follow-up because of the risk of secondary complications, such as rebleeding, increased intraocular pressure, and corneal blood staining.

Remove a superficial corneal foreign body with irrigation, a moistened cotton-tip swab, or a needle tip under slit-lamp guidance. Prior to foreign body removal, assess the patient for a full-thickness penetration. Once the foreign body has been removed, evert the eyelids and sweep the fornices for particulate matter. Treat a simple corneal abrasion with topical antibiotics and a topical nonsteroidal anti-inflammatory drug, such as 1 drop of ketorolac 4 times a day. Treat corneal abrasion in a patient who does not wear contact lenses with erythromycin ointment 0.5%, 4 times a day for 3 to 5 days. If the patient does wear contact lenses, give antipseudomonal coverage, such as ofloxacin 0.3%, 1 to 2 drops every 2 hours while awake, and refer to an ophthalmologist for daily follow-up.

A lid laceration, especially involving the lower lid canaliculus, requires surgical intervention. Depending on the time of the injury and macular involvement, a retinal detachment may also require urgent surgical intervention.

If there is suspicion of nonaccidental trauma, as evidenced by retinal hemorrhages, for example, assess the patient for other potential injuries, contact the local child protective services agency, and proceed with the appropriate evaluation (see Chapter 69, Child Abuse: Physical Abuse and Neglect).

Indications for Consultation

- **Child protection services:** Inflicted or suspected nonaccidental trauma
- **Facial trauma surgical team (may be oral and maxillofacial surgery, otolaryngology, or plastic surgery):** Orbital or facial fractures
- **Neurosurgery:** Orbital roof fracture
- **Ophthalmology:** Acute vision loss, hyphema, lid laceration, open globe, orbital fracture with entrapment, retrobulbar hemorrhage, traumatic iritis

Disposition

- **Interinstitutional transfer:** Subspecialty services not immediately available
- **Discharge criteria:** Vision stable, surgical issues resolved, appropriate follow-up arranged

Follow-up

- **Primary care:** 1 to 2 days
- **Ophthalmology:** Varies, usually within 1 to 3 days, depending on the nature of the injuries

Pearls and Pitfalls

- An open globe, entrapment secondary to orbital fracture, retinal detachment, and retrobulbar hemorrhage all require urgent surgical intervention.
- Maintain a high index of suspicion for open-globe injury and order CT to confirm.
- Watch for white-eyed blowout fracture, and carefully assess the patient for motility restriction, decreased pulse, and other signs of parasympathetic surge in the context of orbital fracture.
- Investigate any abnormality or any change in the ocular vitals: vision, pupils, and intraocular pressure.
- Corneal abrasion in a contact lens wearer requires antipseudomonal antibiotic coverage and daily ophthalmology follow-up.
- If the clinical picture is suspicious for an open globe, cover it with an eye shield (not an eyepatch), but do not place pressure on the globe during examination.

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Red Eye

Introduction

Pediatric red eye is one of the most common inpatient ophthalmologic diagnoses. It describes a large range of infectious or inflammatory conditions that may originate from the lids, conjunctiva, cornea, iris, sclera, or other internal ocular tissues. Serious etiologies of red eye include infectious conjunctivitis in a newborn, keratoconjunctivitis, foreign body, orbital trauma, and systemic or autoimmune diseases. Recognition of the need for emergent referral to an ophthalmologist is critically important.

Clinical Presentation

History

Obtain a thorough history of ocular and systemic symptoms, including onset and duration of symptoms, associated trauma, visual changes, photophobia, diplopia, discharge, burning, pain, itching, and constitutional symptoms. Also ask about contact lens use, ocular medications, prior ophthalmologic surgery, and past episodes of red eye.

Physical Examination

First, observe the patient's spontaneous eye movements. Note areas of color change, edema, or discharge in the periorbital region, conjunctiva, and sclera. Check ocular motility up, down, left, and right. Use a light source to directly evaluate the pupil size, reactivity, and afferent pupillary defect. Assess the presence, symmetry, and color of the red reflex with a direct ophthalmoscope in a dimly lit room. Assess visual acuity, if the patient is able. Perform a fluorescein stain examination to rule out a corneal abrasion/ulcer or herpes keratitis. Evert the lid to look for the presence of a foreign body.

Differential Diagnosis

The priority is to expeditiously diagnose eye- or vision-threatening conditions. Warning signs include altered visual acuity, ocular pain, severe photophobia, excessive tearing, and a ciliary flush (Table 92–1).

Laboratory Workup

Routine laboratory testing is unhelpful in most cases of red eye. If there is a purulent discharge, particularly in the first 2 weeks after birth, swab for

Table 92–1. Differential Diagnosis of Red Eye

Diagnosis	Clinical Features
Allergic conjunctivitis	Itching and tearing Conjunctival bogginess and injection
Blepharitis	Most common among school-aged children Chronic burning and itching but no discharge Can be associated with a chalazion
Chemical conjunctivitis	Starts in the first 24 h after birth Bilateral watery discharge and bulbar injection
Congenital glaucoma	Photophobia, blepharospasm Buphthalmos (enlargement of the eyeball) Increased intraocular pressure
Corneal abrasion/ulcer	Pain, tearing, blepharospasm (+) Fluorescein test Decreased visual acuity
Dacryocystitis	Fever Erythema, swelling, and tenderness inferior and medial to the medial canthus
Herpes keratoconjunctivitis	Pain, photophobia Vesicles on the eyelids (+) Fluorescein test
Hyphema	Pain and photophobia History of blunt ocular trauma
Infectious conjunctivitis	Bacterial: copious purulence at the lid margin Viral: watery discharge, upper respiratory infection prodrome
Keratitis	Pain, photophobia Conjunctival hyperemia (+) Fluorescein test
Ophthalmia neonatorum (chlamydial)	Starts in the first 5–14 d after birth Watery to mucopurulent discharge (+) Direct fluorescent antibody or enzyme-linked immunosorbent assay
Ophthalmia neonatorum (gonococcal)	Starts in the first 2–5 d after birth Hyperacute purulent discharge Chemosis, eyelid edema Gram stain: gram-negative diplococci
Orbital cellulitis	Fever Pain, proptosis, chemosis, impaired ocular movements, ↓ vision or optic nerve dysfunction
Preseptal cellulitis	Fever Pain, swelling
Scleritis	Pain, ↓ vision Violet discoloration of the globe Anterior chamber inflammation
Subconjunctival hemorrhage	Confluent, bright red patch Does not extend past the limbus

Table 92–1. Differential Diagnosis of Red Eye, continued	
Diagnosis	**Clinical Features**
Systemic disease related	Features are related to the specific disease (eg, erythema multiforme, Kawasaki disease, multisystem inflammatory syndrome in children, Stevens-Johnson syndrome, Reiter syndrome, sarcoidosis, tuberculosis)
Uveitis	Pain, photophobia, redness with ciliary flush Constricted and irregular pupil ↓ Visual acuity

+ indicates a positive finding; ↓, decreased level.

culture and Gram stain. If gonococcal ophthalmia neonatorum is suspected, perform a full sepsis workup, including a lumbar puncture. In cases of uveitis or scleritis, obtain a complete blood cell count with differential, C-reactive protein level or erythrocyte sedimentation rate, antinuclear antibody level, rheumatoid factor, and uric acid level. When a systemic disease is being considered, perform the appropriate tests for assigning that diagnosis.

If herpes infection is suspected in an infant younger than 6 weeks, obtain herpes simplex virus DNA via polymerase chain reaction from the serum and cerebrospinal fluid. In addition, obtain swabs of the mouth, oropharynx, conjunctiva, rectum, and any surface lesions. Also perform liver function tests (including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels) and obtain urine for herpes culture.

Treatment

Because of the highly specialized nature of treatment, consult an ophthalmologist prior to initiating therapy for glaucoma, uveitis, scleritis, or infectious/noninfectious corneal disease. If ocular herpes infection is suspected, immediately initiate intravenous (IV) acyclovir (60 mg/kg/d, divided into doses administered 3 times a day) for 14 days. Add a topical ophthalmic antiviral agent (1% trifluridine, 0.1% iododeoxyuridine, 3% vidarabine).

Neonatorum ophthalmia is an ocular emergency and warrants urgent ophthalmology consult. Treat with either IV or intramuscular (IM) ceftriaxone (25–50 mg/kg every day, 125-mg maximum) or IV or IM cefotaxime (50 mg/kg every 12 hours if patient is < 7 days old, every 8 hours if patient is > 7 days old). Order sterile saline eye irrigations every 2 hours to keep the eye surface clear of debris, discharge, and obstruction. Treat chlamydia with oral erythromycin (50 mg/kg/d, divided into doses administered every 6 hours) for 14 days.

Treat acute dacryocystitis with either ampicillin/sulbactam (150 mg/kg/d, divided into doses administered every 6 hours; 8-g/d maximum) or cefuroxime (100 mg/kg/d, divided into doses administered every 8 hours; 4.5-g/d maximum). If methicillin-resistant *Staphylococcus aureus* is a concern, add clindamycin (40 mg/kg/d, divided into doses administered every 6 hours; 4.8-g/d maximum) or vancomycin (40 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum) after performing cultures of the discharge. Linezolid (30 mg/kg/d divided into doses administered every 8 hours; 1,200 mg/d maximum) is an alternative to clindamycin or vancomycin in areas with high clindamycin resistance. Warm compresses may help with disease resolution. Immediate ophthalmology consultation is indicated.

Treat conjunctivitis with a topical antibiotic ointment (bacitracin, polymyxin B, tobramycin) or solution (ciprofloxacin, ofloxacin, polymyxin B, tobramycin) applied 3 times a day. Use a fluoroquinolone (ciprofloxacin, ofloxacin) when treating a *Pseudomonas* corneal ulcer or conjunctivitis in a contact lens wearer.

See Chapter 20, Orbital and Periorbital Cellulitis, for the treatment of preseptal and orbital cellulitis.

Indications for Consultation

- **Ophthalmology:** Moderate or severe ocular pain, abnormal pupil size, altered visual acuity, diplopia, severe photophobia, excessive tearing, ciliary flush, corneal opacity, ophthalmia neonatorum, ocular herpes, dacryocystitis

Disposition

- **Discharge criteria:** Good response to treatment, identification and sensitivity of infection (if any) known, close ophthalmology follow-up arranged

Pearls and Pitfalls

- Proceed with caution when adding steroids to the treatment regimen for infectious conjunctivitis because herpes keratitis will worsen.
- Antibiotic ointment is preferred in children because of difficulty with achieving appropriate antibiotic levels with drops.
- If drops are prescribed, instruct the parents to apply them to the inner canthus (eye closed for best dosing) and then let the child blink them in.
- Suspect a bleeding disorder or nonaccidental trauma if a patient has recurrent or large subconjunctival hemorrhages.

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Orthopedics

CHAPTER 93

Fractures

Introduction

The 3 main causes of fractures are accidental trauma (most common), inflicted trauma (child abuse), and abnormal bone (pathologic fractures). The most common sites of fractures that necessitate inpatient treatment are the femur, tibia-fibula, elbow (supracondylar fracture), and pelvis.

Fractures are categorized as displaced or nondisplaced and open or closed. In a displaced fracture, the bone snaps into 2 or more parts, which may be angulated and not aligned. If the bone is in many pieces, it is called a *comminuted fracture*, and future misalignment is a concern. In a nondisplaced fracture, the bone either partially or completely breaks but maintains its proper alignment. An open fracture is one in which the bone breaks through the skin, creating a portal of entry for infection. A closed fracture is when the bone breaks but there is no open wound in the skin.

The most serious direct complications of a fracture are infection, neurovascular compromise (most common with a supracondylar fracture), fat embolism, and compartment syndrome, which is secondary to ischemia caused by tissue pressure that exceeds the arteriolar and capillary pressures. The causes of compartment syndrome include hematoma, soft-tissue swelling, crushing or high-energy injuries, extrinsic compression, and intravenous (IV) infiltrates.

Clinical Presentation

History

Attempt to determine the mechanism of injury. Ask about the type and direction of the injuring force, the position of the involved body part(s) at that time, and the events immediately following the incident. Other important information includes whether there was any treatment in the field, ongoing medical conditions, previous orthopedic injuries (particularly at the same site), and chronic medication use (eg, steroids). Also ask about any underlying disorders that could predispose the patient to pathologic fractures, such as known bone cysts, osteogenesis imperfecta, chronic steroid use, and other causes of osteopenia. Finally, an inflicted injury or child abuse is a concern when the mechanism of injury does not adequately explain the type or severity of the fracture found, the fracture is inconsistent with the patient's developmental capabilities, there was an unusual delay in seeking medical care, or the patient has a history of previous unexplained fractures.

Physical Examination

Most often, the patient is status post an attempt at reducing the fracture or awaiting either a surgical reduction or resolution of the swelling to allow for optimal reduction. Whether the attempt was successful or not, there will be swelling at the fracture site, which raises the risk of compartment syndrome. Perform a thorough neurovascular examination, including strength and capillary refill distal to the fracture site, which in some cases may be very distal because of the presence of a cast or splint. Check the skin under the edges of a cast for any possible areas of friction or tightness. Also assess active and passive ranges of movement, because pain may be elicited with passive stretching of the muscles within the swollen compartment. Note, however, that pulselessness and pallor can also be secondary to a vascular injury without compartment syndrome, although agitation and pain out of proportion to the injury or increasing pain despite adequate analgesia are particularly concerning for the development of compartment syndrome.

A femur fracture, particularly one resulting from a high-energy injury, has the additional risk of significant loss of blood into the thigh. This may present with tachycardia, hypotension, pallor, or dizziness. Measure the circumference at a fixed point on the thigh at admission, then repeat every 8 hours.

Laboratory Workup

If the patient has a femur fracture or multiple long bone fractures, obtain a complete blood cell count as a baseline value to monitor for continuing blood loss. The need for other laboratory testing for underlying bone abnormalities is dictated by the clinical circumstances, with the possible exception of an evaluation for inflicted trauma (see Chapter 69, Child Abuse: Physical Abuse and Neglect). Do not perform a wound culture of an open fracture before surgical intervention.

Radiology Examinations

Although imaging is usually performed prior to hospital admission, it is important to review the pre- and postreduction images. Further imaging may be necessary if there is ongoing severe pain at the fracture site, since most pain is relieved by reduction and stabilization.

Computed tomography (CT) may be useful in cases of displaced or angulated fractures, complex intra-articular fractures (especially of the ankle), and vertebral and pelvic fractures, and when a pathological fracture is a concern.

Diagnosis

As noted, consider possible inflicted injury or child abuse if the mechanism of injury does not adequately explain the type or severity of the fracture found, if there was an unusual delay in seeking medical care, if there are unexplained fractures in different stages of healing, or if a patient younger than 1 year presents with rib fractures, spinous process fractures, or a fracture of the sternum. Other concerns include epiphyseal and metaphyseal fractures of the long bones and corner or "bucket handle" fractures of the metaphysis in a patient under 1 year of age.

A nondisplaced fracture may not be evident on initial plain radiographs. If there is significant suspicion for a fracture because of extreme pain, limited use of the affected extremity, or mechanism of injury, perform CT or magnetic resonance imaging acutely or follow-up radiography in 10 to 14 days to look for periosteal elevation.

Suspect a pathologic fracture (benign or malignant bone tumor) when it seems unlikely that the mechanism of injury could have caused the fracture.

Complications

Some complications are particularly associated with certain types of fractures, such as nonunion of tibial fractures, thromboembolism and hemorrhagic shock with pelvic fractures, and neurovascular compromise secondary to brachial artery or median nerve injury with supracondylar fractures. Persistence of intense pain after fracture reduction may be an indication of ischemia, compartment syndrome, neurovascular compromise, or a poorly applied cast or splint causing undue pressure.

Compartment Syndrome

The signs of compartment syndrome in older patients, commonly known as the "5 Ps," are pain out of proportion to the severity of injury, pallor, paresthesia, pulselessness, and paralysis. These signs can be less reliable in a child. Instead, use the "3 As": anxiety, agitation, and an increasing analgesia requirement. Maintain a high index of suspicion, because not all of these signs need to be present to diagnose compartment syndrome.

Fat Embolism

Fat embolism and respiratory distress syndrome can occur in a patient with a long bone or pelvic fracture. The risk increases if surgical repair is delayed more than 24 hours and the patient has an open fracture.

Treatment

Analgesia

Treat mild to moderate pain with acetaminophen and/or a nonsteroidal anti-inflammatory drug. For moderate to severe pain, in a patient with no cardiovascular or central nervous system contraindications, add IV or subcutaneous morphine. If the patient requires morphine more frequently than every 2 hours, assess for compartment syndrome, then change to patient/parent-controlled analgesia (see Chapter 103, Pain Management, for dosing and frequency). Effective analgesia will not obscure physical findings and may increase cooperation during the examination.

Immunization Status

For any patient with an obvious open fracture, administer a dose of tetanus toxoid (0.5 mL intramuscular injection) to those who have not received a tetanus immunization within the past 5 years or if their status is unknown.

Fever and Infection

The risk of a surgical site infection (SSI) increases when surgical hardware (nails and fixator pins) is placed into the area or when the patient has an open fracture. High fever or repeated fever spikes, increased pain and swelling, and discharge from the wound or hardware sites are signs of potential infection. Pin sites and surgical wounds can have some serosanguinous, but not purulent, discharge. If an SSI is suspected, prompt initiation of antibiotic therapy, followed by irrigation and debridement, are vitally important. See Chapter 94, Osteomyelitis and Septic Arthritis, for the antibiotic treatment of an SSI.

In addition, discourage the patient from using any devices to scratch under the cast, which can create abrasions. Order an incentive spirometer to promote respiratory expansion in a postoperative or sedated patient.

Neurovascular Monitoring

The key to preventing neurovascular injury is frequent neurovascular checks. Correct mild edema by maintaining elevation of the affected extremity above the level of the heart. Urgent management consists of removal of any splint or cast. Continued or worsening symptoms are an emergency that requires surgical consultation and intervention.

Fat Embolism

The treatment for fat embolism is supportive care, possibly in an intensive care unit (ICU).

Deep Venous Thrombosis

The need for deep venous thrombosis prophylaxis is less clear in children than in adults. Indications include more than one lower extremity long bone fracture and complex pelvic fractures (see Chapter 46, Deep Venous Thrombosis).

Pressure Ulcers and Immobilization

In general, children tolerate immobilization well because they do not have underlying peripheral vascular disease and they continue to move as much as possible. Nevertheless, skin ulcers can occur. Pay particular attention to the areas underneath the ends of a hard cast and attempt to relieve other pressure spots by using special mattresses and frequently turning patients who are not mobile.

Other risks of prolonged immobilization are constipation and hypercalciuria. If a prolonged period of immobilization is expected, immediately begin a bowel regimen. In addition, ensure that the patient is undergoing appropriate physical therapy.

Hypercalciuria is a common cause of microscopic hematuria in an immobilized child. Obtain a weekly spot urine calcium to creatinine ratio (see Chapter 73, Nephrolithiasis) to screen for hypercalciuria. The definition of abnormal varies with age (0–6 months, >0.8; 6–12 months, >0.6; 1–2 years, >0.4; 2–18 years, >0.2).

A problem unique to a patient in a hip spica cast is hypertension, thought to be caused by pressure on autonomic ganglia. Ensure that the cast is scooped off of the abdomen.

Indications for Consultation

- **Child abuse team:** Suspected nonaccidental trauma
- **Orthopedics:** Urgently for any fracture at risk for or with symptoms of neurovascular compromise or suspected pathologic fracture
- **Pain team/anesthesiology:** Difficulty providing adequate analgesia
- **Physical therapy:** As needed, for crutch training and help with other activities of daily living that may be limited by casts or hardware
- **Vascular surgery:** Any concern about vascular compromise

Disposition

- **ICU transfer:** Compartment syndrome, respiratory distress due to fat emboli
- **Interinstitutional transfer:** Pediatric orthopedic specialist not available locally for a patient with a complex fracture
- **Discharge criteria:** Fracture reduced, no risk for neurovascular compromise, pain controlled with oral medication

Follow-up

- **Primary care:** 1 to 2 weeks
- **Orthopedics:** 1 to 2 weeks

Pearls and Pitfalls

- Persistence of intense pain after fracture reduction may be an indication of ischemia from compartment syndrome or nerve entrapment after reduction.
- Always obtain a repeat radiograph after reduction.
- Document neurovascular check results before and after surgery.
- Properly treated physeal injuries are still at risk for longitudinal or angular abnormalities. This is particularly true for the distal femur and distal tibia.
- In a case where nonaccidental trauma is strongly suspected, reporting it to the state child protective services agency is mandatory.
- Document that the patient has demonstrated safe crutch use, if appropriate.
- Initiate discharge planning early in the hospitalization by anticipating equipment needs (eg, walker, hospital bed).

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CHAPTER 94

Osteomyelitis and Septic Arthritis

Introduction

Osteomyelitis and septic arthritis most commonly occur secondary to hematogenous seeding of bacteria in the bone matrix or joint capsule. Other mechanisms include penetrating trauma or the presence of foreign material (eg, spinal rods). In a patient younger than 18 months, end-loop capillaries feeding the immature epiphysis (transepiphyseal capillaries) allow hematogenous extension of the infection from the epiphysis into the joint capsule. In an older child, septic arthritis may complicate osteomyelitis if a subperiosteal abscess ruptures in a joint where the articular capsule extends over the periosteum (shoulder, elbow, hip, knee). In the lower extremities, concurrent osteomyelitis and septic arthritis occur in about 15% to 20% of cases.

Acute hematogenous osteomyelitis is rare after skeletal maturity. Approximately 90% of cases occur in the metaphyses of the long bones (femur, tibia, humerus). Methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA) are the most frequent pathogens in all age groups. Consider other etiologies based on known or suspected risk factors: sickle cell disease (*Salmonella* species); mammalian bites (*Pasteurella multocida*, *Pasturella canis*, *Capnocytophaga* species, *Fusobacterium* species, *Eikenella corrodens*); rodent bites *(Streptobacillus moniliformis, Spirillum minus);* puncture wound of the foot *(Pseudomonas aeruginosa),* and foreign bodies or implants (coagulase-negative staphylococci). Complications of osteomyelitis include subperiosteal abscess, myositis, secondary bacteremia, pathologic fracture, growth disturbance, fistula, and chronic osteomyelitis. Chronic osteomyelitis results from insufficiently treated or debrided acute osteomyelitis, infection with an unusual pathogen, or a predisposing mechanism of injury (pressure ulcer, trauma).

Primary septic arthritis occurs from birth to age 18, with a median age of 2.5 years. More than 90% of cases are monoarticular, with the knee and hip being the most common sites. The causative pathogens vary by age of the patient: birth to 6 months of age, group B *Streptococcus* and *Enterobacteriaceae*; 6 to 48 months of age, *Kingella kingae*, *S aureus*, and *Streptococcus pneumoniae*; over 48 months of age, *S aureus* and group A *Streptococcus*. In adolescents, also consider *Neisseria gonorrhoeae.* Lyme disease is also a concern in endemic areas.

Clinical Presentation

History

In acute long-bone osteomyelitis, the patient presents with a few days of fever and other systemic symptoms, and either a limp or decreased use of the limb, although an infant or disabled child may have only subtle pseudoparalysis of the affected limb. Pelvic osteomyelitis causes buttock or deep perineal pain and refusal to bear weight or sit. Vertebral osteomyelitis leads to back or abdominal pain, decreased back flexion and extension, and decreased weight bearing. In contrast, chronic osteomyelitis at any site progresses over weeks and may not significantly affect function.

Septic arthritis typically presents with acute onset of a painful joint, decreased range of motion, and inability to bear weight, often associated with fever (> 38.4 °C [101.1 °F]) and systemic symptoms. Septic arthritis in an infant or disabled child can appear as a subtle pseudoparalysis of the affected joint at presentation. *N gonorrhoeae* presents in a sexually active adolescent as either an arthritis-dermatitis syndrome or a disseminated infection (polyarthritis, polyarthralgia, tenosynovitis). Arthritis is a late manifestation of disseminated Lyme disease, so that the patient may not recall an earlier manifestation of Lyme disease, such as erythema migrans. With Lyme arthritis, the patient will complain of joint swelling but minimal pain. *K kingae* can have an indolent presentation.

Ask about risk factors for unusual pathogens, including vaccination and immune status, trauma, foreign material, travel, asplenia, sickle cell disease, and sexual activity. Document any exposures (MRSA, unpasteurized dairy products, ticks, bites, tuberculosis, animals [kittens, puppies, rodents, reptiles, amphibians, fowl]). Note any bite wounds and recent dental work, pharyngitis, or enteritis.

Physical Examination

Acute osteomyelitis presents with point tenderness, erythema, warmth, and/or swelling over the bone. These classic symptoms can be subtle or absent, particularly when the affected limb is large because of muscle mass or obesity. Pelvic osteomyelitis causes hip tenderness, in addition to localized bone pain. Vertebral osteomyelitis presents with leg pain, focal bone back tenderness, and neurologic signs of the lower extremities that may suggest spinal cord irritation. Referred pain is common in a child, so examine the joint above and below the affected area. Indolent progression in a minimally weight-bearing, nontoxic preschooler suggests *K kingae* infection. Chronic osteomyelitis appears with point tenderness at presentation but may lack swelling or

warmth, although a draining sinus is sometimes present. Finally, carefully examine all other bone sites to exclude a multifocal infection.

In most cases, the site of septic arthritis is readily apparent. The range of motion is significantly decreased, so that even minimal motion causes severe pain. However, the sole abnormality with a deep joint infection (hip, sacroiliac) can be decreased range of motion. The patient will guard the affected joint in the position of least pain (hip flexed and externally rotated; knee and elbow held carefully in neutral position). Referred pain is common (especially knee pain with a septic hip), so examine the joint above and below the presumed focus. Examine the remaining joints and palpate the long bones for point tenderness.

Polyarticular involvement can occur with *N gonorrhoeae, Neisseria meningitidis,* or *Salmonella* species. Other causes of polyarticular disease include acute rheumatic fever, Lyme arthritis, and juvenile idiopathic arthritis (JIA). A patient with Lyme arthritis often complains of a subacute, monoarticular, swollen ("boggy"), nonerythematous joint (most often the knee) but maintains weight bearing and range of motion with minimal discomfort.

Laboratory Workup

Obtain a complete blood cell count, erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level, and blood culture (yield 10%–40%), ideally prior to starting antibiotics. In acute osteomyelitis the white blood cell count is typically increased, with a left shift in bacterial arthritis. The ESR and CRP level are increased (ESR > 30 mm/h and CRP level > 3 mg/L) in more than 90% of cases of acute osteomyelitis. However, an ESR greater than 100 mm/h suggests autoimmune arthritis.

Order additional tests if a specific organism is suspected: Lyme enzyme-linked immunosorbent assay with reflex to Western blot, nucleic acid amplification tests from urine and cervicovaginal samples for gonococcus and *Chlamydia,* or tuberculin skin testing or interferon-γ release assay for *Mycobacterium tuberculosis*.

If possible, arrange for a bone aspirate for culture prior to starting antibiotics, especially if there is a subperiosteal abscess. In a nontoxic patient, antibiotics can be temporarily withheld if a bone aspirate cannot be immediately obtained. A bone biopsy sample sent for culture and pathologic evaluation is preferred and is especially indicated if there is an unusual history (penetrating trauma, foreign body, treatment failure, mandibular involvement) or unusual risk factors (gram-negative organism, tuberculosis, immunocompromised host).

If septic arthritis is suspected, arrange for an *immediate* percutaneous diagnostic joint aspiration. Ultrasonographic guidance may be warranted, particularly if the hip is involved. Send joint fluid specimens for cell count (Table 94–1), Gram stain, and culture. Polymerase chain reaction testing is available for *Borrelia burgdorferi, N gonorrhoeae,* and *K kingae.* Save any remaining synovial fluid for additional testing.

Immediate surgical irrigation is indicated if the preliminary results are suggestive of bacterial infection. To improve culture yields and detect fastidious organisms such as *K kingae,* some laboratories will inoculate synovial fluid into an aerobic blood culture bottle and incubate for 7 days. Request special cultures for mycobacteria, *S moniliformis, S minus,* and fungal pathogens, if suspected.

Radiology Examinations

Obtain plain radiographs to evaluate the presence of effusion, fracture, and other noninfectious causes, such as bone cyst or neoplasm. Deep soft-tissue inflammation is evident on plain radiographs at more than 3 to 10 days, periosteal elevation at more than 10 days, and cortical changes at 14 to 21 days. Adjacent joint space widening suggests effusion from contiguous septic arthritis.

Ultrasonography of a suspected septic hip is rapid and diagnostic for joint fluid and facilitates therapeutic drainage. Comparison to the contralateral joint can identify subtle abnormalities. Ultrasonography may also be useful for guided aspiration of a subperiosteal abscess.

If osteomyelitis is suspected (with or without contiguous septic arthritis), perform magnetic resonance imaging, which is the best modality for confirming the diagnosis and assessing the anatomic and spatial extent of the

Table 94–1. Interpretation of Synovial Fluid Cell Count

White Blood Cell Count	Polymorphonuclear Neutrophils (%)	Interpretation
$< 200/mm^3$ ($< 0.2 \times 10^9/L$)	< 25%	Normal
$200–2{,}000/mm^3$ ($0.2–2 \times 10^9/L$)	< 25%	Noninflammatory (osteoarthritis)
$2{,}000–50{,}000/mm^3$ ($2–50 \times 10^9/L$)	> 50%	Probably inflammatory, noninfectious (reactive arthritis, JIA) Possibly infectious (Lyme disease, gonorrhea, tuberculosis, brucellosis)
$> 50{,}000/mm^3$ ($> 50 \times 10^9/L$)	> 75%	Probably infectious (*Staphylococcus aureus,* group A *Streptococcus,* Lyme disease, gram-negative rods)

Abbreviation: JIA, juvenile idiopathic arthritis.

infection. This includes the identification of other tissues and spaces (muscle, joint, periosteum, fascia, and subcutaneous) that may be involved. However, do not delay diagnostic arthrocentesis and empirical antimicrobial therapy while awaiting imaging. Computed tomography, while less sensitive, is an alternative if other imaging is not readily available. Computed tomography can be helpful in cases of chronic osteomyelitis to identify cortical bone thickening, sclerotic changes, encroachment of the medullary cavity, and chronic draining sinuses. Alternatively, repeat the plain radiography 2 to 3 weeks after diagnosis to detect underlying osteomyelitis.

Bone scintigraphy can be useful if multiple sites are suspected, occult osteomyelitis is suspected (eg, fever of unknown origin), or the other imaging modalities are unavailable. Focal hyperperfusion, hyperemia, and bone uptake are present in osteomyelitis, although inadequate ossification limits its usefulness in young infants.

Differential Diagnosis

The differential of bone and joint inflammation includes infections, noninfectious inflammatory conditions, and malignancies (Table 94–2). An arthritic joint presents with some combination of erythema, warmth, effusion, and limited range of motion. Once septic arthritis has been ruled out, consider other infectious and noninfectious causes of arthritis.

Vasoocclusive episodes (VOE) in sickle cell disease (see Chapter 48, Sickle Cell Disease) may be difficult to distinguish from infection, so that dual therapy may be necessary. Often VOE pain occurs at multiple or "typical" sites. Multiple, simultaneous sites of involvement suggest a common source (endocarditis) or a systemic inflammatory process (JIA; chronic recurrent multifocal osteomyelitis [CRMO]; synovitis, acne, pustulosis, hyperostosis, and osteitis [SAPHO]; psoriatic arthritis). Chronic recurrent multifocal osteomyelitis presents with recurrent episodes of focal bone pain and swelling at different sites, pain worse at night, bone inflammation at biopsy, negative bone culture, and absence of constitutional symptoms. The average age of onset is 9 to 10 years. Chronic recurrent multifocal osteomyelitis is rare in children younger than 3 years, and girls are affected more often than boys (2:1). Consider CRMO if there is a history of coexisting psoriasis, inflammatory bowel disease, or inflammatory arthritis, or involvement of unusual sites, such as the clavicle or mandible. Synovitis, acne, pustulosis, hyperostosis, and osteitis is an inflammatory syndrome that has recurrent bone involvement, in addition to skin findings. The typical patient is a young female who presents with palmoplantar pustulosis, psoriasis vulgaris, or acute neutrophilic dermatosis.

Table 94–2. Differential Diagnosis of Osteoarticular Infections

Diagnosis	Clinical Features
Osteoarticular Infection	
Chronic recurrent multifocal osteomyelitis	Recurrent episodes of focal bone pain and swelling Multiple sites (−) Culture results, (+) inflammatory markers
Gonorrhea	Patient sexually active Multiple smaller joints and knees affected (+) Urine/cervical nucleic acid amplification test
Lyme disease	History of tick bite or erythema migrans Swollen, "boggy," nonerythematous knee (+) Lyme serologic testing 50% of knee arthritis in endemic areas; 3% in nonendemic areas
Osteomyelitis	Point tenderness of long bone No joint swelling or erythema
Parvovirus	Viral prodrome: fever, fatigue, headache, pharyngitis Typical rash: slapped cheeks followed by lacy appearance on trunk and extremities
Septic arthritis	Erythema, warmth, and decreased range of motion
Tuberculosis	(+) Risk factors (+) Purified protein derivative and/or interferon-γ release assay Joint fluid: lymphocytic predominance, acid-fast bacilli
Malignancy	
Bone neoplasm	Gradual onset Constitutional symptoms: weight loss, fatigue, fever Pain may be worse at night (+) Imaging (onion skin sign, starburst pattern)
Langerhans cell histiocytosis	Failure to thrive Possible chronic seborrheic-like rash and/or otorrhea Lytic skull lesions
Leukemia	Abnormal complete blood cell count Possible pallor or bleeding Constitutional symptoms: weight loss, fatigue
Noninfectious	
Acute rheumatic fever	Preceding GAS pharyngitis Migratory polyarthritis Severe pain out of proportion to examination findings Patient may have carditis (+) GAS antibodies (antistreptolysin O, antideoxyribonuclease B)
Henoch-Schönlein purpura	Palpable purpura of the lower extremities Abdominal pain Patient may have (+) stool guaiac and/or hematuria
Inflammatory bowel disease	Poor growth or weight loss Diarrhea, possibly guaiac (+) Iritis, rash

Table 94–2. Differential Diagnosis of Osteoarticular Infections, continued

Diagnosis	Clinical Features
Juvenile idiopathic arthritis	Prolonged, cyclic fevers Recurrent arthralgia/arthritis Morning stiffness (+) Serologic testing
Postinfectious/postvaccination or reactive arthritis (formerly Reiter syndrome)	Subacute onset over 2–3 weeks May be afebrile Less dramatic erythema, swelling, and pain Urethritis, uveitis, iritis, conjunctivitis, rash Preceding *Chlamydia trachomatis, Campylobacter jejuni,* streptococcal infection
Sickle cell vaso-occlusive episode	Presence or absence of fever Pain in "typical" location(s) Pain may be diffuse rather than point tenderness
Systemic lupus erythematosus	Symmetrical arthritis of the hands and feet Other features (eg, malar rash, proteinuria, laboratory findings) (+) Serologic testing
Transient synovitis	Recent viral illness (eg, parvovirus) Less dramatic joint examination findings, bland arthrocentesis Responds to analgesics
Trauma	(+) History History of trauma can precede bacterial osteomyelitis No fever (+) Radiographic findings

Abbreviation: GAS, group A *Streptococcus*.
+ indicates a positive finding; −, negative finding.

Treatment

If either osteomyelitis or septic arthritis is suspected, consult an orthopedic surgeon for diagnostic biopsy or therapeutic and diagnostic aspiration because identifying the causative pathogen will facilitate definitive treatment decisions. This is critically important with a septic arthritis.

Osteomyelitis

In a stable patient, attempt to obtain a bone culture prior to administering antibiotics, although it may not always be practical or feasible. Sterilization of bone in significant *S aureus* osteomyelitis is unlikely with 24 to 48 hours of antibiotic therapy. Therefore, antibiotic therapy may be initiated if treatment cannot be delayed, either because of the severity of the illness or the unavailability of a timely bone biopsy. Always perform a blood culture prior to starting antibiotics.

For uncomplicated acute hematogenous osteomyelitis, choose empirical intravenous (IV) treatment based on local bacterial resistance to cover the

most common pathogens of *S aureus* and *Streptococcus pyogenes*. Monotherapy with a first-generation cephalosporin or an antistaphylococcal penicillin is the preferred regimen in areas where MRSA is not prevalent. In addition, the increased prevalence of clindamycin-resistant MSSA makes first-generation cephalosporin or antistaphylococcal penicillin the preferred initial option in some areas, but use dual IV treatment with one of these agents *plus* clindamycin (40 mg/kg/d, divided into doses administered every 8 hours; 2.7-g/d maximum) in severe cases. Options include oxacillin (150–200 mg/kg/d, divided into doses administered every 6 hours; 12-g/d maximum [but recent manufacturer labeling suggests a maximum daily dose of 6 g/d]) *or* cefazolin (100–150 mg/kg/d, divided into doses administered every 8 hours; 6-g/d maximum) *or* vancomycin (40–60 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum; target area under the curve [AUC] to minimum inhibitory concentration [MIC], or AUC:MIC, of >400) *or* IV linezolid (<12 years of age, 30 mg/kg/d, divided into doses administered every 8 hours; ≥ 12 years of age, 20 mg/kg/d, divided into doses administered every 12 hours; 1.2-g/d maximum). Do not use ceftriaxone as monotherapy for culture-positive *S aureus*.

If MRSA prevalence in the region is greater than 10% to 15%, start with IV clindamycin (dose as above). If the local MRSA susceptibility to clindamycin is less than 80%, start IV vancomycin or linezolid (doses as above) while awaiting identification and susceptibility.

Because an infant 2 months or younger is at risk of infection with gram-negative organisms (eg, *Salmonella* spp), initiate empirical therapy with IV ceftriaxone (>28 days) or IV ceftazidime or IV cefepime (0–28 days) *and* (depending on the concern for MRSA) either vancomycin *or* an antistaphylococcal penicillin (oxacillin or nafcillin).

Reassess the patient daily, provide adequate analgesia, and monitor improvement in clinical symptoms and resolution of inflammatory markers. Improvement typically begins within 48 hours and is significant in 3 to 5 days. A delay in resolution of inflammatory factors is associated with a poorer prognosis and suggests an ongoing focus of infection or antibiotic failure.

Transition the patient to oral therapy, guided by final susceptibilities, once they are afebrile, bearing weight, or using the affected extremity and have significantly decreased inflammatory markers (eg, 50% decrease from peak value or CRP level <2 mg/L). Use a dose that is 2 to 3 times higher than that given for minor infections to achieve adequate blood levels and bone penetration.

Common choices for definitive oral therapy include clindamycin (40 mg/kg/d, divided into doses administered every 8 hours; 2.7-g/d maximum), linezolid (<12 years of age, 10 mg/kg every 8 hours; ≥ 12 years of age, 600 mg

every 12 hours; maximum, 600 mg per dose), cephalexin (150 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum), penicillin VK (120 mg/kg/d, divided into doses administered every 4–6 hours; 3-g/d maximum), and amoxicillin (100–200 mg/kg/d, divided into doses administered every 6 hours; 3-g/d maximum).

Oral options without culture guidance include a first-generation cephalosporin, clindamycin, or linezolid. Note that doxycycline and trimethoprim-sulfamethoxazole may be less effective for *S aureus* osteomyelitis. *K kingae* is susceptible to cefazolin or ampicillin.

Treat chronic osteomyelitis with oral antibiotics (clindamycin or first-generation cephalosporin) and tailor the therapy to the results of any deep bone cultures. Obtain an infectious diseases consult to determine the treatment of complicated osteomyelitis (penetrating injury, pressure ulcer, or prosthetic material). Relapse of osteomyelitis symptoms warrants reevaluation for repeat cultures, imaging, and possible debridement of bone sequestrate by an orthopedic surgeon.

Treat acute osteomyelitis (IV plus orally) for 3 to 4 weeks, but 6 weeks of therapy may be needed if the patient has extensive or aggressive disease or a slow clinical response. Treat culture-negative osteomyelitis for 3 to 4 weeks, based on the response to therapy. Treat chronic osteomyelitis for 6 to 8 weeks or more, based on clinical improvement and resolution of laboratory test abnormalities. At follow-up, confirm that the CRP level and ESR have normalized (ESR will lag behind the CRP level) prior to discontinuing treatment.

Septic Arthritis

Arrange for an immediate percutaneous diagnostic joint aspiration and culture by an orthopedic surgeon or other skilled personnel. Effective treatment involves empirical IV antibiotics (as above) and urgent orthopedic surgical consultation for possible arthrotomy or arthroscopy. Surgical intervention is based on synovial fluid appearance, cell count and Gram stain findings, clinical course, laboratory results, and suspected pathogen. In nonhip, nonshoulder arthritis in a well-appearing child, a short delay of antibiotic therapy for a few hours can be permitted to perform preantibiotic cultures.

Consider a bacterial infection of a hip or shoulder joint to be a medical/surgical emergency and include vancomycin in the initial antibiotic regimen; perform baseline and weekly renal function testing. For nonhip, nonshoulder joints, include empirical MRSA coverage when community prevalence is greater than 10%; clindamycin is the preferred agent. However, if there is an increased local prevalence of clindamycin-resistant strains of MSSA, use a first-generation cephalosporin, an antistaphylococcal penicillin, or linezolid

for empirical treatment. Add ampicillin, cefazolin, or ceftriaxone for *K kingae*, if clinically indicated, while awaiting culture results. Obtain an infectious diseases consult for a contaminated wound, joint prosthesis, or unusual or resistant organisms.

Administer the initial IV antibiotics, provide adequate analgesia (acetaminophen, or ibuprofen if JIA is not a diagnostic consideration), and reassess the patient daily to look for resolution of clinical symptoms and inflammatory markers. Improvement begins within 72 hours and is substantial by 5 to 7 days. Use the clinical course and organism identification and sensitivity to tailor antibiotic choice and transition to oral therapy. There is no absolute minimum duration of IV antibiotic treatment.

The total (IV plus oral) duration of antibiotics for uncomplicated *S aureus* septic arthritis is typically 3 weeks, although treatment can be as short as 10 to 14 days for *K kingae, S pneumoniae,* or culture-negative non–*S aureus* arthritis with rapid resolution. Consult an infectious diseases expert for atypical pathogens, as longer durations of therapy may be required for *Salmonella* (42 days) and other gram-negative organisms. Treat Lyme arthritis for a total of 28 days. Gonococcal arthritis necessitates susceptibility testing and evaluation and treatment for other sexually transmitted infections.

If there is coexistent osteomyelitis, treat for at least 4 weeks. For culture-negative septic arthritis, treat for 3 weeks. Oral antibiotics are preferred when an oral agent with comparable spectrum to empirical therapy is available and tolerated. In reactive arthritis, treat the primary process. Anti-inflammatories (eg, naproxen) are useful in managing symptoms in these cases.

Indications for Consultation

- **Orthopedics:** All cases of suspected osteomyelitis and septic arthritis
- **Infectious diseases:** Unusual risk factors, organism, or failure to respond to empirical therapy
- **Physiatry/physical therapy:** As tolerated, once surgical issues are resolved

Disposition

- **Intensive care unit transfer:** Possible bacterial sepsis or toxic appearance
- **Interinstitutional transfer:** If orthopedic management is not available, especially if there is a concern about a septic hip
- **Discharge criteria:** Patient afebrile more than 24 hours, surgical issues resolved, significant improvement of joint function, antibiotic regimen narrowed (if sensitivities are known), and improving CRP level and/or ESR

Follow-up

- **Primary provider:** 3 to 5 days
- **Orthopedics:** 1 to 2 weeks; obtain plain radiographs 2 to 3 weeks after diagnosis to identify concomitant osteomyelitis if diagnostic evaluation was not performed or there are other complications (eg, avascular necrosis)
- **Infectious diseases:** 1 to 2 weeks (if involved)
- **Physiatry/physical therapy:** 1 to 2 weeks; coordinate with orthopedics because timing depends on severity of infection and joint involved (eg, more likely necessary with hip or shoulder)

Pearls and Pitfalls

- Whenever possible, perform a biopsy and culture prior to initiating treatment. However, hip and shoulder septic arthritis are emergencies. Urgent arthrocentesis and IV vancomycin are indicated.
- Whenever possible, ensure that at least one blood culture is performed prior to the first dose of antibiotics.
- Review epidemiologic exposures to identify atypical pathogens and local antibiograms to determine prevalence of MRSA and clindamycin-resistant MSSA.
- If there are multiple sites of suspected osteomyelitis, consider a common source (endocarditis) or a noninfectious etiology (rheumatologic, CRMO, SAPHO).
- Consider *K kingae* in preschoolers who are in child care, have negative bone or joint cultures, or show poor response to empirical vancomycin or clindamycin.
- When a young infant has septic arthritis, consider adjacent osteomyelitis of the epiphysis.
- Transition to oral antibiotics as soon as clinical examination findings are improving (increased range of motion, bearing weight, decreased pain, patient afebrile) and laboratory values support resolution.
- Given the risks associated with peripherally inserted central catheters, oral therapy at discharge is preferred when an equivalent oral agent is available and tolerated.

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Pulmonology

CHAPTER 95

Acute Asthma Exacerbation

Introduction

Asthma is a chronic respiratory disease characterized by airway inflammation and obstruction with a recurrent, reversible pattern of symptoms. The prevalence of asthma among American children is 7%, with significant racial, ethnic, and socioeconomic disparities. Acute asthma exacerbations (AAEs) and status asthmaticus, defined as a life-threatening asthma exacerbation with risk for respiratory failure, are among the leading causes of pediatric hospitalizations.

Clinical Presentation

History

In a patient with a known history of asthma, focus the initial history on the frequency and severity of prior exacerbations, compliance with controller medication use, need for oral steroids within the past 12 months, history of food and environmental allergies, and risk factors for death (Box 95–1). Ask about fever and upper respiratory tract symptoms, which can suggest a viral trigger. Once the patient has been stabilized, inquire about chronic asthma symptoms (wheezing, nighttime coughing, and limitation of activity) and the use of short-acting β_2-agonist (SABA) rescue therapy. Also identify any triggers to assess level of control and need for chronic medication adjustment. Obtain a detailed social history and screen for tobacco smoke exposure and, in a patient over 10 years of age, tobacco use, including cigarettes and e-cigarettes/vaping.

Physical Examination

To assess the severity of an AAE, evaluate the respiratory rate (there may be tachypnea or bradypnea), work of breathing, degree of hypoxia (if any), and ability to speak in sentences.

A patient with a moderate to severe AAE often has decreased air movement with diffuse wheezing (classically expiratory but may be both inspiratory and expiratory), a prolonged expiratory phase, tachypnea, dyspnea, accessory muscle use, and coughing. In status asthmaticus, the respiratory examination findings can be misleading, in that the patient may appear to have no wheezing because of lack of air movement ("tight" or "silent" chest). The subsequent onset of wheezing may indicate improved air movement and a

Box 95–1. Risk Factors for Death From Asthma

Asthma History
Difficulty perceiving asthma symptoms or severity of exacerbations
Hospitalization or ED visit for asthma in the past month
Lack of a written asthma action plan
Sensitivity to *Alternaria* fungi
Previous severe exacerbation (eg, intubation or ICU admission for asthma)
$\geq$ 3 ED visits for asthma in the past year
$\geq$ 2 asthma hospitalizations in the past year
Using $>$ 2 canisters of SABA per month

Social History
Illicit drug use
Low socioeconomic status or inner-city residence
Major psychosocial problems

Comorbidities
Cardiovascular disease
Chronic psychiatric disease
Other chronic lung disease

Abbreviations: ED, emergency department; ICU, intensive care unit; SABA, short-acting β_2-agonist.
Adapted from US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Full report 2007. National Heart, Lung, and Blood Institute; 2007.

positive response to therapy. Tachycardia is common and can be secondary to respiratory distress, dehydration, or as a side effect of SABA use.

Laboratory Workup

In most cases, laboratory tests and radiology examinations are not indicated. Obtain a blood gas to assess the Pco_2 if the patient has an increasing oxygen requirement.

Differential Diagnosis

An AAE is a diffuse process that affects the lower airways, producing bilateral wheezing and often hypoxemia. When the diagnosis is in doubt, administer a diagnostic/therapeutic trial of a SABA and monitor the patient for objective clinical improvement. Nonresponse to SABA may be secondary to status asthmaticus or some other non–asthma-related medical condition (Table 95–1). Also consider other potential diagnoses in a patient who has an atypical or prolonged disease course.

Treatment

Treat an asthma exacerbation with a SABA, supplemental oxygen to avoid hypoxemia (oxygen saturation level $<$ 92%), and systemic corticosteroids (Table 95–2). Many institutions use asthma clinical pathways (ie, care process

Table 95–1. Differential Diagnosis of Wheezing

Acute Diagnoses	Clinical Features
Acute viral bronchiolitis	Age < 2 y Often no prior history of wheezing Transmitted upper airway sounds and rales may accompany wheezing No response to SABAs
Community-acquired pneumonia	Tachypnea not responsive to SABAs Might not be hypoxic Asymmetrical breath sounds with focal crackles Chest radiographic evidence of lobar consolidation
Foreign body aspiration	May or may not have a history of an aspiration event Unilateral wheezing No response to SABAs Chest radiographic evidence of asymmetrical hyperinflation
Recurrent or Chronic Diagnoses	**Clinical Features**
Allergic bronchopulmonary aspergillosis	Recurrent AAEs May have chronic sputum production or hemoptysis Complete blood cell count demonstrates eosinophilia Chest radiographic evidence of proximal bronchiectasis
Bronchopulmonary dysplasia	Age < 3 y History of prematurity requiring oxygen therapy for > 28 d Clinical examination findings similar to those of asthma exacerbation
Congestive heart failure	May be acute presentation Dyspnea and fatigue with feeding, poor weight gain Crackles and hepatosplenomegaly Chest radiographic evidence of abnormal cardiac silhouette and pulmonary vascular markings
Cystic fibrosis	Recurrent cough, wheezing, abdominal pain, loose stools Failure to thrive is common
Laryngotracheomalacia	"Noisy" breather since birth Symptoms worse when agitated, when lying flat, or with feedings No response to SABAs
Vascular rings and slings	Chronic dysphagia, wheezing, stridor, and apnea Wheezing not responsive to SABAs Rare diagnosis If clinical suspicion is high, obtain an esophagram
Vocal cord dysfunction	Refractory asthma symptoms with poor response to SABAs No hypoxia or nighttime symptoms Harsh stridor noted over larynx when symptomatic Spirometry demonstrates limitation of inspiratory flow

Abbreviations: AAE, acute asthma exacerbation; SABA, short-acting β_2-agonist.

Table 95–2. Medications for the Treatment of Asthma Exacerbation

Medication	Dose	Comments
Inhaled SABAs		
Albuterol		
MDI, 90 mcg/puff	4–8 puffs every 20 min for 3 doses, then every 1–4 h Inhalation maneuver as needed Use a VHC; add a mask for a patient < 6 y of age	In mild to moderate exacerbations, MDI plus VHC is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel
Nebulizer solution, 0.63 mg/3 mL 1.25 mg/3 mL 2.5 mg/3 mL 5 mg/mL	0.15 mg/kg (2.5-mg minimum) every 20 min for 3 doses, then 0.15–0.30 mg/kg (10-mg maximum) every 1–4 h as needed or 0.5 mg/kg/h via continuous nebulization	Dilute aerosols to ≥ 3 mL at gas flow of 6–8 L/min; use a large-volume nebulizer for continuous administration
Levalbuterol		
MDI, 45 mcg/puff	See albuterol MDI dose	Indicated only for the rare patient with unacceptable side effects from albuterol
Nebulizer solution, 0.63 mg/3 mL 1.25 mg/0.5 mL 1.25 mg/3 mL	0.075 mg/kg (1.25-mg minimum) every 20 min for 3 doses, then 0.075–0.150 mg/kg (5-mg maximum) every 1–4 h as needed	Levalbuterol administered in one-half the milligram dose of albuterol provides comparable effectiveness and safety Levalbuterol delivered via continuous nebulization has not been evaluated
Systemic Corticosteroids		
Dexamethasone		
1 mg/mL	IM, IV, or oral 0.3–0.6 mg/kg doses administered once (16-mg maximum)	Limited data on dosing or benefit of 1 vs 2 doses Advantages include one-time dosing
Methylprednisolone, Prednisolone, Prednisone		
Prednisolone (15 mg/5 mL) Prednisone (2.5-, 5-, 10-, 20-, and 50-mg tablets)	1–2 mg/kg, divided into doses administered twice a day (60-mg/d maximum)	No proven benefit of IV over oral corticosteroid At discharge, administer 1–2 mg/kg/d (60-mg maximum) to complete a 3- to 5-d treatment course, but an extended course may be necessary
Adjunctive Therapies for Status Asthmaticus		
Magnesium Sulfate		
1 g magnesium sulfate = 98.6 mg *elemental* magnesium = 8.12 mEq magnesium	50 mg/kg as IV solution (25–75 mg/kg, 2-g maximum)	Dilute to a concentration of 0.5 mEq/mL (60 mg/mL of *magnesium sulfate*); infuse over 20–30 min; do not exceed 125 mg/kg/h of magnesium sulfate Patient requires continuous monitoring, preferably in an ICU

Table 95–2. Medications for the Treatment of Asthma Exacerbation , continued

Medication	Dose	Comments
Anticholinergics in Combination With SABAs		
Ipratropium Bromide		
MDI, 18 mcg/puff	4–8 puffs every 20 min as needed up to 3 h; use a VHC; add a mask for a patient < 6 y of age	Has not been shown to provide further benefit once a patient is hospitalized; do not use as first-line therapy
Nebulizer solution, 0.25 mg/mL	0.25–0.5 mg every 20 min for 3 doses, then as needed	May mix in same nebulizer with albuterol
Systemic (Injected) β_2-Agonists		
Epinephrine		
1 mg/mL (1:1,000)	0.01 mg/kg up to 0.3–0.5 mg every 20 min for 3 doses, administered subcutaneously	No proven advantage of systemic therapy over aerosol May be useful if the patient is too "tight" to effectively use an inhaler
Terbutaline		
1 mg/mL	0.01 mg/kg every 20 min for 3 doses, then every 2–6 h as needed subcutaneously	No proven advantage of systemic therapy over aerosol

Abbreviations: ICU, intensive care unit; IM, intramuscular; IV, intravenous; MDI, metered dose inhaler; SABA, short-acting β_2-agonist; VHC, valved holding chamber.

Adapted from US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Full report 2007. National Heart, Lung, and Blood Institute; 2007.

models), which promote adherence to best-practice techniques and reduce costs and length of stay but do not decrease readmissions.

Albuterol (4–8 puffs in a valved holding chamber, with a mask for a child < 5 years of age) is the preferred SABA treatment and method of administration. Use the patient's history and prehospital management, emergency department (ED) management, and physical examination findings to determine the initial scheduling of albuterol. In general, begin with more frequent dosing (every 1–2 hours), then wean as tolerated. The greater the intensity of the prehospital and acute management and the more severe the physical examination findings, the more frequent the albuterol dosing.

Frequent reassessment of the patient is crucial, initially with each SABA administration. Check for improvement to taper the frequency of treatments, or for worsening that would necessitate intensifying the therapy. Assessments can be performed by skilled members of the health care team, including respiratory therapists and nurses. A clinical scoring system may improve communication among the health care team and help standardize and facilitate the weaning process. Peak expiratory flows can be useful to assess

changes in a patient who is 5 years or older and experienced in using a peak flow meter.

Provide supplemental oxygen to maintain an O_2 saturation level at or above 92% or if the patient has acute deterioration with worsening respiratory rate, accessory muscle use, or decreased air movement.

Administer systemic corticosteroids, preferably orally, to any patient with an AAE. There is no advantage to using intravenous (IV) or intramuscular steroids, unless the patient cannot tolerate oral medication. Prescribe a single dose of dexamethasone or daily administration of prednisolone or prednisone, for 3 to 5 days. Extend the course if the patient has prolonged symptoms that require a longer hospitalization or recent or chronic steroid use. If the patient received steroids for more than 14 days, a taper is necessary because of the risk of adrenocortical insufficiency.

In a patient with status asthmaticus (severe respiratory distress, respiratory rate $>$ 60 breaths/min, little air movement, O_2 saturation level $<$ 92%) or an acute deterioration, give the patient nothing by mouth and begin maintenance IV fluids. Increase the SABA to continuous therapy via nebulization at 0.15 to 0.30 mg/kg/h (10–15-mg/h maximum). If a patient is receiving continuous SABA therapy for more than 24 hours, obtain electrolyte levels to assess for hypokalemia. If there is no response after 6 hours with treatment intensification, arrange for other therapies, such as heliox (70:30 helium oxygen), ideally in an intensive care unit (ICU). Additional therapies of *unproven* benefit that may be considered in a patient with impending respiratory failure include systemic IV β_2-agonists (IV or subcutaneous [SC] terbutaline or SC epinephrine), ketamine, and noninvasive ventilation.

Treatments that do *not* improve outcomes for an inpatient with uncomplicated asthma exacerbations include theophylline or aminophylline, IV magnesium, chest physiotherapy, and antibiotic therapy without a definite bacterial source. Although nebulized ipratropium bromide has been shown to decrease hospitalization rates for AAE, there is no documented benefit for its use during hospitalization for an uncomplicated AAE.

If the patient does not respond as anticipated or worsens acutely, evaluate for alternative diagnoses and/or complications, such as pneumothorax, pneumomediastinum, or secondary bacterial infections. When there is concern for impending respiratory failure, perform a complete physical examination, blood gas analysis, and chest radiography.

Start discharge planning at the time of admission. A critical aspect of quality inpatient asthma care is transitioning to appropriate outpatient management and facilitating a chronic asthma management plan. Ongoing discussion and communication with the family and primary care provider is

Table 95–3. Discharge Checklist

Intervention	Dose/Timing	Education/Advice
Inhaled medications (eg, MDI with VHC or spacer; nebulizer)	Select agent, dose, and frequency (eg, albuterol) SABA: 2–6 puffs every 4–6 h for 2 d or as needed Inhaled corticosteroids: Dosing depends on the patient's chronic level of severity (generally a low to medium dose, unless an asthma specialist is involved)	Teach purpose Teach and check technique For MDIs, emphasize the importance of VHC or spacer
Oral medications	Select agent, dose, and frequency (eg, prednisone 50 mg every day for 5 d)	Teach purpose Teach side effects
Peak flow meter (PEF)	For selected patients ≥ 5 y and able: Measure PEF in the morning and evening and record the best of 3 tries each time	Teach purpose Teach technique Distribute a peak flow diary
Address triggers, including tobacco use, tobacco smoke exposure, and allergen exposure	Screen caretakers and adolescent patients on tobacco use, which includes cigarettes and e-cigarettes/vape with each clinical encounter	Provide tobacco use treatment (Table 95–4) If an allergen trigger is identified, advise allergen-specific mitigation strategies and follow-up with an allergist
Follow-up visit	Make appointment for follow-up care with primary clinician or asthma specialist within 5 days	Advise patient and caretaker of date, time, and location of appointment
Home management plan (asthma action plan)	Before or at discharge	Educate patient and caretaker on a symptom-specific action plan

Abbreviations: MDI, metered dose inhaler; PEF, peak expiratory flow; SABA, short-acting β_2-agonist; VHC, valved holding chamber.
Adapted from US Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Full report 2007. National Heart, Lung, and Blood Institute; 2007.

essential to these goals. A discharge checklist for AAE is shown in Table 95–3. At discharge, prescribe the appropriate controller medication, as determined by classification of asthma severity. The first-line therapy for persistent asthma is an inhaled corticosteroid (ICS). Updated guidelines (National Heart, Lung, and Blood Institute and Global Initiative on Asthma) recommend as-needed use of a combination of ICS and SABA for the treatment of asthma exacerbations, in certain age groups and chronic levels of severity.

Further information on classification, management, and medications for quick-relief and controller medications can be found at https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates. Provide an individualized written home management plan (ie, asthma action plan), which gives patients and caretakers symptom-specific directions. Sample

Table 95–4. Tobacco Use Treatment Using the 2 As and an R (ASK, ASSIST, and REFER)

	Adolescent Patients	Caretakers (Adults ≥ 18 Y)
ASK	Screen all patients ≥ 10 y for tobacco use. "Do you or any of your friends use tobacco products, including cigarettes, cigars, or e-cigarettes such as JUUL or vape?"	Screen all patients for caretaker use of tobacco. "Does anyone who provides care for your child use tobacco products, including cigarettes, e-cigarettes, or vape?"
ASSIST	Counsel to quit, using personalized, nonjudgmental language. Emphasize short-term health effects and goals with quitting. Nicotine replacement therapy (nicotine patch, gum, and lozenge) is over the counter and Food and Drug Administration–approved for 18 y and older. The American Academy of Pediatrics recommends consideration in those < 18 y with moderate to severe nicotine addiction.	Counsel to quit for the health of the child using personalized, nonjudgmental language. Use motivational interviewing strategies to focus on the tobacco user's reasons to quit. Treatment is most effective when it combines counseling and first-line pharmacotherapy, such as nicotine replacement therapy.
REFER	Enroll patient by phone, online, or fax to 1-800-QUITNOW (resource for tobacco use treatment). Program specific to e-cigarette use is This Is Quitting (TIQ). Enroll by texting DITCHVAPE to 88709. Follow up with primary care provider.	Recommend or enroll caretaker by phone, online, or fax to 1-800-QUITNOW. Follow up with primary care provider or asthma specialist. Other resources: https://smokefree.gov/ https://www.cdc.gov/tobacco/quit_smoking/index.htm
Notes	E-cigarettes are used by more than 1 in 5 high school students. Adolescents who use e-cigarettes have worse asthma symptoms.	More than 30% of children have identified tobacco smoke exposure. Tobacco smoke exposure is a known asthma trigger.

asthma action plans and other patient resources can be found at https://www.nhlbi.nih.gov/resources/asthma-action-plan-2020.

Indications for Consultation

- **Pulmonologist or asthma specialist:** Poor response to therapy or a prolonged, recurrent, or atypical disease course. Moderate to severe persistent asthma with multiple annual admissions and an ICU admission
- **Tobacco use treatment specialist:** Any patient who uses, or has a caretaker who uses, tobacco products, including e-cigarettes and vape devices
- **Social worker:** Barriers to care, including financial or psychosocial stressors that may lead to difficulty with follow-up or nonadherence with medications, as well as if the patient has risk factors for death (Box 95–1)

Disposition

- **ICU transfer:** No response to initial therapy within a 6-hour time frame or an acute deterioration not responsive to intensification of therapy
- **Discharge criteria:** No respiratory distress and stable respiratory status with SABA inhalations at a frequency realistic to perform at home (generally, every 4 hours), adequate saturations in room air at or above 92%, and asthma education with home management plan and follow-up appointments completed

Follow-up

- **Primary care provider:** 2 to 5 days
- **Pulmonologist, allergist, or asthma specialist:** 1 to 2 weeks if the patient has had an ICU admission for asthma or prior asthma admission within the past 12 months, frequent ED visits for asthma, frequent use of systemic corticosteroids, or severe persistent asthma
- **Allergist:** If the patient identifies allergen-related asthma triggers, including pests, indoor allergens, or dust mites for an allergen-specific mitigation strategy

Pearls and Pitfalls

- Address tobacco smoke exposure and adolescent tobacco use in 3 minutes or less by using the "2 As and an R."
- Administer or recommend an influenza vaccination, unless the patient has already received it or there is a contraindication.
- Asthma clinical pathways can standardize and improve inpatient asthma care.
- Begin discharge planning with asthma education upon admission, including a review of both quick-relief and controller medications.
- Chest radiographs are often misread as possible pneumonia. Bacterial pneumonia and asthma rarely occur simultaneously, while wheezing is not a finding in pneumococcal pneumonia.
- Pneumomediastinum is usually an incidental finding that does not need any specific intervention.

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CHAPTER 96

Acute Respiratory Failure

Introduction

Acute respiratory failure (ARF) is an emergency that develops over minutes to hours, so that the situation can become life-threatening if appropriate interventions are not instituted. Infants and toddlers are at higher risk because they have proportionally large tongues and narrow subglottic regions, small and compliant airways, fewer alveoli, more compliant chest walls, more easily fatigued respiratory musculature, and an immature respiratory center. Additionally, children with metabolic, genetic, and developmental disorders have an increased incidence of poor airway control, chronic aspiration, severe muscle weakness, scoliosis, and restrictive lung disease.

Respiratory failure may be hypercarbic, hypoxemic, or a combination of both, which is frequently the case, and one type may lead to the other. Respiratory failure can also be acute, chronic, or acute on chronic, which can occur in chronically ventilated patients.

Clinical Presentation

History

Risk factors for ARF include young age, history of prematurity, underlying diseases (neuromuscular, metabolic, genetic, developmental), and previous respiratory problems or airway issues. The patient may initially present with fever, cough, stridor, accessory muscle use, and/or grunting. Decompensation can present as shock or sepsis, apnea, cyanosis, or depressed mental status. Depending on the etiology, the progression can occur over minutes to days. Note precipitating factors and associated symptoms, such as fever and vomiting. Ask about the nature of and response to the therapies and interventions implemented at home, in the emergency department, in the outpatient setting, in the field by emergency medical services, and during previous hospitalizations.

Physical Examination

Although a thorough physical examination is necessary, do not delay treatment. A focused assessment and initiation of therapy is the priority to prevent clinical deterioration. To evaluate the respiratory pattern while the patient is calm, ask the caregiver to expose the child's chest and abdomen, then observe the patient from a distance while in the parent's arms. Note the general appearance, work of breathing, and mental status. Irritability or anxiety

suggests more severe disease, whereas lethargy occurs with severe hypercarbia or hypoxemia. Extreme tachypnea and work of breathing can lead to fatigue and sudden respiratory arrest. Stridor with poor air movement is an airway emergency, and bradypnea, poor air movement, and grunting are ominous findings of impending respiratory arrest. Hepatomegaly, facial or peripheral edema, jugular venous distention, or a gallop cardiac rhythm raises the concern for heart failure.

Laboratory Workup

A blood gas analysis is rarely helpful or necessary prior to initiating therapy for ARF, and the patient's distress during restraint and phlebotomy can lead to deterioration. In general, defer laboratory testing until the patient has been stabilized. However, in a patient with acute on chronic respiratory failure, a blood gas analysis can document the degree of hypercarbia and the severity of the illness. Otherwise, oxygenation can be assessed with pulse oximetry. Venous or capillary blood gas analysis (if the patient is well perfused) can be used to guide therapy and monitor ventilation status.

Radiology Examinations

Radiographic findings are important and may help suggest a specific and potentially life-saving therapy. Obtain a chest radiograph to explicitly look for pneumonia, effusion, pneumothorax, a widened mediastinum, cardiomegaly, mass lesion, or evidence of a foreign body aspiration. Obtain an echocardiogram if a cardiac etiology is suggested by the history or examination findings.

Differential Diagnosis

Although the list is extensive (Table 96–1), the cause of a patient's acute respiratory disease rarely presents an urgent diagnostic dilemma.

Treatment

The treatment of ARF is directed at the underlying pathophysiology (see Chapter 97, Airway Management and Respiratory Support).

High-Flow Nasal Cannula

High-flow nasal cannula (HFNC) delivers humidified, warmed oxygen at rates from 2 to 60 L/min. It is a therapeutic option for a patient who can maintain their airway but is hypoxic and/or in respiratory distress. Start at a rate of 1 to 2 L/kg/min and then adjust up or down depending on the clinical response. A flow rate between 10 and 60 L/min provides multiple benefits to the patient, including heat and humidification, reliable delivery of increased glottic

Table 96–1. Etiologies of Respiratory Failure	
Pathophysiology	**Diagnosis**
Upper airway obstruction	Adenoidal-tonsillar hypertrophy Choanal atresia/stenosis Croup Epiglottitis/supraglottitis Excessive or inspissated secretions Foreign body Neuromuscular disease and poor airway control Retropharyngeal abscess
Lower airway obstruction	Asthma Bronchiolitis Bacterial tracheitis
Parenchymal lung disease	Acute respiratory distress syndrome Aspiration or inhalation injury Exacerbation of chronic lung disease Noncardiogenic pulmonary edema Pneumonia Pulmonary contusion
Pulmonary edema	Heart failure
Muscle weakness or paralysis	Botulism Guillain-Barré syndrome Muscular dystrophy Spinal cord injury Spinal muscular atrophy Transverse myelitis Underlying neuromuscular condition
Thoracic mass effect	Ascites Effusion or empyema Pneumothorax Tumor

oxygen concentrations, and positive end-expiratory pressure to decrease the work of breathing.

Clinical conditions in which HFNC may be helpful include bronchiolitis, asthma, obstructive apnea, and pneumonia. A patient who improves with HFNC therapy usually does so within the first 90 minutes, with reductions in respiratory rate, heart rate, and work of breathing.

Heliox

Heliox is a low-density gas that flows through narrow airways with less resistance and turbulence. There are 2 concentrations available: 80% helium/20% oxygen and 60% helium/40% oxygen. Heliox may be beneficial in upper airway obstruction, such as severe croup, in an intensive care unit (ICU).

Specific Considerations

Upper Airway Obstruction

A patient with a large tongue, adenoidal-tonsillar hypertrophy, or poor airway control may find their own position of comfort. If not, place the patient in a lateral position, with or without a chin lift or jaw thrust. A mechanical nasal airway, such as a soft nasal trumpet or appropriately sized endotracheal tube, is usually well tolerated and can often provide significant relief. Pretreat with a topical α-agonist nasal decongestant (phenylephrine, oxymetazoline), use the largest diameter that will pass, lubricate well, and insert with gentle twisting and steady pressure to a length equal to the distance measured from the patient's nostril to the tragus. Other helpful modalities include continuous positive airway pressure (CPAP) and HFNC.

Permit a stridulous patient to assume a position of comfort, provide a calm environment, and minimize stimulation. The treatment of stridor (see Chapter 23, Stridor) includes corticosteroids, racemic epinephrine, and, in severe cases, heliox in an ICU. The patient may require endotracheal intubation, but anticipate difficulty and prepare for the possibility of a tracheostomy. Intubation is best performed with subspecialist consultation (intensivist, otolaryngologist, or anesthesiologist), if possible, and it usually requires an endotracheal tube that is at least one size smaller than usual for the patient.

Lower Airway Obstruction

The treatment of asthma (see Chapter 95, Acute Asthma Exacerbation) and bronchiolitis (see Chapter 99, Bronchiolitis) is detailed elsewhere. If respiratory support is needed, use CPAP, bilevel positive airway pressure (BiPAP), or HFNC oxygen. Reserve intubation for a patient with refractory hypoxemia or impending respiratory arrest, which may occur in an infant with severe bronchiolitis. However, even an extreme asthma exacerbation can usually be managed without mechanical ventilation. Do not deliver bronchodilators via HFNC oxygen, because drug delivery decreases substantially as the flow rate increases. Use traditional face mask delivery in addition to HFNC oxygen support.

Parenchymal Lung Disease

The mainstays of treatment are oxygen delivery, positive pressure, and, if needed, antibiotics and diuretics. Although HFNC oxygen may be helpful, a patient with ARF from parenchymal disease often needs CPAP, BiPAP, or intubation with mechanical ventilation. The positive pressure administered with oxygen improves airway recruitment and hypoxemia and decreases the patient's work of breathing.

Heart Failure

The treatment includes oxygen, diuretics, and inotropes (see Chapter 11, Congestive Heart Failure). Noninvasive support and mechanical ventilation improve respiratory symptoms and left-sided heart function. Obtain subspecialist consultation early, because endotracheal intubation can worsen cardiac output and lead to cardiac arrest.

Muscle Weakness or Paralysis

Provide oxygen and mechanical support. The patient may also have an upper airway obstruction that requires treatment.

Thoracic Mass Effect

Drain or treat surgically, as indicated. Obtain appropriate subspecialist consultation (intensivist, surgeon, anesthesiologist) early, especially if sedation is required.

Pulmonary Edema

Provide positive pressure.

Indications for Consultation

- **Anesthesiology:** Patient with croup that requires intubation, epiglottitis, thoracic mass effect
- **Cardiology:** Acute respiratory failure secondary to congestive heart failure
- **Intensivist:** Acute respiratory failure
- **Otolaryngology:** Acute respiratory failure secondary to a foreign body, croup, retropharyngeal abscess, epiglottitis
- **Surgery:** Thoracic mass effect

Disposition

- **ICU transfer:** Acute respiratory failure
- **Discharge from ICU:** Patient maintaining oxygenation and ventilation with just the support available in the respiratory, step-down, or inpatient unit

Follow-up

- **Primary care provider:** 2 to 3 days
- **Subspecialist:** As indicated by any underlying disease

Pearls and Pitfalls

- Do not administer a muscle relaxant to a patient if the success of airway management and ventilation is uncertain. Ketamine and propofol offer

satisfactory intubation premedication while allowing the patient to breathe spontaneously.

- The judicious use of sedation for a patient with extreme respiratory distress can be beneficial. However, anticipate the possibility of deterioration and the need for airway intervention and mechanical ventilation.
- Do not underestimate the importance of unobstructed nasal passages to adequate breathing in infants and other patients with poor airway control.
- Lateral positioning, with or without chin lift or jaw thrust, helps alleviate airway occlusion and may decrease sympathetic activity.
- Hypoxemia in a patient with isolated upper airway disease (croup) is ominous and indicative of extreme hypoventilation and impending respiratory arrest.
- Heart failure is a cause of ARF that is often overlooked.

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CHAPTER 97

Airway Management and Respiratory Support

Introduction

Pediatric patients require ventilatory support for respiratory failure (Chapter 96, Acute Respiratory Failure), cardiac failure (Chapter 11, Congestive Heart Failure), or airway protection. Acute respiratory collapse in children can be rapid, dramatic, and life-threatening, whereas chronic respiratory failure is often insidious.

Ineffective respiration occurs because of pathologic processes in at least one of the following areas:

- Upper airway increased resistance (fixed or dynamic): palatal insufficiency, tonsil hypertrophy, croup, tracheitis, tracheomalacia, craniofacial anomaly, caustic injury, compressing mass, scoliosis
- Lower airway or alveolar pathology: pneumonia, asthma, pneumothorax, inhalation lung injury, chronic lung disease, cystic fibrosis, scoliosis, chronic smoke exposure
- Central nervous system loss of respiratory drive: stroke, traumatic brain injury, narcotics/toxins, posterior fossa tumor
- Peripheral nerve or muscle deficiency: muscular dystrophy, botulism, Guillain-Barré syndrome, myasthenia gravis, spinal muscular atrophy
- Restrictive pulmonary physiology: scoliosis, pneumothorax

A patient with cardiac failure requires respiratory support to decrease energy use and protect the airway.

Clinical Presentation

History

The need for acute respiratory support depends on the patient's history, underlying pathologic processes, and physical examination findings. In a patient with chronic respiratory disease, changes from baseline ventilator settings, blood gas analysis trends, radiographs, and responses to previous illnesses may indicate further respiratory failure.

Physical Examination

The most effective method to determine the level of respiratory deficiency is simple observation of the respiratory pattern. Little or no respiratory effort, despite hypoxia, indicates a problem with respiratory drive, peripheral nerves,

or respiratory muscles. Increased work of breathing is caused by airway resistance or alveolar disease. Auscultation of the airway from mouth to lungs will suggest the level(s) of pathology. Note any structural anomalies that may affect treatment.

- Nose/mouth: Observe the patient for nasal flaring or open-mouth breathing. Listen behind the mandible to assess for upper airway obstruction. If a jaw thrust reduces airway obstruction, the pathology is at the level of the hypopharynx, usually caused by the tongue.
- Neck: Observe the trachea for deviation. Listen for stridor or voice changes, which indicate a problem in the larynx. Listen over the larynx to help differentiate upper airway stridor from lung bronchospasm.
- Chest: Observe chest wall motion for asymmetry, paradoxical movement, and retractions. Listen for rales (alveolar disease), rhonchi (larger airway disease), and/or wheezing (alveolar and small airway disease).

Laboratory Workup

A combination of pulse oximetry, capnography, and blood gas analyses can help identify and monitor respiratory support needs.

Continuous pulse oximetry is the most useful tool to assess hypoxia, so that arterial blood gas oxygen determination is usually not needed. Important oxygen saturation (SaO_2)-arterial oxygen level correlations are

$$90\%\ SaO_2 = Pao_2\ 60\ mm\ Hg \text{ and } 85\%\ SaO_2 = Pao_2\ 50\ mm\ Hg$$

Note that SaO_2 in an anemic patient can be falsely reassuring, because the diminished amount of hemoglobin can be entirely saturated while total oxygen-carrying capacity is low.

Capnography measures carbon dioxide concentration of expired gas. End-tidal carbon dioxide ($EtCO_2$) correlates with $PaCO_2$ (usually within 5 mm Hg) in a closed respiratory system. However, in an open respiratory system (eg, mask or cannula), the correlation is less reliable. Consider correlating $EtCO_2$ with a blood gas when $EtCO_2$ monitoring is initiated. If measured consistently, $EtCO_2$ is useful for trending carbon dioxide retention.

Serial venous blood gases that confirm a rising carbon dioxide (usually $>$ 50 mm Hg) are consistent with respiratory fatigue, impending respiratory failure, and the need to adjust existing respiratory support. Venous blood gas oxygen levels vary dramatically and are not useful in the assessment of respiratory failure.

Other potential laboratory abnormalities include the following:

- An increased hemoglobin concentration suggests chronic hypoxemia.
- Increased serum lactate level may indicate significant tissue hypoxia.

- Increased bicarbonate level occurs with chronic hypercapnia.
- Low concentrations of potassium, calcium, or phosphate can impair muscle function.

Radiology Examinations

Chest radiography provides additional information about pathologic processes in the chest wall and vertebrae, large and small airways, heart and blood vessels, and diaphragm. Indications for chest radiography include an acute change in respiratory status, failure to improve with interventions, or abnormal auscultatory findings. Upper airway imaging is not indicated in croup but may help in the assessment of neck tissue spaces.

Treatment

Mask Oxygen

Additional oxygen can be provided by a simple mask. These supply oxygen mixed with room air, which is entrained into the oxygen flow, diluting the final concentration of oxygen delivered to the lungs. A simple mask provides approximately 50% oxygen to the glottis. A minimum flow rate of 6 L/min is required to prevent the patient from rebreathing exhaled carbon dioxide.

A nonrebreather mask, which can deliver 80% oxygen to the patient, has a reservoir bag attached to the bottom of the mask. A valve between the mask and the reservoir prevents exhaled carbon dioxide or room air from diluting the pure oxygen flowing into the bag. The typical flow rate for a nonrebreather mask is 10 L/min of oxygen.

Both simple and nonrebreather masks are not sealed to the patient's face and do not allow positive pressure ventilation. These types of masks are used solely to increase the patient's oxygen saturation and do not aid in ventilation.

Sealed oxygen masks are designed to provide positive pressure in addition to oxygen. These masks have a silicone, plastic, or rubber cushion that fits snugly onto the patient's face. The adapter of the mask fits an oxygen bag or mechanical ventilator circuit. Sealed masks are used for resuscitation because the clinician can provide positive pressure and a respiratory rate in addition to oxygen.

Nasal Cannula

A standard nasal cannula (NC) provides supplemental oxygen from an oxygen tank or flow meter connected to a wall oxygen source. The source oxygen concentration may range between 0.21 and 1 (fraction of inspired oxygen [FIO_2] 21%–100%). Due to air entrainment, the actual FIO_2 measured at the

glottis is highly variable and ranges between 0.21 and 0.4. Initial flow rates are typically 2 L/min and can be titrated up to 4 L/min. The oxygen supply may be heated and humidified.

Nasal cannula oxygen is the first supplemental oxygen therapy to provide to a hypoxic patient, provided the patient has patent nasal passages and is breathing spontaneously. Add humidification to the circuit, as over time NC oxygen may dry out the patient's nasal passages, resulting in nasal mucosal swelling and reduction of airflow.

High-Flow Nasal Cannula

High-flow nasal cannula (HFNC) utilizes a wide-bore NC, which is softer than a standard NC and is designed to fit snugly into the nose and then be secured in place. Common indications include bronchiolitis, asthma, obstructive apnea, pneumonia, and acute respiratory distress. The oxygen flow is heated and humidified, and the flow rate and FIO_2 can be adjusted independently. Set the initial flow rate using the patient's body weight in kilograms, at 1 to 2 L/kg/min (60 L/min maximum), and then adjust up or down depending on the clinical response. High-flow provides multiple benefits, including heat and humidification, reliable delivery of increased glottic oxygen concentrations, and positive end-expiratory pressure (PEEP) to decrease work of breathing. A patient who improves with HFNC therapy usually does so within the first 90 minutes, with reductions in respiratory rate, heart rate, and work of breathing.

Bilevel Positive Airway Pressure

Bilevel positive airway pressure (BiPAP) provides oxygen, respiratory rate, inspiratory pressure, and expiratory pressure. It is most often delivered via a mask, and less commonly by NC. All 4 of these variables are adjusted in an effort to synchronize the BiPAP support with the patient's respirations and reduce the work of breathing.

Bilevel positive airway pressure masks cover either the nose and mouth or the entire face, and are designed to fit snugly without any leak. Adjust the initial inspiratory positive airway pressure so that chest excursion is visible, typically 8 to 12 cm H_2O. Set the expiratory positive airway pressure high enough to prevent alveolar collapse at end expiration, at about 3 to 5 cm H_2O. Use an FIO_2 that maintains a peripheral oxygen saturation greater than 90% in an otherwise healthy patient. Optimally, the BiPAP rate will be synchronized to the patient's respiratory rate.

Indications for initiation of BiPAP are broad, and its use has resulted in a reduction of respiratory failure requiring intubation and mechanical ventilation. Contraindications include absence of a gag reflex, inability to cough, and insufficient respiratory drive. Severe upper airway obstruction may severely

reduce the effectiveness of BiPAP therapy. Complications of BiPAP utilization include gastric distention, facial pressure sores, aspiration, and pneumothorax.

Laryngeal Mask Airway

The laryngeal mask airway (LMA) device provides a conduit for oxygen from the mouth to the glottis. It offers a more secure airway than a mask and frees the hands of the provider from holding a mask. The LMA is similar to an endotracheal tube (ETT) on the end that *protrudes* from the mouth so that it can connect to a respiratory circuit, either an oxygen bag or ventilator. The cushion on the opposite end of the LMA inflates in the hypopharynx above the glottis to provide a seal for positive pressure ventilation. Mask sizing is weight based: printed on every LMA is the patient weight for which that particular LMA is appropriate.

Laryngeal mask airways are commonly used for surgical procedures but are also extremely valuable as emergency airways. Insertion is simple and does not require special tools or significant training. To insert, introduce the cuff of the LMA into the mouth and advance into the pharynx until resistance is met in the hypopharynx. Inflate the cuff to seal the distal end of the LMA just above the glottis, then attach a breathing circuit to the adapter. Initiate positive pressure ventilation by bag or ventilator, watching for chest rise and oxygen saturation improvement. If the patient's chest does not rise with positive pressure ventilation, deflate the LMA cuff, withdraw the LMA, and reinsert.

The LMA provides a secure upper airway but does not isolate the lungs from the stomach, so gastric aspiration is a complication of LMA use. In addition, maximum peak inspiratory pressures (PIP) of approximately 20 cm H_2O limit the use of LMA in patients with poor pulmonary compliance.

Endotracheal Tube

Successful placement of an ETT requires practice but results in a secure pathway into the lungs. An ETT is useful in a patient who requires high PIP, PEEP, mechanical respiratory rate, or a high FIO_2. Successful ETT placement almost always requires the administration of sedative and muscle relaxant medications followed by laryngoscopy; therefore, it requires a setting with critical care resources.

A relative contraindication to tracheal intubation is the skill level of the practitioner caring for the patient. Prior training and repeated practice at laryngoscopy and tracheal intubation are required for successful tracheal intubation. There are few absolute contraindications to tracheal intubation. It may prove to be impossible when the patient has pathophysiology of the mouth, tongue, mandible, or glottis. In such a case, it may be safer to use noninvasive respiratory support until a definitive airway is obtained by specialists, such

as an anesthesiologist or surgeon. A patient undergoing tracheal intubation requires mechanical ventilation and management in a critical care setting.

Disposition

- **Intensive care unit transfer:** An FIO_2 level greater than 50% is necessary for maintaining an oxygen saturation of 92% or more; progressive fatigue despite respiratory therapy; pH level less than 7.2 and/or climbing $PaCO_2$; need for advanced monitoring, heliox, BiPAP, or intubation; and apnea or irregular respirations.

Pearls and Pitfalls

- Early recognition of impending respiratory failure is more important than determining the cause.
- Tachypnea is the first sign of respiratory distress, but bradypnea is an ominous sign of impending respiratory arrest.
- Altered mental status may indicate the presence of hypoxia and/or hypercarbia.
- Bradycardia is the ultimate sign of catastrophic respiratory compromise.
- Blow-by does not provide any meaningful increase in oxygen content if the oxygen tube is more than 2 cm from the mouth or nose.

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CHAPTER 98

Brief Resolved Unexplained Events

Introduction

A brief resolved unexplained event (BRUE) is defined as an incident that occurs in an infant younger than 1 year, when the observer reports a sudden, brief, and resolved episode of one or more of the following: cyanosis or pallor; absent, decreased, or irregular breathing; marked change in tone (hyper- or hypotonia); and altered level of responsiveness. A BRUE is a diagnosis of exclusion, assigned when there is no explanation for a qualifying event *after* compiling an appropriate history and conducting a physical examination.

It is important to note that, unlike the previously used term *apparent life-threatening event,* a BRUE does not describe a chief complaint from a caregiver prior to medical evaluation or include infants that have ongoing symptoms after the event has resolved (eg, fever or respiratory symptoms). The history is critical for determining whether an event qualifies as a BRUE, because most episodes can be explained as benign, self-limited, or normal physiological phenomena based on caregiver description (eg, acrocyanosis, breath-holding spells, periodic breathing of the newborn). If the history or physical examination reveals an explanation for the event, then it is termed a *brief resolved explained event* and not a BRUE, or unexplained event.

Even when there is no clear explanation for the event and it qualifies as a BRUE, providers and caregivers may fear that the patient's life was or will be at risk. Although BRUEs are not related to sudden infant death syndrome (SIDS), a small number of patients will eventually be diagnosed with a serious underlying condition (eg, seizures, airway abnormalities, head trauma). However, the most common explanations are due to normal infant immaturity and are not life-threatening. The broad differential diagnosis (Table 98–1), potential for a rare but serious underlying etiology, and subsequent uncertainty present unique challenges.

Clinical Presentation

History

Complete a thorough, systematic history to fully characterize what occurred during the event. Distinguish concerning symptoms, such as central apnea, central cyanosis, loss of consciousness, or seizure activity, from more benign ones like obstructive apnea, choking, pallor, "turning red," or cyanosis limited to just the perioral area or distal extremities (acrocyanosis). Understanding

Table 98–1. Differential Diagnosis of Concerning Events in Infants

Diagnosis	Possible Clinical Features
Normal Newborn Behavior and Less Serious Diagnoses	
Acrocyanosis or perioral cyanosis	Lips turn blue (not gums or face) periodically or with choking, gagging, or crying
Breath-holding spell	Crying followed by breath-holding and possible brief loss of consciousness
Gastroesophageal reflux	Vomiting, regurgitation, choking, gagging, respiratory difficulty, or obstructive apnea associated with reflux of stomach contents Signs of Sandifer syndrome (arching of the back) Poor weight gain
Oropharyngeal dysphagia	Choking, gagging, respiratory difficulty, or obstructive apnea associated with descension of feeds Difficulty managing flow from breast or bottle Milk exiting nose or mouth during or shortly after feedings
Periodic breathing	Periodic respiratory pauses < 20 s in duration Typically occurs while asleep
Startle or Moro reflex	Rapid increase in tone and flexing of extremities when startled
Viral respiratory infections	Variable congestion, wheezing, coarse rales, tachypnea, especially if < 2 mo of age
Potentially Serious Diagnoses	
Anatomic abnormalities of the head and neck (eg, cleft palate, laryngomalacia, tracheoesophageal fistula)	Breathing difficulties or noisy breathing since birth, often worse with feeds or sleep Abnormal facial morphology Recurrent respiratory infections
Bacterial infections (meningitis, sepsis, urinary tract infection)	Age < 2 mo or prematurity Delivery complicated by maternal group B streptococcal colonization, chorioamnionitis, or prolonged rupture of membranes History of congenital anomalies of the kidney or urinary tract
Child abuse	History of unexplained death in other children Inconsistent history or events witnessed by a single caretaker Bruising or petechiae on face, trunk, or extremities
Cardiac arrhythmia or congenital heart disease	Family history of arrhythmia, congenital heart disease, or unexplained death Pathologic murmur
Hypoglycemia or inborn error of metabolism	Family history of unexplained death or developmental delay Age < 2 mo May have metabolic acidosis, developmental delay, poor weight gain, or seizures
Seizures and infantile spasms	May be recurrent May be associated with developmental delay and/or focal neurologic findings May have (+) family history

+ indicates positive finding.

the temporal and contextual relationships is also important. For example, central cyanosis without a preceding event is more concerning than obstructive apnea (gagging, choking, turning red, and hypertonia) after spitting up. Perform a careful review of systems, growth and developmental history,

medical history, family history, and social history, as these can identify comorbid conditions, genetic predispositions, or social concerns.

Physical Examination

By definition, the patient is asymptomatic at the time of presentation. Perform a thorough examination to look for subtle findings, focusing on the skin (eg, bruising or petechiae, indicating child maltreatment), head and neck (eg, anatomic abnormalities that contribute to obstructive apnea), heart (eg, pathologic murmur), and nervous system (eg, development and focality).

Risk Stratification: Lower- Versus Higher-Risk BRUE

Use historical and physical examination features to determine if the patient meets lower-risk criteria for BRUE recurrence and a serious underlying diagnosis. These infants are unlikely to benefit from routine hospitalization or testing. Lower-risk criteria include the following:

- Older than 60 days of age
- Gestational age of 32 weeks or more and postconceptional age of 45 weeks or more
- Occurrence of only 1 BRUE (no prior BRUE, and not occurring in clusters)
- Duration of BRUE less than 1 minute
- No cardiopulmonary resuscitation by a trained medical provider required
- No concerning historical features
- No concerning physical examination findings

Laboratory Workup

Routine laboratory testing is unlikely to yield a diagnosis, including in higher-risk BRUE patients. Given the very low prevalence of significant disease in the BRUE population, nonspecific tests are particularly prone to false-positive results, leading to increased parental anxiety. Do not routinely perform a complete blood cell count, sepsis evaluation, gastroesophageal reflux (GER) testing, sleep study, toxicology screening, metabolic testing, brain imaging, electroencephalography, or electrocardiography (ECG). Pertussis testing is indicated based on exposures, vaccination status, and prevalence within the community.

For a patient with higher-risk criteria and no clear explanation, target laboratory testing based on specific findings of the history and physical examination. For example, perform neuroimaging when there is a concern for child maltreatment or an ECG if there is a family history of cardiac arrhythmias or sudden, unexplained death. If the infant is younger than 2 months or was born premature, bacterial testing or a rapid viral respiratory panel may diagnose a subtle infection.

Treatment

Most infants with a BRUE do not have a serious underlying diagnosis, and there is no increased risk of SIDS. Therefore, if the initial history and physical examination are consistent with BRUE, no specific treatment is necessary other than reassurance. A brief period of continuous monitoring or observation is useful if the initial evaluation raises concerns for other diagnoses or the caregiver is unable to characterize the event.

Diagnoses related to normal infant behavior only require parental reassurance or minor interventions (eg, small, frequent feedings and frequent burping if GER is suspected). Reserve specific treatment for patients with other etiologies for the event. Most importantly, reassure the family that a BRUE is not related to SIDS.

If there are symptoms of apnea, rather than BRUE, such as central apneic events, obstructive apnea present since birth, or an anatomic maxillofacial abnormality, consult an otolaryngologist or pulmonologist.

Other chapters cover the management of arrhythmias (Chapter 9, Arrhythmias and Electrocardiogram Interpretation), bronchiolitis (Chapter 99, Bronchiolitis), child abuse (Chapter 69, Child Abuse: Physical Abuse and Neglect), seizures (Chapter 82, Seizures), and sepsis (Chapter 66, Sepsis).

See Chapter 43, Inborn Errors of Metabolism, for the management of a suspected inborn error of metabolism. Immediately stop all feedings and administer an intravenous solution that contains dextrose.

Indications for Consultation (Inpatient or Outpatient)

- **Cardiology:** Abnormal ECG, or family history of congenital disease or sudden death/arrhythmia
- **Child abuse specialist:** Concern for child maltreatment
- **Feeding expert:** Concern for oral dysphagia
- **Gastroenterology:** Recurrent events with GER symptoms not improved with conservative GER management and leading to failure to thrive or respiratory symptoms
- **Metabolic/genetic diseases:** Positive metabolic/genetic screening or family history
- **Neurology:** Focal neurological findings, developmental delay, or suspicion for seizures
- **Otolaryngology:** Concern for airway abnormality, such as noisy breathing worsened by feeding or sleep
- **Pulmonology or sleep study specialist:** Concern for central apnea, apnea of prematurity, or obstructive sleep apnea

Disposition

- **Intensive care unit transfer:** Recurrent, life-threatening events that require high-intensity monitoring or medical intervention
- **Discharge criteria:** Family reassured; risk of hospitalization greater than risk of serious underlying etiology or recurrence; outpatient follow-up planned

Follow-up

- **Primary care:** 1 to 2 days
- **Neurology:** 1 to 2 weeks if seizure disorder is suspected or diagnosed

Pearls and Pitfalls

- A BRUE is a diagnosis of exclusion.
- Do not routinely obtain screening tests. Target testing and treat the patient according to risk determined from the history and physical examination features.

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CHAPTER 99

Bronchiolitis

Introduction

Bronchiolitis refers to the clinical presentation of certain viral lower respiratory tract infections in young children. Although there is some controversy about the age limits of bronchiolitis, most consider this to be a disease observed in children younger than 18 to 24 months. The typical presentation is one of obstructive lung disease caused by edema and increased mucus production involving the small airways. Respiratory syncytial virus (RSV) is the classic (and most common) etiologic agent, but many other viruses are implicated. Coinfection with more than 1 virus can also occur.

In general, bronchiolitis is a self-limited disease, and therapy is supportive. Lack of effective treatments is often a source of frustration for parents and health care professionals alike. Education surrounding the course of illness, which can sometimes reach 2 weeks, is therefore important.

Clinical Presentation

History

Note the timeline of the illness. Typically, a prodromal phase of nasal congestion, often accompanied by fever, is then followed by cough and tachypnea. Obtain a birth history, because prematurity may indicate a risk for a more severe or prolonged disease course, particularly for those with chronic lung disease. Inquire about a prior history of wheezing. Recurrent wheezing may also indicate predilection for a more severe course and/or a differential response to therapies.

Physical Examination

Observe the patient's work of breathing and respiratory rate. There may be a cough and increased work of breathing, characterized by retractions or visible use of accessory respiratory muscles. Periodic reexamination is helpful to assess the disease course. In a young infant who is an obligate nose breather (typically $<$ 3 months of age), an examination after nasal suctioning may reveal significant improvement.

Lung auscultation is usually remarkable for diffuse wheezing and/or rales and tachypnea. In more severe cases, poor air entry may lead to decreased breath sounds. It is important to distinguish the diffuse peripheral lung findings characteristic of bronchiolitis from localized findings or transmitted upper airway sounds, which may suggest an alternate diagnosis. To evaluate

the patient for upper airway transmitted sounds, listen over the patient's nose and mouth, then "subtract" those sounds from what is heard during lung auscultation. Hypoxia is frequently encountered. Less important findings include clear rhinorrhea and middle ear effusion.

Laboratory Workup

Do not perform routine laboratory tests or imaging for a patient who presents with clinical bronchiolitis. Do not perform specific viral testing to confirm RSV unless the patient is receiving RSV prophylaxis or testing is required for cohorting patients in hospital rooms, because the results will not alter the care otherwise. If diagnostic uncertainty exists or the patient is not following the expected clinical course, obtain a chest radiograph to evaluate for other pathologic conditions, including foreign body aspiration and pneumonia. However, be aware that atelectasis may be misinterpreted as pneumonia. The right upper and right middle lobes are frequently affected, and a repeat chest radiograph obtained after 24 hours will often show complete resolution of the "infiltrate" as the affected area reexpands.

There is considerable variation in the management of fever in an infant younger than 60 days (see Chapter 62, Fever in Infants Younger Than 60 Days) who presents with bronchiolitis. A blood culture and lumbar puncture are not routinely indicated in an otherwise well-appearing, febrile infant 22 to 60 days old with clinical bronchiolitis. However, a fever that occurs later in the disease course may be an indication for an evaluation for a secondary bacterial infection, such as pneumonia, otitis media, or urinary tract infection.

Differential Diagnosis

Consider a differential diagnosis to include the common symptoms of wheezing/rales, tachypnea, and fever (Table 99–1). The wheezing and/or rales characteristic of bronchiolitis involve bilateral lung fields. Unilateral or upper airway examination findings may indicate another process, such as aspiration, focal pneumonia, or laryngotracheobronchitis (croup). Other causes of diffuse wheezing and rales include pulmonary edema, perinatally acquired chlamydial infection, pertussis, and parapertussis. Differentiate between adventitial lung sounds that occur in the larger airways (rings and slings) and those that occur in the small airways (wheezing and rales).

Treatment

The mainstay of therapy for children with bronchiolitis is supportive care. Although variation in treatment for this condition remains, the preponderance of evidence demonstrates that medications are ineffective in treating

Table 99–1. Differential Diagnosis of Bronchiolitis

Diagnosis	Clinical Features
Aspiration	History is more chronic Absence of fever and rhinorrhea Possible abnormal tone and/or other neurologic signs that may be predisposing factors
Bacterial pneumonia	Patient may have high fever Hypoxia unusual Unilateral auscultatory findings
Chlamydia	Onset < 3 mo of age Staccato cough Peripheral eosinophilia (> 300/mm^3)
Croup	Inspiratory stridor Unusual in a patient < 3 mo of age Wheezing less common
External airway compression	Monophasic/monophonic wheezing Central rather than peripheral wheeze
Metabolic acidosis	Tachypnea with clear lungs ↓ Bicarbonate level
Pertussis	Paroxysmal cough Wheezing is unusual Whoop may not be heard < 6 mo of age
Pulmonary edema	History of heart disease or murmur Hepatomegaly, facial or peripheral edema

↓ indicates decreased level.

uncomplicated bronchiolitis. Do not use systemic corticosteroids, nebulized albuterol, nebulized racemic epinephrine, or inhaled hypertonic saline.

Hypoxia is a primary reason for inpatient admission of children with bronchiolitis. The routine use of continuous pulse oximetry monitoring may prolong hospitalization without providing other benefits. Therefore, order spot oximetry checks, unless a patient's clinical status is deteriorating. Target a sustained oxygen saturation of 90% or greater. Do not adjust oxygen for transient nonsustained desaturations.

Administration of heated, humidified oxygen via high-flow nasal cannula (HFNC) devices (see Chapter 97, Airway Management and Respiratory Support) can be helpful in supporting a patient with acute respiratory distress from bronchiolitis.

Frequent nasal suctioning is beneficial, particularly before feeding attempts in the obligate nose breather (< 3 months of age). However, avoid aggressive deep suctioning, which may cause edema of the nasopharynx. Also avoid chest physiotherapy, which is ineffective and potentially detrimental in bronchiolitis.

Apnea is a concern in the youngest infants with bronchiolitis, although the patients at highest risk are formerly premature patients and those with underlying neuromuscular disorders. There is no consistent association with a particular virus. In the absence of complicating factors, apnea may still occur in an infant younger than 2 months, although it is very rare. Therefore, do not delay the discharge of an otherwise mildly ill patient solely for apnea monitoring. Treat true apnea in bronchiolitis with close monitoring and stimulation, HFNC oxygen, and continuous positive airway pressure and/or mechanical ventilation, if necessary.

Poor intake that leads to dehydration is a common indication for hospitalization. Closely monitor the safety of oral feeding in a patient with significant tachypnea (> 60 breaths/min) and/or respiratory distress. Support hydration with nasogastric feedings or intravenous fluids as needed.

Administer or ensure appropriate administration of palivizumab, a monoclonal antibody approved for RSV prophylaxis, in high-risk infants.

Indications for Consultation

- **Pulmonologist:** Diagnosis is uncertain, patient has prolonged oxygen requirement or frequent episodes of hospitalization concerning for underlying lung disease

Disposition

- **Intensive care unit transfer:** Persistent hypoxia or respiratory distress despite increasing oxygen delivery; carbon dioxide retention despite tachypnea, apnea
- **Discharge criteria:** Improved respiratory status with decreased work of breathing, oxygen saturation 90% or greater in room air, and adequate oral intake; there is no specific recommendation as to the amount of time that a patient must be without oxygen supplementation prior to discharge

Follow-up

- **Primary care:** As needed based on clinical status

Pearls and Pitfalls

- An infant with bronchiolitis often sounds much worse than their overall appearance (a "happy wheezer").
- Elevation of the minor fissure helps distinguish a radiographic opacity as right upper lobe atelectasis and associated volume loss as opposed to right upper lobe pneumonia.

- Carbon dioxide retention despite tachypnea is an ominous (though rare) sign.
- Bronchiolitis is a prolonged disease by pediatric standards, with a mean duration of symptoms (cough) of more than 2 weeks. Failure to communicate the expected course of the disease contributes to parental frustration and can result in multiple medical visits.
- To prevent readmissions, discuss discharge criteria and the expected disease course with the patient's family and primary care provider.
- Parental tobacco use has been associated with a more severe illness course. Use the hospitalization as an opportunity for tobacco cessation counseling.

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CHAPTER 100

Community-Acquired Pneumonia

Introduction

Community-acquired pneumonia (CAP) occurs in a previously healthy child and is caused by an infection of the pulmonary parenchyma that has been acquired outside of the hospital. This type of pneumonia can be complicated by pleural effusion, abscess, or necrosis, in which case the term *complicated pneumonia* is used. Although the etiology of CAP varies by age, about 15% of cases are bacterial in origin. Viral infections (respiratory syncytial virus in particular, as well as influenza, parainfluenza, adenovirus, and acute COVID-19 disease) are the most common causes of CAP in hospitalized children.

Although universal vaccination against *Streptococcus pneumoniae* has decreased the overall incidence of infections caused by this pathogen, it remains the most common etiology of bacterial CAP in hospitalized children. The pneumococcal 13-valent vaccine (PCV13) has led to significant decreases in invasive, penicillin-resistant serotypes, so that most current pneumococcal isolates among children in the United States remain sensitive to penicillin.

In the PCV13 era, there are far fewer cases of empyema, and most pleural fluid cultures in complicated pneumonias have negative culture findings. However, polymerase chain reaction (PCR) results confirm that *S pneumoniae* and *Staphylococcus aureus* are the first and second most frequent causes of complicated disease, respectively. In particular, methicillin-resistant *S aureus* (MRSA) is now a frequent cause of complicated CAP. Although group A *Streptococcus (Streptococcus pyogenes)* is an uncommon pathogen of pediatric CAP, it is an important cause of severe necrotizing pneumonia.

Pathogens responsible for "atypical pneumonias," such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae,* can be found in patients across all ages, although they are more significant in children older than 5 years. Other bacteria, such as nontypeable *Haemophilus influenzae* or *Moraxella catarrhalis*, are far less common.

Some rare causes of CAP include *Chlamydia trachomatis* (afebrile infants 1–4 months of age), *Coccidioides immitis* or San Joaquin Valley fever (desert Southwest and California), and *Histoplasma capsulatum* or spelunker's lung (central United States, Ohio River valley, lower Mississippi River).

Clinical Presentation

History

There is usually a history of a preceding upper respiratory infection, which is then followed by fever, cough, and dyspnea. A patient younger than 5 years can present with nonspecific symptoms, such as vomiting, headache, and abdominal pain. A history of dyspnea and chest pain may be elicited in a patient with complicated disease. Overall, fever is the most consistent symptom and can often be the sole complaint.

Physical Examination

A patient with CAP can have a range of physical findings, from just fever with or without tachypnea to significant respiratory distress and cyanosis. Tachypnea is the most sensitive sign in children. Findings such as retractions, use of accessory muscles, nasal flaring, and grunting occur with more severe pneumonias. Auscultatory findings include localized, decreased breath sounds and localized, fine, end-inspiratory rales. A patient who presents with wheezing is at low risk for having a radiographically confirmed bacterial pneumonia (especially pneumococcal). This is particularly true if the patient is afebrile.

Laboratory Workup

Obtain a complete blood cell count in a patient with a severe presentation to assess for concurrent anemia and leukocytosis, although the degree of leukocytosis does not differentiate among bacterial, atypical, or viral etiologies.

Obtain viral testing that is sensitive and specific (such as PCR, not rapid antigen) only if a positive result will change management. Do not order viral testing if the history and physical examination are consistent with a bacterial pneumonia needing antibiotic treatment.

The yield of a blood culture is so low that it typically does not influence the clinical management. Perform a blood culture only in a case of severe or complicated disease. When available, perform testing for atypical pathogens in a patient with a higher pretest probability of having an infection with such a pathogen (> 5 years of age, diffuse infiltrates on chest radiographs). A PCR test for *M pneumoniae* of nasopharyngeal or throat swabs is the preferred testing option if an atypical pneumonia is suspected.

Radiology Examinations

Most patients hospitalized with CAP will have undergone chest radiography. An alveolar or lobar infiltrate is most commonly secondary to a bacterial infection. Diffuse or interstitial infiltrates suggest an atypical

pathogen or a virus. However, because the radiographic findings often overlap, they have poor specificity for any particular pathogen. In addition, a normal chest radiographic finding does not rule out CAP. Although repeat chest radiography is usually not necessary, it can be performed if there is no improvement after 24 to 48 hours of adequate treatment and either the clinical course is worsening or a complication, such as an effusion or empyema, is suspected (no clinical improvement, pleuritic chest pain, percussion dullness).

Parapneumonic effusions are most commonly caused by bacteria, although viruses or atypical bacteria are sometimes implicated. Absence of "layering" on a decubitus chest radiograph is an indication of possible septations or empyema. If a complicated effusion or empyema is suspected, perform chest ultrasonography or computed tomography. If pleural fluid is obtained, send it for Gram stain, culture, pH level assessment, and evaluation of lactate dehydrogenase, protein, and glucose levels. A low glucose level (< 40 mg/dL [< 2.22 mmol/L]) and a low pH level (< 7.2) are consistent with an empyema.

Differential Diagnosis

The presentation of pneumonia can overlap with other childhood illnesses (Table 100–1). A combination of the most common symptoms—tachypnea, fever, and cough—can be seen in pulmonary diseases (bronchiolitis), as well as nonpulmonary conditions (congestive heart failure [CHF]) or metabolic disease (diabetic ketoacidosis). Pulmonary effusion can also occur in CHF and many other extrapulmonary (pancreatitis) and neoplastic (lymphoma) illnesses.

Table 100–1. Differential Diagnosis of Community-Acquired Pneumonia

Diagnosis	Clinical Features
Aspiration pneumonia	Chronically ill, special needs, or technology-dependent patient
Bronchiolitis	Patient < 1–2 y of age Wheezing with or without coarse rales
Foreign body aspiration	Patient may have a history of a choking episode Recurrent pneumonia in the same site Localized hyperlucency on chest radiographs
Pertussis	Coughing paroxysms (many coughs without breathing) Whoop (> 3–6 mo of age) Lymphocytosis
Tuberculosis	Presence of risk factors Ghon complex on chest radiographs Purified protein derivative or interferon-gamma release assay (+)

+ indicates a positive finding.

Treatment

Most current pneumococcal isolates are sensitive to penicillin, and resistance to penicillin has not been shown to affect clinical outcomes. Most treatment failures are secondary to the development of complications, such as empyema, noncompliance, and other factors not related to antibiotic susceptibility. As a result, β-lactams remain first-line treatment for suspected bacterial infections. Start treatment with oral amoxicillin (90 mg/kg/d, divided into doses administered every 8 hours; 2-g/d maximum) or intravenous (IV) ampicillin (200 mg/kg/d, divided into doses administered every 6 hours; 6-g/d maximum). Alternatives include a third-generation cephalosporin, such as IV ceftriaxone (50–100 mg/kg/d, divided into doses administered every 12–24 hours; 4-g/d maximum) or cefotaxime (150 mg/kg/d, divided into doses administered every 8 hours; 8-g/d maximum). Add IV clindamycin (40 mg/kg/d, divided into doses administered every 6–8 hours; 4.8-g/d maximum), linezolid (30 mg/kg/d divided into doses administered every 8 hours; 1,200 mg/d maximum), or vancomycin (45 mg/kg/d, divided into doses administered every 8 hours; 4-g/d maximum) if the patient has severe or complicated disease in an area with a significant prevalence of MRSA. When potential penicillin allergy is a concern, administer a closely monitored trial of either cephalosporin or clindamycin (as detailed herein).

If rapid testing for an atypical pathogen yields positive results, or there is a high suspicion of an atypical infection and rapid testing is not available, add azithromycin (10 mg/kg in a single dose, followed by 5 mg/kg daily on days 2–5; maximum, 500 mg per dose). However, do not use a macrolide as monotherapy for CAP, because up to 40% of community-acquired *S pneumoniae* is resistant. Although fluoroquinolones, such as oral or IV levofloxacin (10-mg/kg dose every 12 hours, 500-mg/d maximum), have activity against *S pneumoniae* and atypical pathogens, reserve them for teenagers or a patient with known severe allergies to other first- or second-line agents.

Medically treat an uncomplicated parapneumonic effusion that occupies less than 40% of the hemithorax. Features of a parapneumonic effusion that is likely to fail medical management and require drainage include involvement of more than 40% of the hemithorax, the fluid being loculated, and the initial fluid analysis revealing an empyema (pH level $<$ 7.2). There are many choices for draining a large or complicated parapneumonic effusion, ranging from simple chest tube insertion to open thoracotomy. Early decortication with video-assisted thoracoscopic surgery (VATS) decreases length of stay, need for pain medication, and overall costs. However, chest tube insertion with

instillation of fibrinolytics may be equal to VATS in terms of length of stay and superior in terms of cost. Base the choice of therapy (VATS or chest tube and fibrinolytics) on local expertise and availability.

The length of therapy for CAP caused by typical bacteria is 10 days, although a shorter course may be equally effective. Initiate the transition from IV to oral therapy as soon as there is clinical improvement. There is no established duration of therapy for a patient with complicated disease.

Indications for Consultation

- **Infectious diseases:** Unexpected pathogen identified or patient nonresponsive to the appropriate initial antibiotic regimen
- **Otolaryngology:** Suspected foreign body aspiration
- **Pulmonology:** Recurrent pneumonias or other pulmonary pathologic conditions, such as cystic fibrosis, are suspected
- **Surgery:** Drainage may be necessary (large effusion, loculations, empyema)

Disposition

- **Intensive care unit transfer:** Severe respiratory distress or signs of sepsis
- **Discharge criteria:** No oxygen requirement, defervescing or no fever, patient tolerating maintenance oral fluids, and adequate follow-up assured

Follow-up

- **Primary care:** 2 to 3 days

Pearls and Pitfalls

- Initiation of antibiotic therapy does not mandate completing a full course if subsequent clinical or laboratory evidence suggests a viral infection.
- A patient with a complicated pneumonia can have persistent fever despite receiving adequate treatment.
- Wheezing is not consistent with a classic pneumococcal bacterial pneumonia.
- A rare complication of pneumococcal pneumonia is atypical hemolytic uremic syndrome in a patient whose condition is acutely worsening despite appropriate treatment.

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CHAPTER 101

Complications of Cystic Fibrosis

Introduction

Cystic fibrosis (CF) is a systemic disease that affects multiple organ systems, especially the respiratory and gastrointestinal tracts and the exocrine glands. Comprehensive care is usually delivered at CF centers, but a patient with a complication may present to any hospital. The most common pulmonary complications are pulmonary exacerbations, pulmonary hemorrhage/hemoptysis, and pneumothorax. The most urgent gastrointestinal concern is distal ileal obstruction syndrome (DIOS), an acute intestinal obstruction. Cystic fibrosis–related diabetes (CFRD) is now the most common complication as a result of improved survival. If possible, always coordinate the management of a patient with CF with the staff of the CF center where the child receives routine care.

Clinical Presentation

The presentation of CF complications is summarized in Table 101–1.

History

A patient with a respiratory complication will most often complain of worsening distress, especially shortness of breath and increased respiratory rate.

Table 101–1. Presentation of Cystic Fibrosis Complications

Complications	Clinical Findings	Investigations
CF-related diabetes	Weight loss or poor weight gain/growth Polydipsia/polyuria	↑ Glucose, hemoglobin A1c levels Glycosuria but no ketoacidosis Failed glucose tolerance test
Distal ileal obstruction syndrome	Abdominal pain and distention Emesis No fever	Abdominal radiograph for distal ileal obstruction
Pneumothorax	Acute onset of ipsilateral chest pain and shortness of breath Ipsilateral decreased or absent breath sounds	(+) Chest radiography finding
Pulmonary exacerbation	With or without fever Cough, congestion, dyspnea, and tachypnea Rhonchi and/or rales (diffuse/localized) Change in sputum viscosity or color	Worsening lung function Change in chest radiograph (↓ FEV_1)
Pulmonary hemorrhage	Pallor Cough, shortness of breath Expectoration of bright red blood	N/A

Abbreviations: CF, cystic fibrosis; FEV1, forced expiratory volume in 1 second.
+ indicates positive finding; ↑ increased level; ↓, decreased level.

A pulmonary exacerbation will typically appear with increased cough and secretions at presentation and, with severe lung disease, possibly bleeding. Pneumothorax causes the acute onset of chest pain and difficulty breathing, without an increase in secretions. A patient with hemoptysis/pulmonary hemorrhage will report coughing up frank blood, with or without increased cough and worsening respiratory distress. Fever may occur with a pulmonary exacerbation but is not usually present with pneumothorax or hemoptysis. Ask about previous history of exacerbations, as well as current medications and the pulmonary hygiene regimen.

A patient with DIOS will complain of some combination of distended abdomen, abdominal pain, emesis, and, rarely, blood in the emesis or per rectum. The presentation of CFRD will be more insidious, with fatigue, poor energy, and possibly polydipsia and polyuria.

Physical Examination

Perform a complete physical examination, focusing on the vital signs, pulmonary findings, and abdominal examination.

Laboratory Workup

If a pulmonary complication is suspected, obtain a chest radiograph. This will allow differentiation of pneumothorax from other lung processes. With a pulmonary exacerbation, the radiograph may also demonstrate worsening infiltrates or bronchiectasis in comparison to previous images, if available. Obtain a complete blood cell count to quantify the degree of any blood loss, and check for leukocytosis consistent with an acute infection. Also, if bleeding is present, order coagulation studies (prothrombin time, activated partial thromboplastin time, fibrinogen level).

If a DIOS is suspected, obtain a plain radiograph of the abdomen, which usually demonstrates the diagnostic finding of distended, fluid-filled loops of bowel proximal to the level of obstruction. Alternatively, perform a Gastrografin enema, which will confirm the diagnosis and be therapeutic. Also perform a comprehensive metabolic panel to identify any electrolyte imbalances.

The evaluation of suspected CFRD includes a comprehensive metabolic panel and a urinalysis. Typically, the blood glucose level will be high, especially postprandially, but without associated acidosis or ketosis. For a definitive diagnosis, arrange an oral glucose tolerance test.

Treatment

Always attempt to contact the primary CF provider for specific care recommendations until the patient can be transported to a CF facility.

Pulmonary Exacerbation

The mainstays of treatment are systemic antibiotics and vigorous airway clearance (every 4–6 hours) by using the best tolerated method, such as a high-frequency chest compression vest or flutter valve. Bronchodilators via metered-dose inhaler may also be of benefit and are most useful when given prior to airway clearance. In contrast, steroids and ipratropium have not been shown to be therapeutic in this situation. Inhaled antibiotics are most effective for chronic, maintenance use, but they may be helpful during an acute exacerbation in a patient with a *Pseudomonas aeruginosa* airway infection. For mild to moderate exacerbations, order oral antibiotics directed against pathogens with which the patient is known to be infected. Reserve intravenous (IV) antibiotics for a severe exacerbation, manifesting in increased cough or sputum production, decreased exercise tolerance, increased fatigue, and absenteeism from daily activities, especially if a prior regimen of oral antibiotics has not been effective.

At accredited CF care centers, airway cultures are routinely obtained every 3 months, so information regarding the patient's airway flora will most likely be available. Typical organisms are *Haemophilus influenzae* (infants), *Staphylococcus aureus* (methicillin-susceptible and methicillin-resistant *S aureus* [MRSA]), and *P aeruginosa*, but other gram-negative rods may be present also. Although it is best to focus therapy on organisms known to be present in the patient's airway, if that information is not available, use a regimen that is effective against *P aeruginosa* and *S aureus,* such as tobramycin (10 mg/kg every 24 hours; adjust the dose based on serum levels) *and* an antipseudomonal semisynthetic penicillin (piperacillin/tazobactam, 400 mg of piperacillin component/kg/d, divided into doses administered every 6 hours; maximum, 16 g of piperacillin component/d). If MRSA is present or suspected, add vancomycin (60 mg/kg/d, divided into doses administered every 6 hours; 4-g/d maximum) to the regimen.

Pulmonary Hemorrhage/Hemoptysis

Observation and supportive care are generally sufficient until the bleeding stops. Give the patient nothing by mouth, and administer IV fluid resuscitation with 20-mL/kg boluses of normal saline as needed. Transfuse 20 mL/kg or up to 2 units of packed red blood cells if the hemoglobin level is less than 7 g/dL ($<$ 70 g/L) or if it decreases by 2 g/dL or more ($\geq$ 20 g/L) over 8 hours. Bronchoscopy may be necessary when the bleeding is severe, and embolization may be indicated either acutely or after the hemorrhage has stopped. Consultation with, and possible transport to, a CF provider is necessary if embolization of the bleeding vessel is being considered.

Pneumothorax

If a pneumothorax measuring greater than 2 cm between the lung and chest wall is documented on a chest radiograph, consult a surgeon for chest tube placement. Because the recurrence rate is high, pleurodesis may be the preferred procedure after consultation with a CF specialist.

DIOS

Give the patient nothing by mouth, provide IV fluid resuscitation (if needed), and place a nasogastric tube (NGT), if needed. Treat with polyethylene glycol (PEG) orally (1.0–1.5 g/kg every day, 100-g/d maximum) if the obstruction is mild. Otherwise, administer the PEG orally or via continuous NGT (20–30 mL/kg/h until clear, 1-L/h maximum) if the vomiting is not severe. Alternatively, a therapeutic Gastrografin enema may be necessary. However, consult a surgeon if the obstruction persists or if there is concern about a perforation (rigid abdomen, abdominal guarding, rebound tenderness, increased abdominal pain).

Diabetes

Consult an endocrinologist for dietary and insulin management guidance. Order a standard insulin bolus regimen and a high-calorie, high-fat diet.

Indications for Consultation

- **Endocrinology:** New-onset CFRD
- **Primary CF provider:** All patients
- **Surgery:** Chest tube placement, control of pulmonary hemorrhage needed, bowel obstruction

Disposition

- **Intensive care unit transfer:** Impending respiratory failure, shock, tension pneumothorax
- **Transfer to CF center:** Serious CF-related complication
- **Discharge criteria**
  - — Bowel obstruction: Obstruction resolved, electrolyte imbalances corrected, patient tolerating oral maintenance fluids
  - — Cystic fibrosis–related diabetes: Blood glucose level less than 200 mg/dL (< 11.1 mmol/L), glucosuria resolved, insulin regimen understood by patient, follow-up with CF provider or endocrinologist arranged
  - — Pneumothorax: Affected lung reexpanded without any reaccumulation after chest tube removal

— Pulmonary exacerbation: Patient afebrile for 48 hours with significant clinical and objective improvement in pulmonary function (to near baseline)
— Pulmonary hemorrhage/hemoptysis: Bleeding stopped, hemoglobin level stable

Follow-up

- **Pulmonologist or CF center:** 2 to 3 days

Pearls and Pitfalls

- Have a high suspicion for complications, although they are relatively rare.

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CHAPTER 102

Foreign Body Aspiration

Introduction

Foreign body aspiration (FBA) is potentially life-threatening, as it can lead to complete or partial airway obstruction. Although 80% of cases involve children younger than 3 years, it can occur at any age. Round foods, such as grapes, peanuts, hot dogs, and popcorn, are the most commonly aspirated. Other possibilities include small toy parts, latex balloons, marbles, coins, pen caps, paper clips, pins, and jewelry.

Certain retained foreign bodies are of particular concern because of their ongoing effects on airway tissues. For example, peanuts are irritating to the airway and can cause granulation tissue, whereas vegetable matter (corn kernels) can absorb airway secretions and swell, leading to more severe obstruction. Button batteries can generate electrical current and erode the airway, and sharp objects can puncture the airway.

Clinical Presentation

History

The presentation of an FBA varies, depending on what was aspirated, when, where in the respiratory tree the object lies, and the degree of obstruction. A witnessed episode of choking has the highest sensitivity for predicting FBA.

An acute, life-threatening FBA presents with choking, gagging, respiratory distress, cyanosis, and mental status change. A subacute presentation is more common, characterized by partial airway obstruction hours to days or even weeks later. Possible symptoms include choking, cough, stridor, dyspnea, wheeze, voice changes, and neck or throat pain. In some cases, there may be a history of receiving a previous, but incorrect, diagnosis of asthma or pneumonia. Ask about hemoptysis or fever because these may be signs of airway trauma, foreign body reaction, and/or infection.

Physical Examination

Identify any signs of respiratory distress, including tachypnea or retractions. Extrathoracic airway obstruction may present with stridor, whereas intrathoracic obstruction manifests as cough, focal wheezing, and diminished lung sounds. This classic triad has high specificity but lacks sensitivity. Localized variation in lung aeration (most commonly in the right upper lobe) is an important clue and requires careful auscultation. Small objects lodged past the main bronchi near the terminal bronchioles may present with few, if any,

symptoms. If the history is concerning, further workup may be indicated, even if the physical examination is unremarkable.

Radiology Examinations

If an FBA is suspected and the patient is stable, obtain anteroposterior and lateral radiographs of the chest. Include neck radiographs if a laryngotracheal foreign body is a possibility. Organic objects may be radiolucent and not directly visible on radiographs. In such a case, obtain inspiratory and expiratory radiographs or bilateral decubitus views in a young child who cannot cooperate with inspiratory/expiratory imaging. These radiographs can increase the sensitivity of detecting a foreign body by providing indirect evidence, such as air trapping, localized hyperinflation distal to the obstruction, infiltrate, atelectasis, or mediastinal shift to the contralateral side. Normal radiographic findings do not rule out FBA. If the clinical suspicion remains high, additional imaging is required.

If radiographs are inconclusive, computed tomography (CT) is an option because it has a high negative predictive value for FBA and can detect radiolucent objects. Many centers have ultrafast CT, which requires less radiation, obtains images quickly, and can generate three-dimensional images of large airways. Early use of this modality can reduce the need for bronchoscopy. Discuss with a radiologist the pros and cons, including availability, cost, radiation exposure, and potential delay in performing a diagnostic or therapeutic bronchoscopy.

Differential Diagnosis

The differential diagnosis of FBA is summarized in Table 102–1.

Treatment

Airway stabilization is the immediate priority. In complete airway obstruction, attempt the basic lifesaving (BLS) maneuvers for dislodging a foreign body (for patients <1 year of age, use back blows and chest thrusts; for patients ≥ 1 year of age, use abdominal thrusts or Heimlich maneuver). When BLS maneuvers fail, contact an otolaryngologist for emergent direct laryngoscopy.

Most situations are less acute because the airway is patent but FBA is certain or highly suspected. Contact an otolaryngologist to perform a rigid bronchoscopy, which is the treatment of choice. There is a 95% success rate with few complications. Flexible bronchoscopy, performed by a pulmonologist, is an alternative for older children and adolescents, although the success rate is lower and it carries a risk of dislodging the object. Institutional availability and expertise will determine which procedure to perform.

Table 102–1. Differential Diagnosis of Foreign Body Aspiration

Diagnosis	Clinical Features
Cough/Dyspnea/Wheezing	
Allergic reaction	Known or suspected trigger (often food) Dyspnea, diffuse wheezing, stridor Urticaria, angioedema
Asthma	Recurrent cough and wheezing with known triggers Bronchodilator responsive
Bronchiolitis	Upper respiratory infection prodrome Bilateral rales and wheezing
Pneumonia	Fever, cough, tachypnea Bacterial: localized rales or decreased breath sounds Viral: diffuse wheezing and rales Infiltrate may be seen on chest radiographs
Choking/Dysphagia	
Esophageal foreign body	Decreased oral intake, drooling, dysphagia, cough Substernal discomfort, chest pain
Mediastinal mass	Difficulty breathing and/or swallowing May be seen on chest radiographs (anterior most common)
Stridor	
Croup	Fever, barking cough, hoarse voice
Laryngotracheomalacia	Positional inspiratory stridor Appears in infancy
Peritonsillar abscess	Fever, trismus, "hot potato" voice Uvula or palatal deviation
Retropharyngeal abscess	Fever, drooling, dysphagia Limited neck hyperextension Swelling anterior to cervical vertebrae on lateral neck radiographs

If the diagnosis of a foreign body is unclear, perform diagnostic flexible bronchoscopy first and then proceed to rigid bronchoscopy for object removal.

There is a subset of children in whom FBA is a consideration, but the history is equivocal and clinical suspicion is low. Such patients are asymptomatic, with normal radiographic findings. For this group, observation without bronchoscopic intervention is an appropriate option. Follow up in 1 to 2 days and arrange bronchoscopy if the symptoms persist or have progressed.

Do not prescribe routine antibiotics or corticosteroids after uncomplicated bronchoscopic foreign body retrieval. Postobstructive pneumonia can develop distally after prolonged obstruction of the bronchus by a foreign body. In such a case, Gram stain and cultures of the fluid obtained during bronchoscopy will guide postprocedural antibiotic management.

Indications for Consultation

- **Pulmonology, otolaryngology, or surgery:** Depends on who performs bronchoscopy at a given institution

Disposition

- **Intensive care unit transfer:** Airway instability, respiratory distress, hypoxia, significant airway injury
- **Discharge criteria:** Foreign body removed, normal respiratory status without an oxygen requirement

Follow-up

- **Primary care**
  - — Foreign body removed: 1 to 2 weeks
  - — Low suspicion for a foreign body and clinical status stable: 1 to 2 days
- **Surgical consult:** 1 week with the provider that performed the procedure

Pearls and Pitfalls

- Most airway foreign bodies are in the bronchi, the right bronchus more often than the left.
- Normal chest radiographic findings do not conclusively rule out FBA.
- Consider FBA as a diagnostic possibility in a patient with chronic cough, recurrent pneumonia(s) in one lung, or focal wheezing.
- Accidental FBA does not typically require reporting to the local child protective services (CPS) agency. However, if FBA occurred in the context of a larger or longitudinal pattern of neglectful parenting, file the CPS report.

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Sedation and Analgesia

CHAPTER 103

Pain Management

Introduction

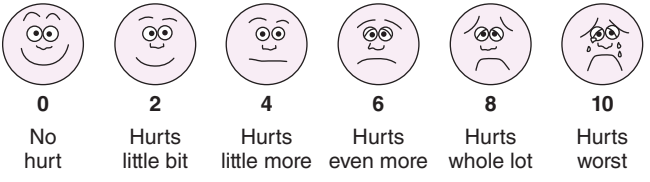
According to the International Association for the Study of Pain, pain is "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." Effective pain management is an essential aspect of inpatient medicine, a clinical performance measure, and a patient right. However, pediatric pain has historically been underrecognized and undertreated. Traditional barriers to providing adequate pain control to children include difficulty assessing pain in young patients, unfamiliarity with scoring instruments to measure pain, fear of adverse effects such as respiratory depression or addiction, and concerns about masking serious conditions.

Pain Assessment

Pain management begins with appropriate assessment, measurement, and documentation of pain. Assess the severity with a developmentally appropriate and validated instrument, supplemented by a thorough pain history and physical examination. The goal is to tailor pain medication dosing to the individual patient and their experience. Therefore, it is important to use standard pain scales in conjunction with assessment of patient and family satisfaction with treatment of the pain. Following a trend in pain score is more helpful than one individual score in assessing the response to an intervention.

In general, 2 types of pain assessment tools are available: self-report and observational-behavioral. Self-report measures depend on the patient's ability to quantify and verbally describe pain. These tools include the Numeric Rating Scale and the FACES Pain Scale (Figure 103–1), which are useful when assessing pain in a school-aged verbal patient. Be aware that there are many

Figure 103–1. Wong-Baker FACES pain rating scale.



reasons why a child might deny feeling pain, including being told to be brave, concern about medication side effects or taste, anxiety that pain means they are getting sicker, inadequate understanding that pain can be treated, worry that pain will prevent discharge home, or fear of injection site pain associated with intramuscular (IM) or subcutaneous pain control.

Assessing pain in a younger child or a patient with developmental disabilities can be challenging. In these cases, observational-behavioral measures that identify the patient's reaction to pain (physiologic signs versus behavior) are helpful. Increased pulse and blood pressure may suggest that a nonverbal child is in pain, although the absence of altered vital signs does not preclude pain, especially if the pain is chronic. Commonly used and validated observational pain scales include the FLACC (Face, Legs, Activity, Cry, Consolability; Table 103–1) or revised FLACC (FLACC-R), Neonatal Infant Pain Scale, and CRIES (C-crying, R-requires increased oxygen, I-increased vital signs, E-expression, S-sleeplessness).

Treatment

There are a number of basic principles in pediatric pain management.

- Pediatric pain practices may rely on extrapolation from adult study data. Medications are frequently used off-label. Use pediatrics-specific, evidence-based practices whenever possible.

Table 103–1. Face, Legs, Activity, Cry, Consolability (FLACC) Scale

Category	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimaces or frowns; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly Normal position Moves easily	Squirming Shifting back and forth Tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily Screams or sobs Frequent complaints
Consolability	Content Relaxed	Reassured by occasional touching, hugging, or "talking to" Distractible	Difficult to console or comfort

Abbreviation: FLACC, face, legs, activity, cry, consolability.

Note: Total all five scores. The interpretation is 0 = relaxed and comfortable; 1–3 = mild discomfort; 4–6 = moderate pain; 7–10 = severe discomfort/pain. From Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs.* 1997;23(3):293–297. Printed with permission of the regent of the University of Michigan.

- Consult the pain service early in the hospital course, particularly if opioids are needed.
- Complementary modalities, such as relaxation and breathing exercises, guided imagery, biofeedback, massage, or distraction (eg, art, pet, play, or music therapy) can greatly reduce the need for pharmacologic management of pain in a child.
- Involve a child life specialist, who is one of the few professionals that is not directly involved with causing emotional stress or physical pain. Treat anxiety, sadness, and fear as components of suffering that increase the child's perception of pain.
- Strive to use the most painless (oral, transdermal, topical, intranasal) route of administration while avoiding IM and rectal medications.
- When treating pain, use a stepladder approach starting with nonopioid medications and escalating to opioids as indicated based on severity of pain. Reassess the patient frequently for continuing pain and the effectiveness of treatment.
- Less medication is required to prevent pain than to eliminate it. Therefore, initially use as much medication as necessary to achieve pain control, and then dose as frequently as needed to maintain adequate analgesia.
- A patient with prior exposure to pain medication (eg, advanced cancer, sickle cell) often requires far higher doses of analgesics and adjuncts to achieve adequate pain control.
- Attempt to achieve control of long-term pain with scheduled or long-acting medications and provide immediate-release medications for incidental or "breakthrough" pain episodes.

Nonopioid Analgesics

Acetaminophen

Acetaminophen is an effective analgesic and antipyretic that is available in oral, rectal, and intravenous (IV) forms. The onset of action occurs within 60 minutes after oral administration and within 10 minutes of IV administration. It is metabolized primarily in the liver and may therefore be contraindicated in hepatic failure. Also, because of a risk of chronic liver toxicity, limit the duration of around-the-clock therapy to 3 days.

Oral or rectal dosage:

- 10 days to 12 years or younger: 10 to 15 mg/kg per dose every 4 to 6 hours (75 mg/kg/d or 4,000-mg/d maximum)
- 12 years and older: 325 to 650 mg every 4 to 6 hours or 1,000 mg per dose, 2 to 3 times a day (4,000-mg/d maximum)

Intravenous dosage:

- Younger than 13 years or weight less than 50 kg: 12.5 mg/kg every 4 hours or 15 mg/kg every 6 hours (750 mg per dose or 75-mg/kg/d maximum, up to 3,750 mg)
- 13 years and older or weight 50 kg or more: 650 mg every 4 hours or 1,000 mg every 6 hours (4,000-mg/d maximum)

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) have analgesic, anti-inflammatory, and antipyretic effects. Side effects include gastritis, nephropathy, and bleeding from platelet antiaggregation.

IBUPROFEN

Ibuprofen is available in both oral and IV forms. The dose of ibuprofen is 10 mg/kg every 6 hours (child) or 400 to 600 mg every 6 hours up to 800 mg every 8 hours (adolescent). The onset of action occurs in 30 to 60 minutes.

NAPROXEN

Naproxen is available in both oral tablets and liquid suspension for use in children 2 years or older. The benefit over ibuprofen is longer duration of action, so dosing is every 8 to 12 hours with 10–20 mg/kg/d.

KETOROLAC

Ketorolac is available in both oral and IV forms. The IV dose is 0.5 mg/kg every 6 hours (maximum 30 mg per dose) and is particularly useful as a parenteral agent when trying to avoid, or minimize, the use of opioids. The onset of action is 30 minutes. Ketorolac shares the same side-effect profile as the other NSAIDs in terms of bleeding risk and potential effect on renal function, with a higher risk in patients with baseline renal impairment or gastric disease. Do not use ketorolac for more than 5 days because of an increased risk of side effects.

Opioid Analgesics

Opioids are available in multiple forms, including IV (which can also be delivered intranasally), oral, and transdermal. The severity of the pain is not an automatic prompt for the use of IV opioids rather than the enteral form. Indications for using IV opioids include, but are not limited to, concern for poor gastrointestinal absorption or inability to administer medications enterally. Commonly used opioids in the pediatric setting, from weakest to most potent, include morphine, oxycodone, hydromorphone, and fentanyl. When a patient is on multiple different opioids, use morphine milligram equivalents (Table 103–2) to determine cumulative intake of opioids in a 24-hour period to gauge overdose potential. Do not use codeine, as genetic variability in

Table 103–2. Morphine Milligram Equivalents	
Opioid (Dose in mg/d, Except Where Noted)	**Conversion Factor**
Fentanyl transdermal (in mcg/h)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20 mg/d	4
21–40 mg/d	8
41–60 mg/d	10
≥ 61 mg/d	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

Morphine milligram equivalent (MME) is an opioid dosage's equivalency to morphine. Do *not* use MME to convert one opioid to another.
From Centers for Disease Control and Prevention. Module 6: Dosing and titration of opioids: how much, how long, and how and when to stop? *Interactive Training Series for Healthcare Providers.* https://www.cdc.gov/drugoverdose/training/dosing/accessible/index.html. Accessed May 10, 2022.

metabolism can result in undertreated pain (rapid metabolism) or respiratory depression (slow metabolism).

Opioids are most effective when administered around the clock (ie, on a schedule) for chronic or persistent pain, with as-needed doses indicated every 2 to 4 hours for breakthrough pain. Start with an as-needed dose that is equal to 10% to 15% of the total daily maintenance dose. If the patient requires more than 4 to 6 as-needed doses, increase the daily maintenance dose, and by extension the as-needed dose, by 50%. If there are side effects, such as severe nausea or sleepiness, decrease the maintenance dose by 25%.

When attempting to rapidly achieve pain control with opioids, it is helpful to do a rapid IV titration by using morphine, hydromorphone, or, occasionally, fentanyl. This process may take several hours and requires close attention to the patient's response to each dose. To treat pain in a patient who is already receiving opioids, increase the dose by 25% to 50% for mild to moderate pain and 50% to 100% for severe pain. Although this approach requires additional physician and nurse presence, the pain relief can be achieved much more effectively with a direct, hands-on approach.

Morphine

Morphine can be administered orally (immediate or sustained release), sublingually, subcutaneously, intravenously, and rectally. Ideally, consult with a pain service before prescribing. Morphine is the preferred initial opioid in opioid-naïve patients for moderate to severe pain. Use with caution in a patient with renal failure.

The starting IV morphine dose for an opioid-naïve patient is 0.05 to 0.10 mg/kg every 3 to 4 hours (maximum, 10 mg per dose). The onset of action is 5 to 10 minutes. The oral dose for immediate-release morphine is 0.15 to 0.50 mg/kg per dose (initial dose of 0.3 mg/kg for severe pain, maximum initial dose 15 to 20 mg) every 3 to 4 hours. The onset of action of oral morphine is 30 minutes.

In a child who has not been given opioids previously, begin at the lower dose and titrate up as needed. However, if the patient has chronic pain management requirements, convert to a long-acting, orally administered opioid once the daily requirement has been established (via either IV or oral administration). This can be a complex process, so consult with the pain service, if available.

Morphine Patient-Controlled Analgesia

Patient-controlled analgesia (PCA) is administered with a programmable pump that allows the patient to control IV analgesia by choosing when to deliver a dose of opioid for quick relief, in addition to facilitating titration to pain needs. The lockout interval for the bolus dose is related to the onset and peak action of the opioid. The patient must be mature enough to understand how and when to push the demand button for boluses.

Patient-controlled analgesia is the safest technique for IV opioid (morphine, fentanyl, or hydromorphone) administration in the treatment of acute postoperative pain. With self-administration, the patient will not request further boluses if sedated and sleeping and therefore cannot self-overdose. Continuous infusion may reduce the safety of PCA, because it is administered independently of the patient's sedation level. Comparative studies show that continuous background opioid infusion in conjunction with PCA does not facilitate improvement in pain scores over PCA-only postoperative analgesia. Therefore, individualize the use of a basal infusion based on the clinical situation. Patient-controlled analgesia with continuous infusion is indicated when analgesia is required for a number of conditions, including (among others) vasoocclusive episodes in a patient with sickle cell disease, severe postoperative pain, or cancer-related pain, or when goals of care have transitioned to primarily palliative.

A typical PCA pump can be programmed with a bolus dose, lockout time, basal (continuous) infusion, and a 1-hour dose limit. Begin a morphine PCA regimen with a loading dose of 0.05 to 0.10 mg/kg per dose. Then start the PCA with a basal (continuous) rate if indicated at 0.01 to 0.03 mg/kg/h. Order an on-demand bolus dose of 0.01 to 0.02 mg/kg per dose with a lockout period of 5 to 10 minutes. For example, give a 25-kg patient a continuous rate of 0.25 to 0.75 mg/h with 0.25-mg PCA demand doses (up to 10 in 1 hour, if the pain persists). Increase the basal rate by 10% if the patient requires more than 3 boluses per hour, and decrease it by the same amount if fewer than 3 boluses

per hour are requested. In addition to the usual tools of pain assessment, calculate the ratio of PCA demands to delivered doses. A ratio greater than 2 may suggest poorly controlled pain, or difficulty understanding the PCA, and the need to investigate why the patient has been pressing the button frequently.

Close monitoring by trained pediatric personnel is required for any patient undergoing the initiation of PCA or IV opioid treatment. Consult with a pain specialist or the palliative care service when more complex pain management is needed.

Oxycodone

Oxycodone is available in oral form and is indicated for mild to moderate pain. If the patient will be receiving other acetaminophen-containing preparations, do not use oxycodone preparations that also contain acetaminophen (due to the risk of acetaminophen overdose). The dose is 0.05 to 0.15 mg/kg every 4 to 6 hours (maximum dose range 5 to 10 mg per dose).

Hydromorphone

Hydromorphone is 5 to 7 times more potent than IV morphine. It is available in oral and IV formulations. The IV dose is 0.015 mg/kg per dose every 3 to 6 hours as needed. The oral dose is 0.04 to 0.08 mg/kg per dose every 4 hours as needed. It may also be used via PCA in place of morphine or in a regimen of planned opioid rotation. Consultation with a pain or palliative care service is helpful in planning a rotation of opioids.

Fentanyl

Fentanyl can be administered IV, with a buccal tab or lozenge, intranasally, or by transdermal patch. Do not use fentanyl as an initial opioid of choice, due to its increased potency and shorter half-life. It is indicated for severe pain, but reserve the transdermal patch for when a long duration of pain is anticipated. Fentanyl administered intravenously, intranasally, and by the buccal route has rapid onset with a relatively brief duration of action, so if a longer period of analgesia is necessary, use a continuous infusion. The IV dose is 0.5 to 1.0 mcg/kg every 1 to 2 hours as needed, and the intranasal dose is 1.5 mcg/kg (maximum 100 mcg per dose).

Side effects of rapid administration in some patients are glottic and chest wall rigidity. Therefore, follow a careful monitoring protocol and have resuscitation equipment available when administering the drug via bolus or infusion. Because of its high lipophilicity, fentanyl tends to accumulate in adipose tissues, leading to a prolonged elimination in a patient receiving long-term treatment. Discontinuation of fentanyl after as few as 3 days of use has been associated with abstinence syndrome, necessitating close observation and consideration for weaning in patients receiving long-term treatment.

Opioid Side Effects

It is important to note that reactions to one opioid are not predictive of reactions to another, so if severe side effects, such as uncontrolled pruritus, occur, change to another opioid.

RESPIRATORY DEPRESSION

Sedation is far more common than respiratory depression. However, naloxone, an opioid antagonist, is indicated when a patient receiving narcotics is unresponsive to physical stimulation, has shallow respirations (< 8 breaths/min and at risk for intubation), and pinpoint pupils. If the patient is hypoxemic or hypoventilating, or if there is hemodynamic compromise, discontinue the opioid and provide face-mask oxygen. For life-threatening opiate overdose, the initial dose of naloxone is 0.1 mg/kg (maximum, 2 mg per dose). Administer the naloxone slowly, and monitor the patient closely for a response. The onset of IV action is about 2 minutes, and the dose can be repeated every 2 to 3 minutes until the patient responds. If there is no response to the naloxone, assess for other causes of respiratory depression.

Administering higher doses of naloxone may precipitate acute abstinence syndrome in a patient receiving long-standing opioids, with adverse physical and psychological consequences. Cardiac decompensation or pulmonary edema may also occur when fully reversing opiates acutely. Discontinue the naloxone as soon as the patient responds. However, continue to monitor the patient because the effective duration of action of naloxone is about 30 minutes, which is frequently shorter than the opiate, necessitating additional doses of naloxone. The patient will then require nonopioid pain relief. Once the patient is easily arousable with a respiratory rate greater than 9 breaths/min, consult with a pain specialist to determine the best way to restart the opioid.

NAUSEA

In a patient over 1 month of age, treat with IV or oral ondansetron (0.05–0.15 mg/kg every 6 hours as needed; maximum, 4 mg per dose).

CONSTIPATION

Always start a bowel regimen if the patient will be receiving opioids for more than 1 day (see Chapter 35, Constipation).

PRURITUS

This is a common side effect of all opioids. In general, the more potent the opioid, the less histamine release. Isolated pruritus is not an allergic reaction and is therefore *not* a contraindication to continuing the drug. Treat with diphenhydramine (5 mg/kg/d, divided into doses administered every 6 hours; 300 mg/d maximum) or hydroxyzine (2 mg/kg/d, divided into doses administered every 6 hours; 50 mg per dose maximum). In addition, consult with a

pain specialist to determine whether a low-dose naloxone infusion would be beneficial in treating the pruritus.

Opioid Tolerance

Opioid tolerance is the development of the need to increase the dose of the medication to achieve the same sedative or analgesic effect. Cross-tolerance among all opioids occurs, but not on a 1:1 basis. Therefore, in conversion to another opioid, it is best to administer a percentage of the equianalgesic dose (25%–50% for a short-acting medication) and then titrate up. Every child is different, and dosage must be individualized. However, to minimize tolerance, rotate opioids or, in severe cases, use adjuncts such as a ketamine infusion, which enhances the response to opioids. In such complex pain management situations, consult with a pain specialist or the palliative care service.

Weaning and Withdrawal

Opioid withdrawal may occur in a patient who has been receiving opioids at regular intervals for longer than 7 days. The goal of weaning is to prevent withdrawal symptoms (abstinence syndrome), which can occur within 24 hours of abrupt cessation of the medication or immediately if the patient is given naloxone. The symptoms peak within 72 hours of cessation and include cramping, vomiting, diarrhea, tachycardia, hypertension, diaphoresis, restlessness, insomnia, movement disorders, and seizures. Use a validated scoring tool to assess for withdrawal such as the Withdrawal Assessment Tool Version 1.

Consult with a pain specialist to determine the best weaning regimen, which can vary based on the indication for, and duration of, the opioid treatment. One approach is to begin the weaning process when the patient is receiving 0.025 mg/kg/h or less of morphine (basal rate plus bolus). The initial step is to lower the total opioid by 10% to 30%, either by decreasing the IV rate or converting from continuous IV to around-the-clock bolus treatment. Continue the weaning process by no more than 20% per day. Discontinue IV analgesia when the patient is tolerating an oral regimen, with normal gastrointestinal function (patient tolerating oral intake and passing gas) and pain typically quantified as 6 or lower on a scale of 10.

When transitioning from PCA to oral medication, administer a dose of the oral analgesic first, and then discontinue the basal infusion 30 to 60 minutes later. Concurrently, reduce the IV bolus dose by 25% to 50%. Then discontinue the PCA if the patient has not required a bolus dose in more than 6 hours. If the patient requires 1 to 3 bolus doses over a 6-hour period and is in persistent pain after evaluation, increase the oral analgesic dose by 25% to 50%. Increase by 50% to 100% if 3 to 6 boluses are required over a 6-hour period, or add an oral adjuvant, such as acetaminophen. However, always assess whether there are other, psychologically based motivations why the patient continues to push the button.

Some institutions have protocols for converting the patient to oral methadone. This generally takes several days to achieve complete conversion after the parenteral opioids have been weaned to an acceptably low level. Monitor for excessive sedation, as methadone can accumulate due to its long half-life. When pain management is no longer needed, do not stop the medication abruptly. Reduce the dose by 10% to 20% every 48 hours to prevent withdrawal.

Special Considerations in Pain Management

Orthopedic Pain

The proper management of orthopedic pain permits earlier mobilization, which can lead to decreased morbidity and shortened hospital stay. Around-the-clock opioids, such as IV morphine, provide optimal analgesia, which can then be tapered accordingly. Ensure that adequate analgesia is given prior to mobilization or physical therapy.

Postoperative Pain

Initially manage postoperative pain with around-the-clock analgesics, and then taper the medication, as tolerated, to as-needed dosing. If the patient underwent abdominal surgery or cannot tolerate oral medications, IV morphine administered every 3 to 4 hours or via PCA is useful, with appropriate monitoring. Intravenous acetaminophen is sometimes used in this situation to reduce or avoid opioid use.

Patient With Neurocognitive Impairment

Pain is often underrecognized and inadequately treated in this population due to the complexity of identifying pain in a child who cannot communicate their experience. Sources of pain include both acute causes and chronic recurrent conditions such as reflux, spasticity, and neuropathic pain. Use validated behavioral pain-assessment tools to identify presence of pain in these patients (Table 103–1). Furthermore, avoid using terms such as "agitation" or "irritability" to describe children with neurocognitive impairment (NCI) in distress, as this can shift the focus from true pain behaviors and undermine the urgency of pain management. Chronic recurrent pain behaviors in a patient with NCI are typically best treated using an empiric approach, with some evidence of benefit from adjuvant medications that target the central nervous system, such as gabapentin. When managing pain, consider the patient's home medications to avoid harmful drug interactions. If symptoms remain intractable after first-line interventions, arrange for an interdisciplinary approach with input from palliative care, physical medicine and rehabilitation, complex care specialists, and/or neurology.

Neuropathic Pain

Neuropathic pain can be described as burning, tingling, or numbness. In these cases, consult with a pain specialist to determine whether the addition of gabapentin would be helpful. Titrate by starting at 5 mg/kg oral (up to 300 mg per dose) once a day at nighttime, increasing to twice daily the next day, and then 3 times a day on the third day. Make further adjustments by dosage increases, rather than frequency.

Newborn Procedural Pain

Procedural pain in neonates can be assessed by physiologic or behavioral pain indicators. Use oral sucrose (1–5 mL) to reduce procedural pain from single events such as heel sticks, venipuncture, and intramuscular injections. Oral acetaminophen (10–15 mg/kg/dose every 6–8 hours) is also effective.

Sickle Cell Pain

Manage vasoocclusive pain episodes aggressively, and ask the patient/parents what has worked well in the past. Depending on the patient's age and the severity of the pain and disease, it may be best to start with morphine PCA. If the patient is too young to use a PCA, order around-the-clock IV morphine. For a patient of any age, ketorolac may also be necessary (after confirmation of normal serum creatinine level; see Chapter 48, Sickle Cell Disease). Be aware that a patient with sickle cell disease may have previously received multiple courses of opioids and may therefore require higher doses than an opioid-naïve patient.

Pearls and Pitfalls

- When managing pediatric pain, do it "by the child, by the mouth, and by the clock." That is, individualize an analgesia regimen for a specific patient that is administered around the clock (every 3–6 hours) and is ideally delivered orally (painless administration).
- Do not undertreat pain because of fear of adverse effects. Consult with a pain specialist when the pain severity requires you to practice outside your comfort zone.
- Do not overlook the benefit of nonpharmacologic techniques to aid in relief of both pain and anxiety (ie, using child life specialists, creating an "ouchless" environment).
- When choosing a pain assessment tool, keep in mind the child's physical, social, and emotional development.
- A trend in pain score is more helpful than an individual score in assessing the response to a given intervention.

- Intravenous acetaminophen may be limited by the pharmacy due to expense. It may help reduce opioid use, but switch to oral dosing as soon as possible.
- Ketorolac has minimal anti-inflammatory effects, so if that is desired, then ibuprofen or naproxen is a better choice.

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Sedation

Introduction

The goal of pediatric sedation is to allow diagnostic and therapeutic procedures to be performed as safely, comfortably, and efficiently as possible. Consider each situation on an individual basis to determine the appropriate level of sedation needed and to address the individual patient's needs regarding control of pain, anxiety, memory, and motion during the procedure.

Definitions

The level of drug-induced sedation is divided into 4 different states.

Minimal Sedation/Anxiolysis

The patient can respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are maintained.

Moderate Sedation

The patient can respond purposefully to verbal commands, either alone or accompanied by light to moderate tactile stimulation. No interventions are required to maintain a patent airway; adequate spontaneous ventilation and cardiovascular functions are usually maintained.

Deep Sedation

The patient cannot be easily aroused but responds purposefully to repeated verbal or painful stimulation. Ventilatory function and protective airway reflexes may be impaired, and the patient may require assistance in maintaining a patent airway and/or require positive-pressure ventilation. Cardiovascular function is usually maintained.

General Anesthesia

The patient cannot be aroused, even by painful stimulation. Ventilatory function is often impaired, and the patient will often require assistance in maintaining a patent airway. Positive-pressure ventilation may be needed because of depressed spontaneous ventilation or neuromuscular function. Cardiovascular function may also be impaired.

Principles

The guiding principles for safe and effective sedation are

- Maximize patient comfort and minimize pain and distress.
- Use nonpharmacologic interventions as an adjunct. Whenever possible, supplement sedation with other pain-reducing modalities, such as topical analgesia and nerve blocks, and nonpharmacologic techniques, such as involving a child life specialist.
- Prepare the child and family.
- Ensure health provider competency in performing procedures and sedation.
- Use appropriate monitoring to ensure safety.

Training

Each institution must develop a specific training and certification program, ideally in conjunction with the institution's department of anesthesiology. This will help ensure the competence of medical providers in performing safe sedation techniques and will also clearly delineate hospitalist roles and limitations. Specific guidelines must include the medications that may be used, American Society of Anesthesiologists (ASA) physical status classes that may be sedated (see Table 104–1), and the timing and location of hospitalist-run sedations. The training program must also ensure that the hospitalist is comfortable with and prepared to manage contraindications, common side effects and complications, and basic rescue mechanisms, including airway management.

Each patient's responses to different medications can vary, so be prepared to manage deeper levels of sedation than what was planned. For example, if moderate sedation is intended, be qualified and prepared to manage a patient who is deeply sedated. Become familiar with a small number of anesthetic agents to be able to simplify sedation plans and maximize safety and efficiency. For example, ketamine is useful for painful procedures, whereas dexmedetomidine is a reasonable option for imaging procedures that require a motionless state.

Institutional needs and resources will dictate what levels of training are available for hospitalists, and a tiered system may be appropriate in some cases. For example, a first tier of hospitalists may be approved to sedate ASA class I–II patients in the emergency unit where multiple resources are available, whereas a second tier may be approved to sedate ASA class I–III patients in specified specialty units during daytime hours when anesthesia is available for backup, and a third tier may be approved to use a wider variety of agents or sedate patients after hours.

Table 104–1. American Society of Anesthesiologists Physical Status Classification		
Class	**Definition**	**Examples**
I	A normal healthy patient	Healthy (no acute or chronic disease) Normal body mass index for age
II	A patient with mild systemic disease	Asymptomatic congenital cardiac disease, asthma without exacerbation, well-controlled epilepsy, oncological disease in remission, mild obstructive sleep apnea
III	A patient with severe systemic disease	Uncorrected stable congenital cardiac disease, asthma with exacerbation, poorly controlled epilepsy, severe obstructive sleep apnea
IV	A patient with severe systemic disease that is a constant threat to life	Symptomatic congenital cardiac abnormality, active sequelae of prematurity, sepsis, severe respiratory distress
V	A moribund patient who is not expected to survive without a procedure	Respiratory failure or arrest, decompensated congestive heart failure, malignant hypertension

Adapted from the American Society of Anesthesiologists Committee on Economics. ASA Physical Status Classification. https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system.

Presedation Evaluation

Perform a screening evaluation prior to the induction of sedation. Include a focused history guided by the mnemonic SAMPLE (Box 104–1). At physical examination, pay particular attention to airway, respiratory, and cardiovascular status. Screen the patient for a personal or family history of complications from sedation or anesthesia; a history of snoring, wheezing, or stridor; recent illnesses; obesity; and anatomic abnormalities (small jaw, short neck, large tongue) that may make airway obstruction more likely and rescue procedures more difficult. Evaluate the patient's ASA physical status (Table 104–1), and arrange an anesthesia consultation prior to sedation if the ASA class is III, IV, or V.

As with any procedure, observe and document a time-out before sedation is initiated. Encourage the presence of the family, provided they can tolerate the procedure and understand that they cannot interfere with the medical care.

Box 104–1. SAMPLE Mnemonic for Patient History
S: Signs and symptoms
A: Allergies to medications, food, or latex
M: Medications used regularly or recently
P: Past medical and surgical history, including history of sedations
L: Last liquid and solid intake
E: Events leading to current illness, injury, or need for procedure

Presedation Fasting

It is generally believed that fasting decreases the likelihood of aspiration. Therefore, follow the ASA recommendations for nil per os (nothing by mouth) times (Table 104–2) for all elective procedural sedations. For emergent sedations, carefully balance the risks of sedation with the benefits of completing the procedure quickly. In an emergent case, when the fasting interval is insufficient, use the lightest effective sedation.

Presedation Preparation

To optimize patient safety, ensure the presence of a medical provider with advanced resuscitation skills at all times during sedation. This person may also perform the procedure during moderate sedations, provided there is an assistant present who can closely monitor the patient and record vital signs data. Ideally, this assistant will have skills for the recognition and rescue of airway obstruction. During deep sedations, the sedation provider may offer brief, interruptible assistance to a separate proceduralist if it does not interfere with the ability to closely monitor the patient at all times.

Before beginning sedation, confirm that all potentially needed rescue equipment and medications are easily accessible. Keep a crash cart nearby, with precalculated doses of common rescue medications and airway rescue equipment, such as laryngoscopes with appropriately sized blades, endotracheal tubes, stylets, and laryngeal mask airways. Have an anesthesia or continuous positive airway pressure bag readily available and connected to

Table 104–2. American Society of Anesthesiologists Recommendations for Preoperative Fasting[a]

Ingested Material	Minimum Fasting Period[b]
Clear liquids[c]	2 h
Breast milk	4 h
Infant formula	6 h
Nonhuman milk[d]	6 h
Light meal[e]	6 h
Fried foods, fatty foods, or meat	Additional fasting time (eg, 8 or more hours) may be needed

[a] These recommendations apply to healthy patients who are undergoing elective procedures. They are not intended for women in labor. Following the guidelines does not guarantee complete gastric emptying.

[b] The fasting periods noted above apply to all ages.

[c] Examples of clear liquids include water, fruit juices without pulp, carbonated beverages, clear tea, and black coffee.

[d] Since nonhuman milk is similar to solids in gastric emptying time, the amount ingested must be considered when determining an appropriate fasting period.

[e] A light meal typically consists of toast and clear liquids. Meals that include fried or fatty foods or meat may prolong gastric emptying time. Additional fasting time (eg, 8 or more hours) may be needed in these cases. Both the amount and type of foods ingested must be considered when determining an appropriate fasting period.

Excerpted from Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration. *Anesthesiology.* 2017;126:376–393.

an oxygen source with an appropriately sized face mask attached. Connect a large-bore suction catheter to wall suction in case of emesis. The SOAPME mnemonic is useful for patient care during sedation: Suction, Oxygen, Airway, Positioning, Monitoring, and End-tidal carbon dioxide.

Sedation and Recovery Monitoring

During minimal and moderate sedation and recovery, continuously monitor the patient's heart rate, ventilation (auscultation), and pulse oximetry data. Also, monitor the end-tidal carbon dioxide ($EtCO_2$) level when the sedation practitioner is at a distance and cannot directly observe the patient (eg, during magnetic resonance imaging). Reassess blood pressure and respiratory rate every 5 minutes once a stable level of sedation has been achieved. Obtain intravenous (IV) access for moderate or deeper sedation.

For deep sedation and recovery, monitor the patient as detailed earlier, always with IV access. Monitor $EtCO_2$ level during the sedation and recovery period if feasible, because ventilatory function is often compromised before oxygenation. Perform deep sedation only in an area that is both familiar to the sedation provider and properly supplied with all necessary equipment. Do not perform deep sedation in a routine inpatient bed.

In addition to the abovementioned monitoring, directly observe the patient during sedation, paying particular attention to the level of consciousness, color, airway patency, ventilatory effort and adequacy, and perfusion. Continue to monitor the patient after sedation and ensure that the institutional recovery criteria are met before the patient is discharged or returned to the inpatient floor. Follow the hospital's protocols for appropriate documentation of patient monitoring data during both sedation and recovery, specifically noting in the medical record all vital signs and patient information mentioned earlier.

Discharge Criteria

The patient may be discharged from monitoring 30 minutes after the final medication administration if all of the following discharge criteria are met:

- Patent airway without respiratory depression
- Return to baseline vital signs, motor function, and level of consciousness
- Adequate hydration and no spontaneous vomiting (although nausea may be expected)
- Adequate pain control

Pearls and Pitfalls

- Consent for sedation is separate from consent for the procedure.

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Surgery

Abdominal Masses

Introduction

Abdominal masses may be caused by a range of conditions, from benign (eg, constipation) to life-threatening (eg, neuroblastoma), and many are found incidentally by a parent or health care provider. Masses can be associated with solid organs, the mesentery, or the bowel. A mass may also represent organomegaly, which may suggest an infiltrative disorder. The initial hospitalization is usually focused on the diagnostic evaluation, with imaging (often ultrasonography [US]) findings as the mainstay of diagnosis.

Clinical Presentation

History

Presenting symptoms will vary, based on the size and location of the mass. These may include abdominal pain (localized or diffuse), abdominal distention, early satiety, anorexia, vomiting, constipation, fever or night sweats, hematuria, and weight loss or failure to thrive. Significant distention can limit diaphragmatic excursion, resulting in respiratory distress. Ask about any systemic symptoms, such as fever and lethargy. The dietary history may suggest a diagnosis of constipation or bezoar. Some masses are secondary to genetic conditions, so the family history may be important.

Physical Examination

Superficial venous distention suggests impingement on deep venous drainage by a large mass. Similarly, a large mass may cause lower extremity edema and scrotal or labial swelling. Hypertension is a common finding, particularly among patients with a primary kidney tumor (most commonly Wilms tumor) or when a suprarenal mass (most commonly neuroblastoma) results in compression of the kidney(s) and/or renal vasculature. A mass involving the liver may appear with jaundice and edema or signs of a coagulopathy at presentation, if synthetic function is affected. The presence of cutaneous hemangiomas in an infant may be associated with an occult infantile hepatic hemangioma. When these infantile hepatic hemangiomas are large and symptomatic, they may cause high-output heart failure.

Laboratory Workup

If a malignancy is suspected, obtain a complete blood cell count with differential and lactate dehydrogenase, uric acid, and electrolyte levels. Then choose laboratory tests based on the location of the mass and the patient's associated symptoms (Table 105–1). Always perform a urine pregnancy test early in the workup of a postmenarchal female subject (prior to imaging).

Radiology Examinations

Imaging is essential to the diagnosis of an abdominal mass. Often, abdominal radiographic findings will have confirmed the presence of a mass, or mass effect, prior to hospital admission. However, the key test is abdominal US, which will differentiate cystic from solid masses, thereby narrowing the differential diagnosis. Ultrasonography is useful for imaging the liver, biliary tract, kidneys, pylorus, and female reproductive organs. However, image quality is dependent on the skill of the sonographer and may be limited by obesity or excessive bowel gas. Computed tomography (CT), magnetic resonance imaging, or nuclear medicine can subsequently be performed to further characterize the mass and extent/spread of disease. If possible, discuss the clinical concerns and examination findings with a radiologist to determine the most appropriate imaging study. A summary of imaging modalities is included in Table 105–2.

Differential Diagnosis

The differential diagnosis is age dependent. For example, a liver mass in an infant is most likely infantile hemangioendothelioma; in a young child, it is likely a mesenchymal hamartoma or hepatoblastoma; and in an adolescent (especially a teenage female subject using oral contraceptives), it is likely a

Table 105–1. Initial Laboratory Tests in the Evaluation of an Abdominal Mass

Type or Source of Mass	Initial Laboratory Tests
Liver	Liver function tests, including alanine transaminase, aspartate transaminase, γ-glutamyltransferase, albumin, and total and direct bilirubin levels PT/PTT AFP level
Kidney/adrenal	BUN and creatinine levels Urinalysis, urine HVA/VMA levels
Ovary	AFP level Quantitative β-HCG level
Pancreas	Amylase and lipase levels

Abbreviations: AFP, α-fetoprotein; BUN, blood urea nitrogen; HCG, human chorionic gonadotropin; HVA, homovanillic acid; PT, prothrombin time; PTT, partial thromboplastin time; VMA, vanillylmandelic acid.

Table 105–2. Choice of Imaging Modality for Evaluation of Abdominal Masses

Imaging Modality	Indications	Limitations
Abdominal radiography	May confirm presence of mass May help rule out acute obstruction or perforation	Limited ability to demonstrate exact anatomic location and structure of mass
Computed tomography (with contrast material)	Suspect malignancy (also obtain pelvic and chest images) Suspect teratoma Suspect focal hepatic lesion Suspect infection/abscess	Radiation exposure (decreased with newer technology)
Magnetic resonance imaging (with and without contrast material)	Evaluate hepatobiliary masses Suspect Kasabach-Merritt syndrome	Potential need for sedation or anesthesia
Ultrasonography	Initial evaluation of most abdominal masses Particularly useful for: Renal and adrenal masses Vascular malformations	Dependent on skill of sonographer Imaging may be limited by obesity or bowel gas

hepatic adenoma. The most common masses palpated in children involve the kidney, with hydronephrosis or multicystic dysplastic kidney being frequent diagnoses. Hydronephrosis has many potential underlying etiologies, but consider ureteropelvic obstruction, ureterovesicular obstruction, vesicoureteral reflux, and renal duplication. Wilms tumor is the most common renal malignancy in children and occurs mostly between 2 and 8 years of age. Other relatively common solid tumors in young children include neuroblastoma and rhabdomyosarcoma, both of which may appear with an abdominal mass at presentation. Hepatosplenomegaly may be caused by a diffuse infiltrative process, which may be oncologic (eg, leukemia), metabolic (eg, glycogen storage disease), or infectious (eg, viral or fungal disease). Table 105–3 includes common diagnoses to consider in children who present with an abdominal mass.

Treatment

Treatment is dependent on the etiology of the mass. Consult hematology/oncology if a malignancy is suspected. Consult surgery if a biopsy is needed for diagnosis or if total resection is the treatment of choice. If the mass is associated with a solid organ, refer the patient to the relevant specialist (eg, a pediatric gastroenterologist or nephrologist). Begin venous thromboembolism prophylaxis if the patient has signs of venous obstruction and/or other risk factors for thrombosis (see Chapter 46, Deep Venous Thrombosis).

Table 105–3. Differential Diagnosis of an Abdominal Mass

Organ System	Most Likely Diagnoses		
	Infant	Child	Adolescent
Adrenal	Adrenal hemorrhage Congenital neuroblastoma	Neuroblastoma	Rare
Bowel	Duplication cyst Intussusception Pyloric stenosis Volvulus	Appendicitis Constipation Intussusception	Appendicitis Constipation
Genitourinary	Germ cell tumor Teratoma	Germ cell tumor Rhabdomyosarcoma Teratoma	Germ cell tumor Ovarian cyst Pregnancy Rhabdomyosarcoma
Hepatobiliary	Choledochal cyst Hamartoma Hemangioma Hepatoblastoma	Hamartoma Hepatoblastoma Hepatomegaly Sarcoma	Focal nodular hyperplasia Hepatocellular adenoma Hepatocellular carcinoma
Kidney	Congenital mesoblastic nephroma Hydronephrosis Multicystic dysplastic kidney Polycystic kidney disease	Multilocular cystic nephroma Renal abscess Pyelonephritis Renal vein thrombosis Wilms tumor	Renal abscess Renal vein thrombosis Pyelonephritis
Mesentery	Meconium pseudocyst	Mesenteric cyst	Non-Hodgkin lymphoma
Pancreas	Congenital pancreatic cyst	Pancreatoblastoma Pancreatic pseudocyst	Pancreatic pseudocyst
Spleen	Congenital splenic cyst	Posttraumatic cyst Splenic abscess Splenomegaly	Posttraumatic cyst Splenic abscess Splenomegaly

Indications for Consultation

- **Gastroenterology:** Hepatobiliary or pancreatic disease
- **Hematology/oncology:** Concern for a malignancy
- **Nephrology:** Renal or suprarenal mass
- **Surgery:** Surgical emergency (appendicitis, intussusception, pyloric stenosis, volvulus); mass biopsy or removal necessary

Disposition

- **Intensive care unit transfer:** Shock, toxic appearance, respiratory compromise secondary to distention, tumor lysis syndrome
- **Discharge criteria:** Definitive diagnosis with treatment underway or planned, presenting symptoms managed effectively, adequate oral intake, and follow-up plans arranged

Follow-Up

- **Primary care:** 1 to 3 days
- **Surgery (if patient underwent a procedure or one is to be scheduled):** 1 to 2 weeks
- **Subspecialist:** Per subspecialist recommendations

Pearls and Pitfalls

- *Do not administer corticosteroids* without consulting an oncologist if there is any possibility that the patient has a malignancy.
- To avoid radiation exposure and the need for sedation, perform abdominal US as the initial imaging examination, especially in a patient younger than 4 years.
- Masses complicating abdominal trauma, such as pancreatic or splenic pseudocysts, can appear weeks after the trauma.

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CHAPTER 106

Acute Abdomen

Introduction

Acute abdomen, also known as surgical abdomen, is a surgical emergency. It is imperative to identify this diagnosis early. However, this can be a difficult task, given the wide range of etiologies and presentations, especially among young children.

Appendicitis is the most common surgical cause of pediatric acute abdomen, but the differential diagnosis includes nonsurgical entities, such as constipation. Age is a major determinant of the diagnoses to consider (Box 106–1). For example, the most common causes of acute abdomen in infants include intussusception and incarcerated inguinal hernia, but for adolescents appendicitis, pelvic inflammatory disease, and ovarian torsion are more common.

Clinical Presentation

History

The symptoms associated with acute abdomen typically evolve over hours. The description of the abdominal pain, along with the associated signs and symptoms, help to differentiate among potential causes. For example, recent contact with sick persons who had a similar illness would make infectious conditions, such as acute gastroenteritis (AGE), more likely.

Box 106–1. Common Etiologies of Abdominal Pain[a]

Infant	Toddler/Child	Adolescent
AGE	AGE	AGE
Constipation	Appendicitis	Appendicitis
Hirschsprung disease	Constipation	Constipation
Intussusception	Henoch-Schönlein purpura	Dysmenorrhea
Incarcerated hernia	Pneumonia	Ectopic pregnancy
Nonaccidental trauma	Strep throat	Irritable bowel disease/irritable bowel syndrome
UTI	Trauma[b]	Mittelschmerz
Volvulus	UTI	Ovarian torsion
		Pancreatitis
		Pelvic inflammatory disease
		Pneumonia
		Strep throat
		Trauma
		UTI

Abbreviations: AGE, acute gastroenteritis; UTI, urinary tract infection.

[a] This table is a guide to the most common causes and is not a comprehensive list.

[b] Includes nonaccidental trauma.

It is important to develop the pain history. Pain location can suggest a potential cause, such as appendicitis (initially periumbilical then migrating to the right lower quadrant) or biliary disease (right upper quadrant). However, being able to localize pain is a developmental milestone, so younger children may not be capable of doing it. The pain time course can also be helpful. For example, appendicitis pain tends to be constant and made worse with movement. Alternatively, the pain of intussusception, nephrolithiasis, and volvulus is episodic or colicky. In general, younger patients are more likely to have an atypical presentation of surgical diagnoses.

Physical Examination

Abdominal pain can be focal or generalized, and it is typically worse with movement. The patient may refuse to walk or walk hunched over, splinting from the pain. Bowel sounds may be present or diminished. Typically, there are peritoneal signs, such as rebound tenderness. Later, as with appendiceal rupture, there can be signs of generalized peritonitis, including abdominal distention and rigidity. Bloody stool is a late finding of ischemia and necrosis that can occur in conditions such as intussusception and volvulus, although this also occurs in nonsurgical conditions such as AGE.

Depending on the child's age and level of cooperation with the examination, it may be necessary to try several different approaches to evaluate peritoneal signs, such as bumping into the bed, asking the child to jump, and distracting the child with a stethoscope. The absence of rebound tenderness suggests that appendicitis is much less likely.

A patient with appendicitis tends to find a position of comfort and lie still. In contrast, episodes of intense pain and movements aimed at finding a comfortable position suggest other etiologies, such as nephrolithiasis or ischemia (ovarian torsion, intussusception, volvulus, incarcerated hernia). A patient with retrocecal appendicitis may not have rebound tenderness, because the overlying distended cecum protects the appendix, resulting in less pain. To determine if there is retroperitoneal inflammation, look for the psoas and obturator signs. Test for a positive psoas sign via passive hip hyperextension and the obturator sign by passive internal rotation of the hip while it is flexed.

As the utility and reliability of radiologic studies continue to evolve, there is less reliance on the digital rectal examination (DRE). For example, pain with DRE is not a reliable sign of appendicitis, and DRE is no longer required for every patient with functional constipation. However, DRE can provide insight into alternative diagnoses, such as helping to determine when diarrhea is more likely caused by encopresis rather than gastroenteritis.

A genitourinary examination is important for children with abdominal pain. Perform testicular examination and cremasteric reflex in boys. Perform external examination in girls with consideration of pelvic examination in patients with vaginal discharge or other findings suggestive of pelvic process.

Laboratory Workup

There is no universal standard for the laboratory evaluation of possible acute surgical abdomen. The diagnosis remains a clinical one, although younger children often have an atypical presentation, which makes this difficult. Some laboratory testing is usually required to eliminate important diagnoses, such as pregnancy or a urinary tract infection (UTI).

In general, if a surgical abdomen is in the differential diagnosis, obtain blood for a complete blood cell count (CBC), C-reactive protein (CRP), electrolytes, lipase, and liver enzymes. Obtain urine for urinalysis. A pregnancy test is a priority for any female who is postmenarchal or sexual maturity (Tanner) stage of 3 on examination (median age: 11 years).

The absence of leukocytosis and a left shift does not conclusively rule out appendicitis but makes it much less likely, especially when coupled with a low index of suspicion based on history and physical examination findings. However, initial laboratory findings can sometimes be misleading. For example, an inflamed appendix or abscess in contact with the bladder can cause pyuria and/or hematuria, resulting in the misdiagnosis of a UTI.

Multisystem inflammatory syndrome in children (MIS-C), which can present weeks after development of acute COVID-19, can include abdominal pain as a primary feature. By definition, there is more than one body system involved, with findings such as conjunctivitis, rash, adenopathy, shock, and/or headache. If MIS-C is a concern, obtain a COVID-19 polymerase chain reaction test and serology and, in addition to labs mentioned above, an erythrocyte sedimentation rate, D-dimer test, ferritin, B-type natriuretic peptide, and troponin, as well as an electrocardiogram (see Chapter 65, Multisystem Inflammatory Syndrome in Children [MIS-C]).

Radiology Examinations

Appropriate radiologic studies depend on clinical suspicion based on history and physical examination. Ultrasonography (US) is the preferred initial screening tool for appendicitis, although its accuracy is dependent on the skill of the operator, and it is notably less sensitive among children who are overweight. Use US for gynecologic diagnoses, especially if there is a possible ovarian torsion.

Classic appendicitis is a clinical diagnosis that can be assigned solely on the basis of physical examination findings, without the use of imaging. If

the physical examination findings and laboratory evaluation results are not diagnostic, perform US. If there is a high level of suspicion, but the appendix is not visualized on US, obtain a computed tomography (CT) scan, even if no signs of inflammation were seen on US. Order the CT scan with both intravenous (IV) and oral contrast (if the patient can tolerate it). However, if the physical examination and laboratory results suggest just a low or moderate concern for appendicitis, do not order secondary imaging studies. Perform serial abdominal examinations and monitor the patient's clinical status.

With the exception of chest radiography for a patient with notable respiratory symptoms, plain films are not helpful. Although abdominal radiography is often performed to look for obstruction, free air, or other gross abnormalities, in about 50% of cases of appendicitis there are no abnormal findings. If intussusception is possible, obtain prone and supine radiographs to look for the absence of air in the colon (particularly the descending) and rectum. See Table 106–1 for radiologic testing suggestions based on clinical suspicion.

Differential Diagnosis

Nonsurgical conditions, such as AGE, severe constipation, strep throat, and lower-lobe pneumonia, can all cause severe abdominal pain and mimic acute abdomen.

The likelihood of appendicitis increases with each additional component of the classic picture: initially periumbilical pain that migrates to the right lower quadrant, increased white blood cell (WBC) count, increased neutrophil percentage (left shift), and increased CRP level. However, a normal WBC count and CRP level do not rule out appendicitis. These classic criteria are represented in appendicitis scores, such as the Alvarado score, which can help

Table 106–1. Radiologic Tests Based on Clinical Suspicion

Suspected Diagnosis	Radiologic Study
Appendicitis	US (preferred) or CT with IV, oral, and/or rectal contrast material MR imaging if available and sedation not required
Constipation	Left lateral decubitus and supine radiography or KUB radiography (NASPGHAN guidelines do not recommend radiography as routine evaluation)
Ileus	Left lateral decubitus and supine radiography or KUB radiography
Intussusception	US (diagnostic only) Air (or contrast-enhanced) enema (diagnostic and therapeutic)
Malrotation Volvulus	Emergent UGI study or CT with IV contrast material
Ovarian torsion	US with Doppler
Pneumonia	PA and lateral chest radiography
Renal stone	CT without contrast material

Abbreviations: CT, computed tomography; IV, intravenous; KUB, kidney, ureter, bladder; MR, magnetic resonance; PA, posteroanterior; UGI, upper gastrointestinal; US, ultrasonography.

identify patients with appendicitis. However, these scoring rubrics are confounded by atypical presentations, which are especially common in younger patients. Furthermore, many other serious entities, such as volvulus and intussusception, can have normal laboratory evaluation findings. The differential diagnosis of acute abdomen is summarized in Table 106–2.

Consider diagnoses based on the history and presenting symptoms. Bilious emesis suggests intestinal obstruction, ileus, or volvulus. These are emergencies that require prompt surgical consultation. Bloody stool is most commonly associated with bacterial gastroenteritis but can be a late finding of intussusception or other bowel ischemia. Consider ovarian torsion, ovulatory pain (mittelschmerz), imperforate hymen, pelvic inflammatory disease, and pregnancy in a postmenarchal female subject. Prior abdominal surgery can increase the risk of adhesions and bowel obstruction. Food intake typically decreases the pain in ulcer disease and gastritis but worsens the discomfort in pancreatitis and biliary disease. Henoch-Schönlein purpura can present with severe abdominal pain that precedes the typical purpuric rash, and it rarely is associated with intussusception and/or gastrointestinal (GI) bleeding. Meckel diverticulum is classically described as presenting with painless GI bleeding, although 30% of patients can have obstruction or perforation that results in pain, vomiting, and distention.

Functional abdominal pain often involves underlying dysmotility issues, such as gastroparesis, in the context of an amplified pain response, often along with anxiety and other psychological factors. Typically, the patient has recurrent bouts of periumbilical abdominal pain without fever, vomiting, or diarrhea. However, this is a diagnosis of exclusion that requires an extensive evaluation of other possible causes.

Treatment

When the symptoms are consistent with acute abdomen, give the patient nothing by mouth, request surgical consultation, and start antibiotics with piperacillin/tazobactam (350 mg/kg/d, divided into doses administered every 6 hours; 12-g/d maximum) *or* IV meropenem (20 mg/kg every 8 hours, 6-g/d maximum) *or* cefoxitin (30 mg/kg every 6 hours, 12-g/d maximum) *or* cefotetan (30 mg/kg every 12 hours, 6-g/d maximum).

If the patient is nontoxic with a presentation inconsistent with acute abdomen, conduct serial abdominal examinations and repeat the laboratory studies (CBC count, CRP level) as dictated by the degree of clinical suspicion. It is often prudent to give the patient nothing by mouth and defer starting antibiotics until the diagnosis is more certain. For example, a patient with isolated nonbilious emesis, anorexia, generalized abdominal pain, fever, and

Table 106–2. Differential Diagnosis of Acute Abdomen

Suspected Diagnosis	Clinical Features
Abdominal migraine	Moderate to severe abdominal pain Nausea, vomiting, anorexia Recurs every 3–4 wk, episodes last 18 h on average
Acute gastroenteritis	Fever, nausea, vomiting, diarrhea Pain may be relieved by vomiting Contact with sick persons, travel, contact with certain animals
Appendicitis	Anorexia and fever (most patients) Patient remains still for comfort Pain precedes vomiting (nonbilious) Pain migration periumbilical moving to right lower quadrant
Constipation	History of infrequent, painful stools Patient afebrile Pain does not migrate Hard stool in the ampulla
Intussusception	Episodic pain with drawing up of the legs or intermittent lethargy Patient afebrile Bloody stool or frank blood (late finding) Lead point more likely in patients $>$ 2 y of age
Inflammatory bowel disease Malignancy (uncommon)	Weight loss Recurrent episodes of abdominal pain Bloody stools
Nephrolithiasis	Episodic severe pain radiates to flank or groin Patient afebrile Hematuria
Ovarian torsion	Episodic and unilateral lower quadrant pain (can be generalized) Patient afebrile Associated nausea and vomiting
Pancreatitis	Epigastric pain that may radiate to the back Pain relieved by leaning forward Elevated lipase level
Pelvic inflammatory disease	Sexually active female subject Vaginal discharge, fever Cervical motion tenderness
Pneumonia	Fever, tachypnea, cough, chest pain Auscultation: rales or decreased breath sounds
Small-bowel obstruction	Anorexia, bilious vomiting Crampy periumbilical pain without migration Peritoneal signs Air-fluid levels on abdominal radiographs
Urinary tract infection	Dysuria, urgency, frequency May have costovertebral angle tenderness Pyuria, bacteriuria
Volvulus	Episodic pain Patient afebrile Bilious emesis

increased WBC count could have AGE, appendicitis, or a UTI. In such a case, it is useful to observe the patient for changes in symptoms (such as the onset of diarrhea), physical examination findings, fever curve, CRP level, and possibly abdominal radiography findings, depending on the level of concern.

If appendicitis is likely, start antibiotic treatment (as noted above), because it is becoming increasingly common to defer surgery until the next morning, when the patient and hospital staff are better prepared.

About one-quarter of patients with appendicitis, particularly those younger than 5 years, will have a ruptured appendix before presentation, and this typically occurs within 72 hours of the start of symptoms. There is continuing controversy over the best treatment of a patient with a ruptured appendix. After consultation with surgery, one approach is to treat with parenteral antibiotics until there is clinical improvement (patient afebrile > 24 hours, patient tolerating maintenance oral intake, and decreased inflammatory markers), then transition to an oral regimen. Specific drug regimens vary by institution, but one approach is to add IV metronidazole (7.5 mg/kg every 6 hours, 4-g/d maximum) to one of the antibiotics detailed earlier. At discharge, change to amoxicillin/clavulanate (90 mg/kg/d of amoxicillin, divided into doses administered twice a day; 4-g/d maximum) with or without metronidazole (oral dose same as the IV dose herein). Interval appendectomy may be scheduled after about 6 weeks per surgical preference, especially if there was a fecalith.

There is no reason to withhold analgesia. Although pain medication can change some aspects of examination, it will not hinder identification of surgical candidates and may actually facilitate a more thorough examination. Administer IV morphine (0.05–0.20 mg/kg every 2–4 hours; maximum, 8 mg per dose) as needed for pain.

There is no evidence to support the routine use of antiemetics for the patient with abdominal pain, outside of the diagnosis of AGE.

Indications for Consultation

- **Gynecology or pediatric surgery:** Possible ovarian torsion
- **Surgery:** Rebound tenderness, abdominal rigidity, bilious emesis, or presence of other findings of acute abdomen
- **Urology (or surgery):** Possible testicular torsion

Disposition

- **Intensive care unit transfer:** Shock, toxic appearance
- **Discharge criteria:** Definitive diagnosis, treatment, and recovery have occurred and the patient is tolerating adequate oral intake and medications, if needed

Follow-up

- **Primary care:** 1 to 3 days
- **Surgery (if patient underwent a procedure or if one is to be scheduled):** 1 to 2 weeks

Pearls and Pitfalls

- Laboratory tests and radiographs alone cannot be used to rule out the diagnosis of acute abdomen.
- The younger the child, the less likely the symptoms will conform to the classic presentation of appendicitis.
- Do not withhold pain medication.
- Not all cases of acute abdomen require immediate surgery. A perforated appendix may be treated medically, with or without interval appendectomy.
- Be circumspect of assigning the diagnosis of AGE when nausea and vomiting are not accompanied by diarrhea.

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CHAPTER 107

Pyloric Stenosis

Introduction

Pyloric stenosis is the most common cause of upper gastrointestinal (UGI) obstruction in infancy, with an incidence of 2 to 4 per 1,000 live births. Male infants are 4 to 6 times more likely to be affected, with 30% of patients being first-born males. With prompt diagnosis and intervention, pyloromyotomy can prevent complications such as significant metabolic derangements, failure to thrive (FTT), shock, and death (rare).

Clinical Presentation

History

The patient typically presents at 10 days to 8 weeks after birth, with progressively forceful, nonbilious emesis after feedings. The vomiting may be described as projectile and is nonbilious and nonbloody.

Depending on the duration of symptoms, the patient may have a range of presentations, from vigorous and ravenous (especially immediately after vomiting) with adequate weight gain to listless and emaciated with profound FTT. Other complaints may include irritability, colic, and constipation. A careful history can often diagnose an infant with pyloric stenosis.

Physical Examination

The physical examination findings may be completely normal. However, if symptoms have progressed over several weeks, the patient may appear dehydrated with significant weight loss or inadequate weight gain. Focus on assessing the degree of dehydration.

The classic finding is a palpable "olive," which is the hypertrophied pylorus, in the epigastric region or right upper quadrant. To appreciate the mass, place the patient supine with the hips flexed. Examine from the patient's left side and attempt to "slip" a hand under the edge of the right rectus muscle. The presence of the olive is pathognomonic; however, its absence does not exclude the diagnosis. The olive is best palpated after a child has vomited and the pylorus is contracted. Another unique finding is a visible abdominal peristaltic wave seen while the infant is sucking.

Laboratory Workup

Obtain serum electrolyte levels. An infant with pyloric stenosis characteristically develops a hypochloremic, hypokalemic, metabolic alkalosis (bicarbonate level > 24 mEq/L [> 24 mmol/L]). Note that a normal bicarbonate level in

this age group is 18 mEq/L (18 mmol/L). However, early in the disease course, electrolyte levels may be normal.

Radiology Examinations

Abdominal ultrasonography (US) has replaced contrast-enhanced studies as the modality of choice for diagnosing pyloric stenosis. However, if US is unavailable, classic findings of a UGI series are the "string sign" (pyloric channel filled with a thin stream of barium) or the "shoulder sign" (extrinsic compression of the stomach by a hypertrophied pylorus) in the presence of significant stenosis.

Pyloric US will allow measurements of both canal length and thickness. Pyloric stenosis is confirmed if the muscle width on a cross-sectional image is greater than 3 mm, whereas 2 to 3 mm is equivocal and less than 2 mm is a negative finding. Pyloric stenosis is also confirmed if the pyloric length is longer than 14 to 15 mm. However, pyloric stenosis is a progressive process, so a negative or equivocal pyloric US finding may be seen during the early stages of disease. If symptoms persist, arrange a repeat study in 1 week.

Differential Diagnosis

Pyloric stenosis causes unopposed (ie, no diarrhea), nonbilious vomiting. A number of conditions, ranging from mild (gastroesophageal reflux) to life-threatening (acute adrenal insufficiency), can appear with unopposed vomiting (Table 107–1).

Other causes of hypochloremic metabolic alkalosis in an infant include Bartter syndrome, diuretic use, cystic fibrosis, exogenous alkali ingestion, and a chloride-deficient diet.

Treatment

Preoperative

Consult a surgeon to arrange a pyloromyotomy, which is not an emergent procedure. The priority is correcting dehydration and any electrolyte abnormalities. Generally, the anesthesiologist will defer surgery until the bicarbonate level is 30 mEq/L or less ($\leq$ 30 mmol/L), the chloride level is 100 mEq/L or greater ($\geq$ 100 mmol/L), and the potassium level is greater than 3.5 mEq/L ($>$ 3.5 mmol/L).

Treat significant dehydration ($\geq$ 10%) with a normal saline (NS) bolus (or boluses) to restore intravascular volume. If renal function is normal and the patient remains alkalotic, administer 5% dextrose one-half NS with

Table 107–1. Differential Diagnosis of Pyloric Stenosis	
Diagnosis	**Clinical Features**
Antral web	Similar presentation
Congenital adrenal hyperplasia Adrenal insufficiency/crisis	Clitoromegaly or hyperpigmented scrotum Hyperkalemia, hyponatremia No alkalosis
Gastroenteritis	Patient may have fever Diarrhea Patient not ravenous after vomiting
Gastroesophageal reflux	Lower-volume vomitus Nonprojectile emesis May be positional
Increased intracranial pressure	Bulging fontanelle Sunsetting eyes Cranial nerve VI palsy
Overfeeding	Good/robust weight gain Nonprojectile emesis Normal electrolyte levels
Sepsis	Fever, lethargy Acidosis ↑ or ↓ White blood cell count
Volvulus	Bilious spit-up or nonprojectile vomiting No alkalosis

↑ indicates increased level; ↓, decreased level.

2 mEq (2 mmol) potassium chloride/100 mL or 5% dextrose NS with 2 mEq (2 mmol) potassium chloride/100 mL at 150% of the maintenance rate until urine output is adequate. This will help correct the alkalosis, which is chloride responsive. Once the patient's hydration status and electrolyte levels have normalized, switch to a maintenance intravenous solution and rate. It is not necessary to give the patient nothing by mouth until the appropriate time has arrived for preoperative fasting.

Surgical

Depending on individual preference, a laparoscopic (most common) or traditional open pyloromyotomy will be performed.

Postoperative

There is no single approach to the reinstitution of feedings. Options include starting immediately after the infant awakens from anesthesia to withholding feedings for 4 hours postoperatively, then advancing to ad libitum feedings.

Regurgitation after surgery occurs in most patients. This may be secondary to anesthesia, gastritis, irritation from the long-standing obstruction, residual inflammation after the pyloromyotomy, or an incomplete repair. If the infant

continues to vomit for more than 5 days after surgery, repeat the abdominal US examination and contact the surgeon, who may want to perform a UGI series. Consult the surgeon if fever with abdominal distention occurs within the first 24 hours, because this may be caused by an unsuspected perforation.

Acetaminophen usually suffices for postoperative analgesia.

Disposition

- **Interinstitutional transfer:** Pediatric surgeon not available
- **Discharge criteria:** Adequate oral intake

Follow-up

- **Primary care:** 1 week
- **Surgeon:** 1 to 2 weeks

Pearls and Pitfalls

- Always consider pyloric stenosis in a young infant with unopposed vomiting with or without weight loss.
- Pyloric stenosis is not an emergency. Correct any electrolyte abnormalities before surgery.
- Postoperatively, some emesis is to be expected.
- Due to the availability and reliability of US, many cases are diagnosed early, before electrolyte abnormalities have developed or the olive can be palpated.

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CHAPTER 108

Wound Care Basics

Introduction

Wounds are common among pediatric inpatients and may be the reason for admission or a consequence of some other issue or its treatment (Box 108–1). Comorbid conditions, such as diabetes, immunocompromise, poor perfusion, limitation of movement, poor nutrition, or obesity can increase the risk of a patient developing a wound or having poor wound healing. Wounds and burns may be evidence of nonaccidental trauma (NAT), so maintain a high level of suspicion if the presenting wound injury is inconsistent with the history and/or the developmental level of the patient (see Chapter 69, Child Abuse: Physical Abuse and Neglect).

Optimal wound healing requires an environment with adequate moisture, temperature, perfusion, and pH, as well as appropriate pain control. Prevention of injury to the surrounding skin and management of issues causing delayed healing, such as exudate, infection, and devitalized or necrotic tissue, are critical.

Clinical Presentation

History

Determine the mechanism of injury and when the wound was first sustained or noted. Ask about prior treatments or therapies, whether there is any drainage or signs of infection, and if the wound is improving or worsening. Note any comorbid conditions that might compromise healing, and assess pain using an age-appropriate pain scale. Consider whether the pattern of injury is consistent with the reported history and the patient's developmental level.

Box 108–1. Wound Types

Bullae formation: Stevens-Johnson syndrome/toxic epidermal necrolysis
Burns
Incontinence-associated dermatitis
IV infiltration and extravasation injury
Ostomy/peristomal skin breakdown
Pressure ulcers
Skin irritation/damage from medical devices (eg, tracheostomy ties, peripheral IV catheters)
Skin-stripping from medical taping or frictional injuries (premature babies and infants)
Staphylococcal scalded skin syndrome
Surgical wounds and dehiscence
Traumatic lacerations and abrasions

Abbreviation: IV, intravenous.

For pressure ulcers, determine the source of the pressure, such as medical device/equipment, chairs with hard surfaces, and beds with improper pressure redistribution. Inquire about home turning practices or schedule for shifting weight.

In the case of thermal burns, assess for risk of inhalation injuries, such as exposure to toxic gas (including carbon monoxide and/or hydrogen cyanide) and airway injury following inhalation of high-temperature gases, steam, or hot liquids. For chemical burns and intravenous (IV) extravasations, determine the causative agent.

Physical Examination

Assess the wound for size, location (exercise particular caution if over a joint, due to the risk for developing contractures), depth of involvement, and whether the site is clean or dirty. Evaluate the surrounding tissue for maceration, friability, erythema, edema, and track formation. Evaluate for moisture and whether the wound is too dry and flaking. Determine if there is any active drainage, attempt to quantify volume, and note if it is purulent, serosanguineous, or from an ostomy site. Assess the wound site for signs of fungal or bacterial superinfection. Evaluate for any necrotic or devitalized tissue, such as slough or eschar that may need debridement. Other specific physical examination findings are summarized in Table 108–1.

Laboratory Workup

Minor wounds do not require laboratory testing. For wounds that are more significant, obtain a complete blood cell count (CBC) and comprehensive metabolic panel. To assess and monitor nutritional status for a patient with extensive burns or wounds, trend the prealbumin and C-reactive protein (CRP) levels (as prealbumin is a negative acute phase reactant). If wound infection is a concern, obtain a CBC with differential, wound culture, inflammatory markers such as CRP and/or erythrocyte sedimentation rate and/or procalcitonin. For a patient at risk of inhalation injury or airway burns, obtain a blood gas and carboxyhemoglobin level. Additional evaluation may be necessary depending on wound type.

Treatment

Initial treatment involves ensuring hemostasis and adequate wound irrigation. Clean with normal saline or a wound cleanser (normal saline base with surfactant). Wounds with devitalized or necrotic tissue will need debridement. For shallow wounds with sloughing, use dressings that promote autolysis, hydrogels, or enzymatic debridement (collagenase, papain, or bromelain). Larger and deeper areas of devitalized tissue and necrotic wounds will need surgical debridement. Treat wounds with excessive exudate, large defects, and

Table 108–1. Physical Examination by Wound Type	
Type	**Physical Examination Findings**
Burns	
All	Assess for patterns concerning for NAT and other injuries indicative of NAT Estimate TBSA Determine depth
Superficial (first degree)	Erythematous, hypersensitive, painful No sloughing
Partial thickness (second degree)	Erythematous and blistered Wet or weeping Edematous
Full thickness (third degree)	White or charred skin Eschar formation
Fourth degree	Eschar formation Indented wound shape
Ostomy Site and Peristomal Skin Breakdown	
Ostomy tube	Determine stoma size relative to tube Note leaking of gastrointestinal secretions Note excessive granulation tissue
Ileostomy Colostomy	Examine ostomy pouch seal Assess for proper size, type of wafer, leakage around barrier Assess whether stoma is flush or recessed against skin level Assess for allergic type reaction to wafer material
Pressure Ulcers	
Evaluate for pressure from medical devices such as wheelchairs, knee-ankle-foot orthosis, beds, respiratory devices (positive pressure ventilation masks) Ischial wound: Determine degree of stool and urine soiling and presence of incontinence Stage the pressure ulcer Stage 1: Nonblanchable erythema Stage 2: Partial thickness loss of dermis Stage 3: Visible subcutaneous fat Stage 4: Exposed muscle, tendon, or bone Unstageable: Wound bed is covered by slough and/or eschar	
Surgical Wounds	
Note any wound tension from suture placement or pressure Note signs of wound site infection and drainage Assess for allergic type reaction to suture material	
Surgical Wound Dehiscence	
Determine depth of wound Evaluate condition of wound margins and skin surrounding the wound Assess for granulation tissue, sloughing, and eschar formation Determine if there are exposed sutures, hardware, tissue, and organs Assess for infection and quantify drainage, if any	
IV Infiltrate/Extravasation Injury	
Monitor site every 2 hours for erythema, edema, blanching, necrosis, drainage, pain, warmth	
Epidermal Loss	
Estimate TBSA Assess for involvement of mucosal surfaces	

Abbreviations: IV, intravenous; NAT, nonaccidental trauma; TBSA, total body surface area.

significant edema (eg, dehisced wounds, high-stage pressure injury, compartment syndrome, abdominal wall defects) with negative-pressure wound therapy (NPWT), under the direction of a wound ostomy team.

Significant anemia may compromise wound healing, so that transfusion may be necessary at a higher hemoglobin level than what is typically used for cardiovascular instability.

Wound Dressings

Factors to take into consideration when choosing a specific wound dressing or product (Table 108–2) include depth of the wound, whether or not the wound requires debridement, infection and contamination risk, exudate level, and risk of adherence to the wound. Ensure a moist wound environment, which will promote epithelization and granulation tissue formation. However, too much moisture can cause skin breakdown and maceration, increase risk of infections, and impede healing. Use absorptive dressings for exudate and moisture management, and emollients, collagen matrix, or hydrogel for a wound that is too dry. Select dressings that will maintain the integrity of peri-wound skin. Medical-grade honey and silver-impregnated products offer antimicrobial properties. Medical-grade honey also promotes autolytic debridement. Reassess the type of dressing used at every dressing change, because as the wound evolves, product needs will change.

Burns

Transfer the patient to a dedicated burn center if they have burns covering more than 10% total body surface area (TBSA), full-thickness burns, electrical or chemical burns, circumferential burns, or burns that involve the face, hands, feet, genitalia, perineum, or major joints.

Use lactated Ringer (LR) or normal saline for fluid resuscitation. Calculate the amount of fluid using the formula 3 mL × kg × % TBSA of partial and full-thickness burns. Administer half of the total volume in the first 8 hours and the remainder over the next 16 hours. If the patient weighs less than 30 kg, also provide hourly maintenance fluids containing 5% dextrose and LR (or normal saline), using the "4-2-1" formula (4 mL/kg/h for the first 10 kg of body weight + 2 mL/kg/h for the second 10 kg of body weight + 1 mL/kg/h for the remainder of body weight). Titrate fluid rate and volume as needed to maintain a urinary output of 1 mL/kg/h.

The initial approach to burns involves the same procedures as general wound care, cleansing, and debridement. Unroof blisters larger than 2 cm and use sterile equipment to remove any dead skin. Do not routinely

Table 108–2. Wound Dressings

Dressing Type	Indications	Contraindications and Limitations	Dressing Change
Nonadherent Dressings			
Contact layer (silicone or lipo-colloid matrix)	Burns: superficial and partial thickness Partial and full-thickness wounds Pressure ulcers Superficial tears and wounds with limited exudate	Does not absorb moisture Requires a secondary dressing	Daily
Hydrating Dressing			
Hydrogel	Burns Partial and full-thickness wounds Tunneling or deep wounds with minimal exudate Pressure ulcers	May cause peri-wound maceration Do not use with highly exudative wounds Requires a secondary dressing	Daily or twice daily
Moisture Maintenance			
Collagen matrix	Partial and full-thickness wounds Tunneling wounds with minimal exudate	Do not use with dry wounds Use cautiously on infected wounds Do not use with full-thickness burns Requires a secondary dressing	2–3/d (depends on product)
Hydrocolloid	Partial and full-thickness wounds Pressure ulcers	Do not use with dry wounds Use cautiously on infected wounds Do not use with burns May cause peri-wound maceration and epidermal stripping	3–7/d (depends on product)
Absorptive Dressings			
Hydrofiber Alginate Polyurethane foam	Exudative wounds Infected wounds Partial and full-thickness wounds Tunneling wounds Wound dehiscence Pressure ulcers	Requires a secondary dressing Do not use with dry wounds, eschars, full thickness burns, grafts, or wound with heavy bleeding	Every 3 d pending exudate

For more specific information on types of wound dressing products, see www.woundsource.com.

use systemic prophylactic antibiotics, and do not employ dressings that will adhere to the burn site. Use an absorbent dressing (foam, hydrofiber) for superficial burns during the first 3 days, as they are highly exudative. Use hydrogels and honey dressings for partial thickness burns that are sloughing, as these will promote autolytic debridement. Ensure moisture balance.

Intravenous Infiltrates and Extravasations

Immediately stop the infusion and remove the IV line after attempting to aspirate as much of the drug as possible. Elevate the site and provide warm or cool compresses depending on the type of medication. Cold compresses may reduce pain and local inflammation and promote local constriction, which may be beneficial to limit the spread of hyperosmolar solutions such as parenteral nutrition. However, cold compresses are contraindicated for the extravasation of vasopressors, vinca alkaloids, etoposide, and contrast media. Use warm compresses to promote vasodilation, increased blood flow, and dispersion of drug. Treat extravasation of aminophylline, amiodarone, calcium solutions, contrast media, dextrose, mannitol, nafcillin, parenteral nutrition, potassium solutions, sodium bicarbonate, sodium chloride (> 1%), and vinca alkaloids with hyaluronidase subcutaneous or intradermal injection (5 separate 0.2-mL injections of a 15-U/mL or 150-U/mL solution into the extravasation site). Use phentolamine (subcutaneous injection of 0.2-mL aliquots of a 0.5- to 1-mg/mL solution into the extravasation site) for extravasation of dopamine, epinephrine, norepinephrine, and phenylephrine.

Incontinence Dermatitis or Ostomy Site Leakage

Use a barrier ointment such as petrolatum, zinc oxide, dimethicone, or cyanoacrylate. If there is copious drainage around an ostomy site, use an absorbent foam dressing or alginate to control the moisture.

Tetanus

Assess tetanus immunization status. Wounds with higher risk for tetanus include dirty wounds, penetrating or puncture wounds, and wounds with devitalized tissue. If the patient is unvaccinated, begin a primary vaccine series with an age-appropriate tetanus vaccine. Assess the need for tetanus immune globulin and administer 250 units intramuscularly if the patient meets criteria (Table 108–3).

Pain Control

Pain control is critical (see Chapter 103, Pain Management), especially with dressing changes. For smaller wounds, use acetaminophen (15 mg/kg every 4 hours, as needed) and/or ibuprofen (10 mg/kg every 6 hours as needed for patients > 6 months of age). Give oral sucrose 24% solution (0.1–0.5 mL/dose) to neonates for minor injuries. Use an opioid (morphine 0.1–0.5 mg/kg/dose every 3 to 4 hours, as needed) for more significant injuries and with dressing changes. Sedation (see Chapter 104, Sedation) is required for painful

Table 108–3. Indications for Tetanus Prophylaxis		
Lifetime Tetanus Doses	**Tetanus Immunization Indicated**	**Tetanus Immune Globulin Indicated**
Clean Minor Wounds		
< 3 or unknown	Yes	No
> 3	> 5 years since last dose: Yes < 5 years since last dose: No	No
All Other Wounds		
< 3 or unknown	Yes	Yes
> 3	> 5 years since last dose: Yes < 5 years since last dose: No	No

Adapted from Tetanus: for clinicians. Centers for Disease Control and Prevention. https://www.cdc.gov/tetanus/clinicians.html. Updated August 29, 2022. Accessed December 8, 2022.

dressing changes or complex wound management (debridement or scald/burn assessment).

Antibiotics

Do not routinely start antibiotic prophylaxis for burns or wounds. Provide optimal wound care to prevent infection. If a wound infection is suspected, give empiric therapy that covers the typical pathogens (*Staphylococcus aureus* and *Streptococcus pyogenes*). Choose antibiotics based on local antibiogram resistance patterns for *S aureus*. Options include clindamycin, linezolid, and vancomycin. Dirty, soiled, or bite wounds may need broader-spectrum antibiotic coverage.

Monitor for signs and symptoms of toxic shock syndrome. Wounds may be colonized with toxin-producing bacteria and not appear infected. If toxic shock is suspected, use the same antibiotics for wound infection, but add clindamycin for the theoretic benefit of reducing toxin production.

Nutrition

Nutrition is an important aspect of healing. Proteins, carbohydrates, and fats are important macronutrients, and vitamin C, vitamin A, and zinc are important micronutrients. Implement a high-protein diet that is 1.5 to 2 times the recommended daily allowance, and start a daily multivitamin. For extensive burns or wounds, place an enteral feeding tube for supplemental feeds to meet increased caloric demands for adequate healing.

Indications for Consultation

- **Pediatric surgery or plastic surgery:** Surgical debridement and skin grafting
- **Nutritionist:** Underlying malnutrition, poor wound healing, planning of a high-protein diet, suspected vitamin C or zinc deficiency

- **Child abuse:** Suspected NAT
- **Wound ostomy nurse:** Complicated ostomy pouch fitting or drainage from ostomy site; NPWT
- **Child life, if available:** Wound dressing changes

Disposition

- **Intensive care unit transfer or dedicated burn unit, if available:** Burns and denuding conditions covering more than 10% TBSA; those involving hands, feet, face, perineum, genitalia, joints, and circumferential injuries; full-thickness burns; chemical and electrical burns; and inhalation injury
- **Discharge criteria:** Adequate fluid and nutritional intake, enteral antibiotics, adequate pain control with enteral medications, provision of home care supplies, manageable home dressing change frequency, and competent care provider

Follow-up

- **Primary care:** 1 week
- **Various subspecialists:** Depending on wound type

Pearls and Pitfalls

- Wounds can be a sign of inflicted trauma.
- Careful attention to exudate and moisture management will aid wound healing. Moisture balance is critical.
- Burns and epidermal loss covering more than 10% TBSA, full-thickness burns, and high-complexity burns require transfer to a burn center or pediatric intensive care unit.
- Significant skin injury over a joint can result in loss of function from contractures.
- Pain management is especially critical during dressing changes. Use play and child life consults to limit pain and anxiety.

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