Pulmonology

20

Tanya Martínez-Fernández, Yadira Rivera-Sánchez, and Preeti Sharma

DIAGNOSTIC TESTING FOR RESPIRATORY CONDITIONS

Pulmonary Function Testing (PFT)

Definition of lung volumes and capacities:

- 4 volumes:
  - IRV inspiratory reserve volume
  - TV tidal volume
  - ERV expiratory reserve volume
  - RV residual volume: Volume at maximal expiration
- Capacities are sums of volumes
  - TLC total lung capacity (all four volumes) – volume at maximal inspiration
  - IC inspiratory capacity: (TV + IRV)
  - FRC functional residual capacity (RV + ERV) – resting volume at the end of normal expiration
  - VC vital capacity: (RV + ERV + TV = TLC – RV)

Spirometry

- Provides objective measurements that can be tracked over time
- Forced maneuver breathing from full inspiration (TLC) to RV capturing VC
- Displays volume exhaled and flow rates
  - FVC—volume after full-forced exhalation
  - FEV1—volume exhaled during first sec
  - FEV1/FVC ratio—low with obstruction
  - FEF 25–75—average flows between 25% and 75% of the maneuver
- Interpreted to show obstruction (low flow), restriction (low volume), or mixed process (Fig. 20.1)
  - Obstruction: N ↓ FVC, ↓ FEV1, ↓ FEV1/FVC, ↓ FEF 25–75
  - Restriction: ↓ FVC, ↓ FEV1, N FEV1/FVC, ↓ FEF 25–75
- Consider further testing if spirometry is normal, but positive for asthma-type symptoms:
  - Measurement of spirometry pre and post bronchodilator can be used to evaluate for airway reactivity
    - Increase in FEV1 after bronchodilator (significant if > 12% change)
  - Bronchial challenge testing to measure bronchoconstriction
  - Inhalation challenge or exercise challenge (e.g., methacholine, histamine, cold air, exercise)

Lung Volumes

- Useful in evaluation of restrictive lung disease (low TLC)

T. Martínez-Fernández (✉) · Y. Rivera-Sánchez · P. Sharma
Division Respiratory Medicine, Department of Pediatrics, University of Texas Southwestern Medical Center/Children's Medical Center Dallas, Dallas, TX, USA
e-mail: tanya.martinez@utsouthwestern.edu

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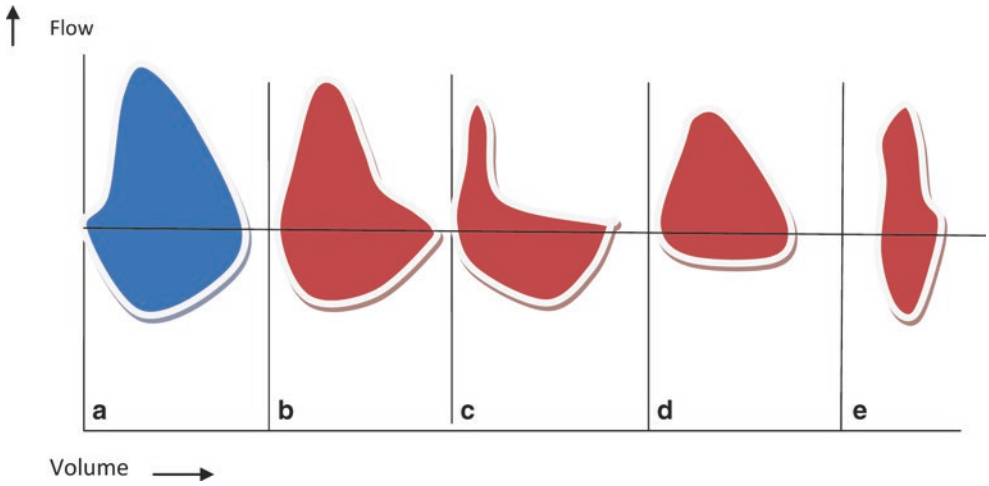

Fig. 20.1 Flow volume loop configurations in normal and different pulmonary disorders. Loop above line is expiratory loop; loop below line is inspiratory. (**a**) Normal; (**b**) early small airway obstruction; (**c**) chronic obstructive disease; (**d**) variable extrathoracic large airway obstruction, e.g., vocal cord pathologies; (**e**) restrictive diseases

- Measurement of RV impossible with spirometry
  - Evaluated by
    - Plethysmography (body box)—most accurate
    - Nitrogen washout, underestimates volume, if obstructive process present

Diffusion capacity measured with use of carbon monoxide gas

- Measure of gas transfer across alveolar-capillary barrier
  - May be decreased in interstitial lung disease, after lung resection

Pulse Oximetry

- Noninvasive, continuous, and rapid measure of peripheral oxygen saturation (SpO2)
- SpO2 estimates percentage of hemoglobin bound by oxygen
- Oxyhemoglobin curve dissociation curve = relation between partial pressure oxygen (pO2) and hemoglobin saturation (Fig. 20.2)
  - In hypoxia, pO2 is on steep part of curve = small pO2 changes, but large SpO2 changes
  - Acidosis, hyperthermia, increase in CO2 shifts curve to the right (lower SpO2 for same pO2)

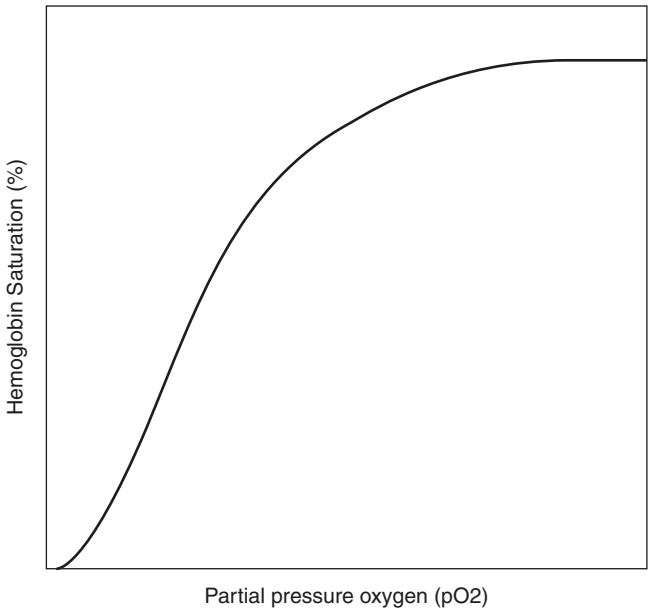

Fig. 20.2 Oxyhemoglobin saturation curve

- Limitations of pulse oximetry
  - Inaccurate readings with poor perfusion, severe anemia, motion artifact, shifts in oxyhemoglobin dissociation curve (e.g., acidosis), deep pigmentation of the skin, dark nail polish
  - Presence of methemoglobinemia and carboxyhemoglobin not recognized by most oximeters and may overestimate SpO2
  - Co-oximeter used to measure effect of dyshemoglobinemias

Blood Gas Analysis

- Gold standard for blood gas analysis is an arterial blood gas (ABG) sample.
- ABG interpretation (see Table 20.1 for ABG values associated with various conditions)
- Upper airway obstruction
  - Early increase in pCO2 and proportionate decrease in pO2. Initially responds well to supplemental oxygen
- Intrapulmonary airway obstruction
  - Mild: Decrease in pCO2, normal to decreased pO2
  - Moderate: Normal pCO2, decrease pO2 moving toward failure
  - Severe: Increase pCO2 and decrease pO2
  - Supplemental oxygen will support patient, but imperative to monitor carbon dioxide as well
- R-L shunt
  - Early decrease in pO2
  - Normal or low pCO2, high pCO2 with development of fatigue
  - Testing with 100% oxygen helps to define: Response to supplemental oxygen is fair to poor, depending on degree of shunt

Limitations of capillary blood gases (CBG)

- Arterialized CBG obtained by warming of a well-perfused heel or earlobe
- CBG is more easily attainable than arterial sample
- Values are comparable to arterial pH and pCO2, but pO2 measurement in CBG is less reliable
- Inaccuracy of blood gas measurements increased if sample processing is delayed, white blood cell (WBC) metabolism continues to consume oxygen and results in acidosis

Chest Imaging

Suggested modalities for various issues

Table 20.1 Arterial blood gases: values associated with various conditions

Acid-base abnormality	pH	pCO2	HCO3	Possible causes
Normal range	7.35–7.45	35–45	21–27	
Respiratory acidosis				Hypoventilation, neuromuscular disorders, severe asthma exacerbation, airway obstruction, intrinsic lung disease, pneumonia
Acute	↓	↑	N	
Compensated	N↓	↑	↑	
Respiratory alkalosis				Pain, hyperventilation, pulmonary embolism, high altitude
Acute	↑	↓	N	
Compensated	N↑	↓	↓	
Metabolic acidosis				Methanol, diabetic ketoacidosis, inborn error of metabolism, lactic acidosis, salicylates, diarrhea, shock
Acute	↓	N	↓	
Compensated	N↓	↓	↓	
Metabolic alkalosis				Vomiting, diuretics, primary aldosteronism
Acute	↑	N	↑	
Compensated	N↑	↑	↑	

N Normal

- **Plain chest radiograph (CXR)**
  - Upright views: Atelectasis, pneumonia, pneumothorax
  - Inspiratory and expiratory or bilateral decubitus views for suspected foreign body may be able to see asymmetric hyperinflation inside with foreign body due to check valve effect
    - Most foreign bodies not seen, as they are radiolucent
    - In bilateral decubitus views, dependent side should have lower volume (like expiratory view) than upright side
  - Decubitus views: Pleural fluid, pneumothorax
- **Fluoroscopy:** Tracheomalacia, diaphragmatic movement
- **Upper gastrointestinal (UGI) series:** Vascular ring, tracheoesophageal fistula
- **Video swallow study:** Aspiration
- **Ultrasound:** Pleural effusion, complicated pneumonia, diaphragm
- **Computed tomography (CT) scan:**
  - Best at providing images of lung anatomy, airway tree, parenchyma, and vascular structures
  - High resolution: Better to evaluate parenchyma like in bronchiectasis or interstitial lung disease
  - Contrast: Used to evaluate for lymphadenopathy, masses, vascular abnormalities, arteriovenous malformations, pulmonary embolism
- **Positron emission tomography (PET) scan:** Anterior, middle mediastinal masses, lymphoma
- **Ventilation-perfusion scan:** Pulmonary embolism
- **Magnetic resonance imaging (MRI):** Vascular lesions, mediastinal and chest wall masses

GENERAL SIGNS AND SYMPTOMS

Stridor/Wheezing

Background

- Wheezing
  - A musical, high-pitched whistling sound produced by airflow turbulence
  - One of the most common symptoms in asthma (see amplified discussion)
- Stridor
  - High-pitched, harsh sound often audible without the stethoscope
  - Results from rapid, turbulent airflow through a partially obstructed airway
- Inspiratory versus expiratory
  - *In*spiratory—*Ex*trathoracic swelling or obstruction will lead to airway collapse on inspiration. Example: Laryngomalacia
  - *Ex*piratory—*In*trathoracic swelling or obstruction will lead to airway collapse on expiration. Example: Tracheomalacia
  - *Biphasic stridor*—Indicates fixed airflow obstruction, subglottic space obstruction

Differential Diagnosis of Acute Stridor

- **Croup or laryngotracheobronchitis** (see amplified discussion)
- **Foreign body aspiration** (see amplified discussion)
  - Most common between 1 and 3 years of age
  - Sudden onset with cough, stridor, or wheezing
- **Bacterial tracheitis** (see amplified discussion)

- **Spasmodic croup or acute spasmodic laryngitis**
  - Children 6 months to 5 years
  - No viral etiology but symptoms similar to viral croup
  - May be triggered by gastrointestinal (GI) reflux
- **Retropharyngeal abscess**
  - Preschool age group
  - Abrupt onset of high fevers, difficulty swallowing, refusal to feed, sore throat, hyperextension of the neck or torticollis, and respiratory distress
- **Peritonsillar abscess**
  - Preadolescents and adolescents
  - Severe throat pain, trismus, muffled voice, trouble swallowing or speaking
- **Allergic reaction or anaphylaxis**
  - Associated with itchiness or hives
  - History of allergy

Differential Diagnosis of Chronic Stridor

Laryngomalacia

- Most common cause of stridor in infants
- Accounts for up to 75% of all causes of stridor

Clinical presentation

- Onset shortly after birth, minimal respiratory distress, positional effects, and marked reduction of noise when infant is at rest
- May present with apnea and feeding difficulties
- Stridor improves in prone position with head elevated and worsens in supine position
- Associated with normal voice quality and pitch

Diagnosis

- Diagnosis cannot be established on the basis of standard radiograph of the neck
- Flexible laryngoscopy can confirm the diagnosis but may miss tracheal abnormalities that can be identified with bronchoscopy
- If moderate to severe obstruction, difficulty with feeding and breathing, or unable to gain weight, flexible or rigid bronchoscopy to rule out other associated airway anomalies

Management

- Usually benign and self-limiting and improves as the child reaches 1–2 years of age
- Careful observation and growth monitoring for most patients
- Surgical correction may be considered in severe cases
- Resolution of symptoms for most patients without therapy in early childhood

Choanal Atresia

- 50% associated with congenital anomalies (i.e., CHARGE association, mnemonic for ***C***oloboma, ***H***eart defects, ***C***hoanal atresia, ***R***etarded growth and development, ***G***enital abnormalities, and ***E***ar anomalies)
- Bilateral—medical emergency during neonatal period, intermittent respiratory distress relieved by crying
- Unilateral—chronic mucoid nasal discharge on affected side in older infants/young children
- Diagnosis: Inability to pass a 6F catheter into oropharynx through nose
- Management: Surgical

Vocal Cord Paralysis (VCP)

- Second most common cause of stridor in infants
- May result from local trauma
- Left side VCP may result from trauma to the recurrent laryngeal nerve at birth or surgical trauma
- Unilateral—congenital or secondary to birth or surgical trauma such as cardiothoracic surgery

- Bilateral—associated with central nervous system abnormalities such as Arnold-Chiari malformation, tumors, or increased intracranial pressure

Clinical presentation

- Unilateral VCP—hoarse voice, weak cry, and biphasic stridor that is louder when awake. Improves when lying with the affected side down
- Bilateral VCP—high-pitched biphasic stridor that may progress to severe respiratory distress. Rarely associated with abnormal vocalization
- Bilateral VCP is associated with increased risk of recurrent aspiration
- VCP may be an early sign of brain stem or spinal cord compression

Imaging

- MRI of the upper spinal cord and brain stem may be required in evaluating patients with unexplained bilateral VCP

Management

- Presence of aspiration and the degree of airway obstruction—primary indicators of need for therapy in patients with VCP
- Continuous positive pressure may provide temporary relief of symptoms of VCP
- Decompression surgery is required to relieve VCP secondary to Arnold-Chiari malformation
- Traumatic VCP should improve in 6 months and, if not, unlikely to improve thereafter

Laryngeal Web

- Strong association with velocardiofacial syndrome (chromosome 22q11.2 deletion)
- Posterior glottic webs are acquired from prolonged intubation
- Laryngeal webs may be associated with anterior subglottic stenosis
- Weak cry and biphasic stridor

Management

- Surgery can be curative if significant obstruction occurs
- Emergency tracheostomy is required to relieve obstruction caused by a complete laryngeal web

Subglottic Stenosis (SGS)

- SGS may be congenital (rare and usually associated with other genetic syndromes or conditions) or post-traumatic (due to airway instrumentation or more commonly, intubation)
  - Even brief periods of intubation may result in chronic SGS
- Airway inflammation secondary to trauma may lead to acquired SGS
- The cricoid cartilage, being a complete ring, is predisposed to traumatic injury and stenosis

Clinical presentation

- History of recurrent croup, a protracted croup illness, previous intubation or airway instrumentation
- Biphasic stridor
- Retractions, flaring, high-pitched stridor, and diminished air entry are associated with significant SGS
- Hypoxemia or carbon dioxide retention in a child with SGS indicates a severe obstruction leading to marked hypoventilation

Diagnosis

- Spirometry will demonstrate flattened inspiratory loops
- Endoscopy will demonstrate narrowing of the subglottic space
- No correlation between the radiographic appearance of SGS and actual degree of narrowing on direct visualization

Management

- If subglottic space only allows an endotracheal tube (ETT) two sizes smaller than expected, consider surgical intervention
- A cricoid split procedure may provide an alternative to tracheostomy in infants with SGS

Subglottic Hemangioma

- Rare cause of upper airway obstruction in children

Clinical presentation

- Considered in the differential diagnosis of chronic upper airway obstruction
- 50% accompanied by cutaneous hemangiomas of head and neck
- Inspiratory or biphasic stridor that worsens as hemangiomas enlarge
- Likely to shrink with age and usually do not require therapy

Diagnosis

- Upper airway endoscopy—asymmetric compressible bluish mass in the subglottic space

Management

- Treatment options include steroids, laser, intralesional steroid injections, and open surgical excision
- Propranolol from months to years by center with expertise
- Tracheostomy in severe obstruction

Laryngotracheoesophageal Cleft

- Associated with tracheoesophageal fistulas
- Rare cause of recurrent aspiration
- Neonates with severe clefts may present with respiratory distress
- Defect involves the anterior wall of the upper esophagus and the posterior aspect of the larynx, with the defect lying in the interarytenoid space

Clinical presentation

- Recurrent aspiration and cyanosis with feeding are the most common clinical presentation

Diagnosis

- Direct laryngoscopy rather than transnasal fiber-optic endoscopy is the diagnostic method of choice

Management

- Type 1—Conservative management with swallow therapy and thickening of feedings
- Types 2–4—Surgical intervention and swallow therapy

Macroglossia

- Macroglossia predisposes patients to obstructive sleep apnea (OSA)
- Lateral-view radiograph to evaluate anatomic relationship between tongue and airway
- Prone positioning may help in the acute management of airway obstruction due to macroglossia
- Airway obstruction may improve with age

Cough

Background

- Cough sensors present in upper and lower airway mucosa, paranasal sinuses, upper GI tract, external auditory canal
- Nocturnal cough is rare in normal children

Clinical presentation

- Differential is wide, so narrow possible diagnoses with history and physical:
  - Age, exposures, family history of asthma, allergies, or lung disease
  - Type of cough
    - Wet, dry, frequency, diurnal, nocturnal, length of cough, seasonality, quality, presence of hemoptysis
    - Sputum production (bronchitis, cystic fibrosis [CF], primary ciliary dyskinesia [PCD], bronchiectasis)
    - Quality
      - Brassy (tracheal irritation, tracheomalacia)
      - Barky (croup)
      - Honking (habit cough)
      - Staccato (chlamydia, mycoplasma)
      - Paroxysmal/whoop (pertussis, CF, foreign body)

  - Association to feedings and exercise (aspiration, exercise-induced asthma)
  - Associated with persistent rhinitis: allergies, PCD
  - Recurrent pneumonia—immunodeficiency
  - If not present during sleep in school age/adolescent, consider habit cough
  - Nighttime cough: asthma, sinusitis
  - Response to medications
  - Useful physical findings: stridor, wheezing, clubbing, poor growth, eczema, tachypnea, focal auscultatory findings, chest wall abnormalities
- Acute cough usually resolves in 1–3 weeks in 90% of children
- Subacute cough lasts 3–8 weeks and chronic cough > 8 weeks

Differential diagnosis

Considerations by length of cough:

- *Acute:* Allergies, foreign body, upper respiratory tract infections
- *Subacute:* Postinfectious cough, viral, pertussis
- *Chronic cough:*
  - All age groups: Gastroesophageal reflux (GER), exposures (tobacco smoke, pollution)
  - Other considerations by age:
    - Infants: Aspiration, congenital airway abnormalities, CF (even if neonatal screen is normal), neonatal infection, chlamydia, congenital heart disease (CHD)
    - Toddlers/preschoolers: Upper respiratory infection (URI), asthma, foreign body, postinfectious cough, pertussis, mycoplasma, immunodeficiencies, bronchiectasis, CF
    - School age/adolescents: Asthma, upper airway cough syndrome, smoking, tuberculosis (TB), bronchiectasis, habit cough

Evaluation of chronic cough

Look for clues and pointers and tailor evaluation according to most likely diagnoses:

- CXR
- Pulmonary function (spirometry)
- Sputum culture
- Allergy testing
- Swallow study
- Sweat test
- Immune function testing, including complete blood count (CBC) with differential, immunoglobulins
- Purified protein derivative (PPD) test
- Consider chest CT if cough is productive
- Echocardiogram
- Refer to specialists for further evaluations, e.g., laryngoscopy, bronchoscopy, echocardiogram

Management

- Recurrent respiratory tract infections/postinfectious cough: Symptomatic therapy
- Upper airway cough syndrome: Antihistamines, nasal steroids
- Dry cough/wheezing: Trial bronchodilators with environmental modifications. If positive response, consider trial with inhaled corticosteroids (ICS)
- GER: Antacids
- Psychogenic cough: Behavioral modifications
- Further management based on diagnostic findings: Refer to specialists for complicated diagnoses

Tachypnea

- Definition by age (breaths/min):
  - Birth to 30 days > 60
  - 2 to 12 months > 50
  - 1 to 5 years old > 40
  - Older than 5 > 20
  - Subtract 10 if the child is febrile

Exercise Intolerance

- The reference standard is the maximal oxygen consumption (VO2 max)
- Pulmonary conditions
  - Most common: Exercise-induced asthma (EIA) and CF
- Less common: Interstitial lung diseases
- Cardiovascular conditions
  - Congestive heart failure and CHD (most common CHD = tetralogy of Fallot)
- Muscular conditions, especially those associated with neuromuscular weakness
  - Duchenne muscular dystrophy
- Hematologic disorders
  - Iron deficiency anemia
  - Sickle cell disease
- Vocal cord dysfunction
  - Paradoxical motion of vocal cords
    - More common in adolescent females
    - May mimic EIA—Need to consider if not responding to EIA treatment
- Sedentariness—Leads to deconditioning, muscle weakness, and obesity

Respiratory Failure

- Type 1 respiratory failure characterized by low blood oxygen levels (hypoxemia, low pO2, normal or decreased pCO2, and alveolar-arterial oxygen gradient (pA-aO2) is increased)
  - Causes: V/Q mismatch, decreased minute volume, diffusion impairment or shunt
- Type 2 respiratory failure affects both oxygen and carbon dioxide levels
  - Low pO2, high pCO2, normal pA-aO2
  - Causes: Reduced breathing effort, increased airways resistance, neuromuscular disease
- Treating the underlying cause is paramount. In severe cases, intubation and mechanical ventilation are required
- If related to respiratory depression is related to narcotics, reversal can be of benefit

Apnea

- Defined by reduced or cessation in respiratory airflow

Three main types

- ***Central***
  - Cessation of airflow secondary to reduction or lack of excitatory signals from central nervous system (brain stem) to respiratory muscles
  - No chest wall effort
  - Prolonged episodes (> 20 s) are more clinically significant and usually associated with cyanosis and/or bradycardia
  - Shorter episodes can be seen in periodic breathing, which is common in premature infants and decreases with age/maturation
- ***Obstructive***
  - Airway (usually upper airway) obstruction/collapse leading to partial or complete obstruction of airflow in spite of chest wall effort
- ***Mixed***
  - Combination of both central and obstructive components
  - Usually central component followed by obstructive

Differential diagnosis of central apnea

- Neonates/infants:
  - Can present with central or mixed apnea
  - Most common cause: Apnea of prematurity or apnea of infancy
    - Associated with immature respiratory centers, laryngeal reflex, and, when mixed, underdeveloped upper airway musculature
    - Usually resolves by 48–53 weeks postconceptional age
    - Can be treated with respiratory stimulants (e.g., caffeine) or continuous positive airway pressure (CPAP)
    - Further evaluation warranted in younger infants (< 2 months) and severe presentations requiring resuscitation

  - Other causes of apnea during infancy usually more severe and include:
    - Infection (e.g., sepsis, pneumonia, meningitis, pertussis, bronchiolitis, botulism)
    - Head trauma, intraventricular hemorrhage, seizure, medications
    - GER, necrotizing enterocolitis
    - Metabolic derangements such as hypoglycemia and acidosis, inborn errors of metabolism
    - Hyper- or hypothermia
    - Heart failure
    - Anemia
    - Congenital central hypoventilation syndrome
- Older children
  - Causes: Cerebral hemorrhage or infarction, brain tumor, seizures, hypoxic injury, spinal cord injury, drugs, medications

Evaluation

- Guided by history (see amplified discussion for ALTE/BRUE)
- If severe presentation, young infant or older child, consider:
  - CBC, serum glucose, electrolytes
  - Sepsis workup
  - Electrocardiogram (ECG)
  - Neuroimaging, electroencephalogram if clinically indicated
  - Consult pertinent specialists
  - OSA (see amplified discussion for OSA)

Cyanosis

Background

- Bluish tint of the skin, either centrally or peripherally, related to respiratory causes, central nervous system causes, or hematologic causes
- Pulmonary causes are a result of poor oxygen delivery
- Cardiac causes include CHD and heart failure
- Hematologic causes include methemoglobinemia and polycythemia
- Can be caused by high altitude and hypothermia

Evaluation

- Assessment of respiratory status—wheezing, distress
- Cardiac assessment to include echo, and if concern for intrapulmonary shunt, consider contrast (bubble) echo
- ABG
- Methemoglobin assessment

Chronic Hypoxia

Causes

- Pulmonary venous desaturation
  - Lung disease with diffusion impairment (interstitial lung disease)
  - Intrapulmonary right-to-left shunting (pulmonary arteriovenous malformations)
- Extrapulmonary/intracardiac right-to-left shunting
  - Cyanotic CHD (tetralogy of Fallot, pulmonary atresia)
  - Pulmonary hypertension can present with intracardiac right-to-left shunting
- Hemoglobin disorders with decreased oxygen affinity
  - Methemoglobinemia (see expanded discussion)

Diagnosis

- Hyperoxia test
  - Give 100% oxygen and obtain a preductal blood gas (i.e., right upper extremity)
  - Normal PaO2 > 500 mmHg
  - Pulmonary disease PaO2 > 150 mmHg, but < 500 mmHg
  - Right-to-left shunting PaO2 < 150 mm Hg
- CXR to evaluate for pulmonary pathology
- CBC—If chronic, will show polycythemia

Methemoglobinemia

Background

- Methemoglobin (MetHb) cannot carry oxygen to tissues
- Methemoglobin occurs with oxidation of ferrous (Fe2+) to ferric (Fe3+) hemoglobin
- Methemoglobinemia can be acquired or inherited
  - Acquired
    - Most common after exposure to exogenous oxidizing agent like nitrites
      - Intestinal bacteria can convert nitrates in well water and pureed leafy vegetables to nitrites
    - Dehydration
  - Inherited
    - Deficiency cytochrome-b5 reductase
    - Hemoglobin M disease

Clinical Presentation

- Presents as cyanosis with MetHb levels > 15%
- Cyanosis with normal pulse oximetry, no respiratory or cardiac findings on physical exam

Evaluation

- Pulse oximetry—May be normal, but does not increase with use of oxygen
- Blood gas—Chocolate-colored blood
- Co-oximetry

Management

- Oxygen
- Severe cases: Methylene blue, N-acetylcysteine, exchange transfusion

Clubbing of Digits or Hypertrophic Pulmonary Osteodystrophy

Causes

- The most common cause is cyanotic heart disease
- The most common pulmonary causes are CF and bronchiectasis (usually more advanced disease)
- Biliary cirrhosis
- Infective endocarditis
- Normal variant as a familial trait

Diagnosis

- Obliteration of the angle between the proximal nail and soft tissue of the digit (Schamroth sign)
- Normal anatomy shows a diamond-shaped space when placing the distal phalangeal joints in mirrorlike fashion

Hemoptysis

Background

- Hemoptysis (coughing blood) is uncommon but can be a serious manifestation of pulmonary disease in children
- Pulmonary vasculature composed of two-pressure system:
  - Bleeding from low-pressure pulmonary vessels (e.g., diffuse hemorrhage) leads to small-volume hemoptysis, while bleeding from systemic pressure bronchial vessels (e.g., bronchiectasis) tends to be profuse

Clinical presentation

- Differentiating from hematemesis (vomiting blood) and epistaxis (nasal bleeding) can be tricky
- Most common reason for symptom usually not true hemoptysis but bleeding from upper airway (e.g., nasal bleeding)
- Diffuse hemorrhage is frequently slow and may present only with anemia and fatigue

Differential Diagnosis

- Most common etiology of true hemoptysis is inflammation or infection
- More common
  - Upper airway and GI bleeding
  - Infection such as bronchitis, pneumonia, lung abscess, TB, fungal infections
  - Foreign body
  - Cystic fibrosis, bronchiectasis

- Less common
  - Airway trauma
  - Tracheostomy
  - Cardiac (CHD, pulmonary hypertension, pulmonary embolism)
- Rare
  - Airway tumor (e.g., carcinoid)
  - Arteriovenous fistula
  - Bleeding disorder
  - Idiopathic pulmonary hemosiderosis
  - Pulmonary renal syndromes (usually in older children)
    - Granulomatosis with polyangiitis, Goodpasture syndrome, systemic lupus erythematosus, microscopic polyangiitis, Henoch-Schönlein purpura
  - Factitious hemoptysis

Evaluation

- History and physical exam not usually helpful; other guided studies frequently useful in the investigation
  - Imaging including CXR or chest CT with contrast to localize lesion or find evidence of pulmonary hemorrhage
  - Helpful labs: CBC for anemia; erythrocyte sedimentation rate (ERS), kidney function, urinalysis for renal involvement or inflammatory disease
  - Bronchoscopy can identify area of active bleeding and should include upper airway evaluation. Bronchoalveolar lavage for evidence of infection or hemosiderin-laden macrophages (presence indicates previous bleeding)
  - Echocardiogram for cardiac disease

Management

- Massive blood loss requires acute resuscitation with volume, blood products, and supportive care with oxygen and mechanical ventilation
- Evaluation by subspecialists (ear/nose/throat (ENT), pulmonologist, gastroenterology, rheumatology), depending on suspected cause

RESPIRATORY CONDITIONS OF THE UPPER AIRWAY

See discussion on stridor for general considerations

Viral Croup (Laryngotracheobronchitis)

Background

- Most common cause is parainfluenza
- Causes subglottic narrowing
- Common between 3 months and 3 years
- Spasmodic croup similar without viral prodrome or other identifiable cause
- Cricoid cartilage has a complete ring and is the narrowest part of the airway in infants
  - Edema at this level will lead to further narrowing, increased airway resistance, and possible airway compromise

Clinical presentation

- Barking or brassy cough
- URI with or without fever, which may be high (39–40 °C)
- Respiratory distress with retractions with hypoxia and hypercapnia in severe upper airway obstruction
- Child may prefer to sit or be held upright
- Mild—no stridor at rest
- Moderate—stridor at rest but no agitation
- Severe—stridor and agitation
- Recurrent croup: Consider underlying anatomic airway abnormality, GER, or atopy

Diagnosis

- Clinical diagnosis
- In typical cases**,** CXR is not required
  - CXR findings—steeple sign on frontal view is a common finding but may be absent

Management

- Reassurance, observation, and hydration

- Dexamethasone 0.6 mg/kg beneficial in mild croup (may decrease need for hospitalization)
- Oxygen and racemic epinephrine in moderate or severe cases
- Racemic epinephrine does not lead to rebound worsening of obstruction, but patient may worsen when drug effects subside. A 2-h observation is important. Worsening of obstruction is unlikely to occur if patient does well after 4 h.
- Racemic epinephrine should be used cautiously in patients with left ventricular outlet obstruction
- Low-density gas such as helium-oxygen (heliox) may be effective in children with severe croup
  - Turbulent flow through large airways is density-dependent.
  - By decreasing gas density, airflow resistance can be decreased.
- Admit for severe distress, hypoxia, and inability to feed/drink or if requiring 2 or more racemic epinephrine treatments
- Endotracheal intubation recommended before patient is restless and cyanotic
- Endotracheal intubation using an ETT one size smaller than predicted tube size (based on age and weight) is the preferred method of establishing an artificial airway in patients with viral croup
- Intubation more likely for bacterial tracheitis and epiglottitis and rare in croup
- If intubation needed, consider measles or influenza A

Prognosis

- Course of viral croup in infants younger than 1 year of age is prolonged
- Symptoms often improve during the day with recurrence of symptoms in the early hours of the morning

Epiglottitis

Background

- Most common pathogen *Haemophilus influenzae*
- Rare in children due to *H. influenzae* vaccination, which leads to individual and herd immunity
- More common in the elderly and immune-compromised children than in the general population
- Uncommon pathogens that can cause epiglottitis: Herpes viruses and fungi
- Pathology involves the epiglotis and other supraglottic structures, but the subglottic space and trachea are usually spared

Clinical presentation

- Rapid onset of illness (hours) with high fever, sore throat, drooling with difficulty swallowing, and difficulty breathing
- Patient sitting up and leaning forward position to enhance airflow
- Stridor is not a prominent feature
- Radiograph lateral neck view: Thumb sign

Management

- Patients with acute epiglottitis should undergo endotracheal intubation to ensure an adequate airway until inflammation subsides
- In severe cases, avoid unnecessary studies until airway is secured
- A skilled provider needs to remain with a patient with epiglottitis until the airway is visualized and secured

Bacterial Tracheitis

Background

- Most common organisms are *Staphylococcus aureus*, *Moraxella catarrhalis,* and *Streptococcus*

- Mean age is 4 years (range 4 weeks to 13 years, typically about 2 years)

Clinical presentation

- Brassy and barky cough, but the patient has high fever and appears very toxic with respiratory distress and stridor
- Patient may lay flat and does not have drooling or dysphagia associated with epiglottitis
- Rapid progression and purulent secretions may mandate early endotracheal intubation
- Does not respond to racemic epinephrine or corticosteroids

Diagnosis

- CXR not needed but may show the classic findings of pseudomembrane detachment in the trachea
- High fever, purulent airway secretions, absence of findings of epiglottitis

Management

- Intubation, especially for younger patients; 50–60% do not require intubation
- Humidification and careful suctioning of the ETT are important
- Antistaphylococcal treatment (i.e., nafcillin or vancomycin)
- Prognosis is good
- Complications can include ARDS, toxic shock, septic shock, pulmonary edema, and subglottic stenosis

RESPIRATORY CONDITIONS OF THE LOWER AIRWAY AND PARENCHYMA

Congenital Airway and Pulmonary Malformations

Pulmonary Sequestration

Background

- *Extralobar:* More common in males; 65% in the left lung, covered by pleura, fed by systemic artery, and drained via systemic vein. May be associated with diaphragmatic hernia and colonic duplication
- *Intralobar:* Typical in the lower lobe, systemic arterial supply, variable venous drainage, and airway connections

Clinical presentation

- Dullness on percussion, decreased breath sounds over the lesion, continuous murmur may be heard on the back, and crackles if infected

Evaluation

- Fetal ultrasound or ultrasound following birth may detect pulmonary mass
- CT scan with contrast confirms diagnosis

Management

- Surgical removal because retained sequestrations have a small possibility of becoming malignant
- Consultations: Pulmonology and surgery

Bronchogenic Cyst

Background

- Arise from abnormal budding of the tracheal diverticulum
- Patient may become symptomatic if the cyst enlarges or becomes infected
- May be asymptomatic and found incidentally

Clinical presentation

- Fever, chest pain, and productive cough are the most common presenting symptoms
- Dysphagia, if causing pressure on the surrounding structures
- CXR can show the cyst, but CT or MRI demonstrates anatomy (usually medial mediastinum)

Management

- Surgical removal

Vascular Ring/Sling

Background

- Congenital anomalies of the large vessels (such as aortic arch)

- May involve airway and/or esophagus
- Variable severity and timing of presentation but, if significant, usually presents during infancy

Clinical presentation
- May cause stridor or wheezing, cough, apnea, failure to thrive, and/or dysphagia
- Imaging:
  - Echocardiogram, CT, and MRI help define anatomy. Can be associated with tracheomalacia secondary to airway compression
  - Esophagogram may indirectly diagnose by demonstrating compression of abnormal vessel upon esophagus

Management
- Surgical intervention

Tracheal Stenosis

Background
- Narrowing of tracheal lumen frequently associated with complete tracheal rings
- Can vary from short- to long-segment stenosis
- Condition is rare

Clinical presentation
- Varies depending on degree of obstruction
- If severe, presents during neonatal period or infancy with respiratory distress, cyanosis, stridor, cough, and dysphagia

Diagnosis
- Direct visualization via rigid bronchoscope
- CT scan could be used to reconstruct via "virtual bronchoscopy"
- Echocardiogram to evaluate associated CHD

Management
- Surgical intervention
- Refer to pediatric ENT or airway surgical specialist

Congenital Pulmonary Adenomatoid Malformation

Background
- More prevalent in the left lower lobe
- 5 subtypes
  - Most are Type 1 (70%): Large (> 5 mm) single or multiple cysts
  - Type 3 (10%): Microcystic, solid, and associated with other anomalies. Worse prognosis

Clinical presentation
- Asymptomatic to respiratory distress depending on extent

Evaluation
- Can be identified by prenatal ultrasound
- CT scan is diagnostic

Management
- Resection if respiratory distress, markedly symptomatic
- If asymptomatic, can observe, but eventually most are surgically removed
  - Even if asymptomatic, there is increased future risk for infections and small risk for malignancy

Congenital Lobar Emphysema

Background
- Congenital bronchial obstruction leads to air trapping and distention of involved lung
- Rare
- Prevalence: Left upper lobe > right middle lobe/right lower lobe

Clinical presentation
- Usual presentation in infancy with respiratory distress, tachypnea, hypoxemia

Diagnosis
- CXR

  - Initially may present in neonate with opacification due to fluid
  - Subsequently, there is hyperinflation with shift to contralateral side
- Confirmation with CT scan

Management

- Surgical resection/lobectomy

FOREIGN BODY (FB) ASPIRATION

Background

- Nuts, particularly peanuts, make up one-third of cases
- Round, globular FBs (hot dog, grapes, nuts, hard candies) are the most frequently found, causing a complete airway obstruction
- Most common in age < 3 years

Clinical presentation

- Initial event: Violent, paroxysmal coughing, choking, gagging, possible airway obstruction if the FB is large
- Asymptomatic interval: FB becomes lodged, reflexes fatigue, immediate irritation subsides. This stage is most dangerous and accounts for delayed diagnosis
  - In this stage, FB might be missed, as physician is reassured by the absence of symptoms
- A positive history must never be ignored, and negative history can be misleading
- Coughing or choking episode accompanied by wheezing is highly suggestive of FB in the airway.
- Must question about nuts, small toys, other small items
- 58% lodge in the right bronchus

Diagnosis

- CXR is negative in 10–30% of cases
- If there is suspicion for FB, patient should undergo inspiratory and expiratory CXRs; in the uncooperative patient, consider doing bilateral decubitus films
- A lack of radiographic findings does not exclude an airway FB; many objects are organic and likely to be radiolucent
- Positive radiographic findings include hyperinflation, atelectasis, or infiltrate
- Soft tissue film of the neck can be of benefit to detect objects in the upper airway
- Patients with tracheostomy are at a higher risk

Management

- Ideal treatment is prompt removal with rigid bronchoscopy
- Can defer bronchoscopy until proper hydration and emptying of the stomach

Complications

- Retained foreign body can lead to hemoptysis, lung abscess, and ultimately bronchiectasis

PULMONARY HEMOSIDEROSIS

Background

- Repeated episodes of intra-alveolar bleeding that leads to abnormal accumulation of iron (hemosiderin) in the alveolar macrophages
- Subsequent development of pulmonary fibrosis and severe anemia

Causes and associated conditions

- Idiopathic pulmonary hemosiderosis (IPH)
- Secondary pulmonary hemosiderosis
  - Cardiovascular:
    - Congestive heart failure
    - Pulmonary hypertension
    - Mitral valve stenosis
  - Inflammatory/autoimmune
    - Goodpasture syndrome
    - Rheumatoid arthritis
    - Wegener granulomatosis
    - Henoch-Schönlein purpura
  - Allergic
  - Heiner syndrome (cow's milk hypersensitivity)

Clinical presentation

- Iron deficiency anemia
- Hemoptysis (helpful if occurs, but infrequent)
- Alveolar infiltrate
- Presence of hemosiderin; it takes 48–72 h for macrophages to convert erythrocyte to hemosiderin
- Widely variable from asymptomatic with infiltrates and anemia to shock and sudden death
- After episode of hemorrhage, the patient will present with wheezing, cough, dyspnea, bronchospasm, and alteration of blood gases

Diagnosis

- Best guided by consulting pulmonologist
- Recurrent "pneumonia", fever, cough, CXR abnormalities
- Hypochromic microcytic anemia
- Elevation of plasma bilirubin
- Infiltrates are typically bilateral and may spare the apices, often with hyperaeration
- IgE, cow's milk antibody levels, stool specimen for heme
- Urinalysis for nephritis
- Antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), and anti-glomerular basement membrane (GBM)
- Lung biopsy if diffuse alveolar hemorrhage (DAH)

Management

- Corticosteroid is the treatment of choice for IPH
- Treatment is highly dependent on the underlying cause

ACUTE BRONCHIOLITIS

Background

- Viral bronchiolitis is the most common lower respiratory tract infection in those under 2 years of age
- Respiratory syncytial virus (RSV) is responsible for more than 50% of acute bronchiolitis
- Other common causes are human metapneumovirus, parainfluenza, adenovirus, influenza, rhinovirus, and mycoplasma

Risk Factors

- Maternal asthma
- Maternal smoking
- Persistent rhinitis
- Eczema at < 1 year of age

Clinical presentation

- Nasal congestion, rhinorrhea, and cough
- Tachypnea or elevated respiratory rate is the earliest and most sensitive vital sign change
- Nasal flaring, grunting (in infants), and suprasternal, intercostal, and subcostal retractions are evidence of increased respiratory effort
- Nasal suctioning and repositioning may allow for a more accurate assessment of lower respiratory tract involvement
- Common: Crackles, wheezing, and referred upper airway sounds upon auscultation
- Apnea may be more prominent than wheezing in infants < 2 months or former preterm infants
- Symptoms can range from mild tachypnea to frank respiratory failure
- Clinical course is expected to worsen, with peak symptoms noted around days 3–4 of illness ("day of illness")
- "Day of illness" is an important variable for providing anticipatory guidance for outpatient management and in making decisions regarding admission and discharge of patients

Diagnosis

- Clinical symptoms lead to diagnosis; subsequent evaluation is important in determining treatment
- Initially must assess respiratory rate and oxygen saturation because work of breathing, tachypnea, and hypoxia are most clinically significant in determining severity
- CXR warranted for infants in respiratory distress
- CXR commonly demonstrates hyperinflation, patchy atelectasis, and infiltrates

- In infants under 30 days old, the risk for serious bacterial infection (SBI) warrants full evaluation for SBI and administration of empiric antibiotics
- Recognize that infants older than 30 days with bronchiolitis are at a lower risk for SBIs, thus allowing for decreased invasive testing and observation without administering antibiotics to patients who have classic presentations

Management

- Mainstay of treatment is supportive: Oxygen for hypoxia, hydration, nasal suctioning, and positioning to elevate chest to 30°
- When feeding adequately and work of breathing improves, oxygen can be discontinued if saturations are 90–92% for most of the time
- Infants with respiratory distress and desaturation or dehydration should be hospitalized
- The American Academy of Pediatrics does NOT recommend the use of bronchodilators or systemic steroids in the routine treatment of bronchiolitis
- However, those with recurrent wheezing may respond to bronchodilator therapy
- Corticosteroid medications, inhaled or administered systemically, should not be routinely used in the treatment of bronchiolitis
- If bronchodilator makes the wheezing worse or increases work of breathing, consider pulmonary consultation for trachea or bronchomalacia
- Sweat chloride testing for patients with recurrent wheezing and who are resistant to treatment is recommended
- Ribavirin should not be used routinely in the treatment of bronchiolitis

Prevention

- Palivizumab (Synagis®) 15 mg/kg intramuscular (IM) for premature and high-risk infants as monthly IM monoclonal antibody injection
- Handwashing is best measure to prevent nosocomial infection

BRONCHOPULMONARY DYSPLASIA (BPD)

Background

- Definition has changed since initial description in the 1960s
- "Old" BPD in late premature infants treated with high peak inspiratory pressures and high oxygen concentrations leading to necrotizing bronchiolitis, pulmonary hypertension, alveolar overinflation, atelectasis, cystic disease, and pulmonary fibrosis
- "New" BPD definition revised in 2000 after use of CPAP, gentler ventilation, antenatal steroids, and surfactant instituted as standard
  - *Immature lung* resulting in alveolar arrest and dysmorphic pulmonary vasculature; *lung injury* from oxygen therapy, positive-pressure ventilation, infection, inflammation, and fluid overload; and *inadequate lung injury repair* with ongoing inflammation
  - Other risk factors: lower birthweight, gestational age (< 32 weeks), chorioamnionitis, and *Ureaplasma* colonization

Clinical Presentation

- Need for oxygen, which can progress to respiratory failure leading to increased or progressive need for ventilatory support
- Grading of "new" BPD based on ongoing need for oxygen in premature infants who required oxygen at 28 days
  - On reassessment at 36 weeks postmenstrual age:
    - Mild: On room air
    - Moderate: FIO2 < 30%
    - Severe: FIO2 > 30% or on positive-pressure ventilation
- CXR can present with areas of opacification, atelectasis, hyper-expansion, and pulmonary edema
- Sequelae of BPD and associated conditions include:
  - Tachypnea, retractions

  - Suboptimal growth, increased caloric requirements
  - Dysphagia and GER can lead to aspiration
  - Neurodevelopmental delays with cerebral palsy being the most common presentation
  - Heart failure secondary to pulmonary hypertension, ventricular hypertrophy, pulmonary overcirculation from right-to-left shunting

Management

- Prevention: Good prenatal care, prevention of prematurity
- Postnatal management leading to reduced incidence of BPD:
  - Use of gentle ventilation, permissive hypercapnia, noninvasive forms of airway pressure/ventilation
  - Assure growth and adequate nutrition
  - Vitamin A supplementation in extremely low birthweight infants shown to reduce incidence of BPD
  - Screen for and treat for pulmonary hypertension
  - Use of systemic steroids postnatally decreases risk of BPD and improves extubation success. However, **routine use is contraindicated** due to increase in long-term risk of neurodevelopmental impairment
- Management once BPD diagnosed:
  - Multidisciplinary follow-up of neurodevelopmental, cardiovascular, and nutritional sequelae
  - Bronchodilators, inhaled steroids, diuretics are frequently used
  - Insufficient data related to long-term outcomes
  - Short course of steroids for acute exacerbations
  - Prevent infections; prophylaxis with palivizumab decreases frequency of RSV-related hospitalizations

ASTHMA

Background

- Heterogeneous disease characterized by chronic inflammation of the airways
- US prevalence of childhood asthma ranges from 10% to 15%
- Wheezing observed in about 3% of infants before 3 years of age
- Several asthma phenotypes have been described based on onset of symptoms and natural course of the disease process:
  - Transient
    - Early onset at < 1 year old
    - Decreased lung function at birth
    - Resolved symptoms by mid-childhood
    - No further reductions in pulmonary function
  - Nonatopic
    - Early onset at < 3 years
    - Variable clinical course
  - Late onset
    - Onset > 3 years
    - Variable clinical course
  - Persistent
    - Early onset < 3 years
    - Abnormal lung function by 3 years
    - Most patients are atopic
- Asthma symptoms are more common in boys before puberty, but more severe in girls after puberty
- The **asthma predictive index** was developed to help predict which children would be likely to develop persistent asthma symptoms
  - Its negative predictive value is better than its positive predictive value
  - Positive if:
    - 1 or more major risk factors: Parental history of asthma, atopic dermatitis, sensitization to aeroallergen

OR

- 2 or more minor risk factors: Sensitization to food, more than 4% eosinophilia, wheezing apart from upper respiratory tract infections

Pathophysiology

- Inflammation plays a key role in asthma pathophysiology
- Important contributors to the inflammatory response include:
  - Cell types including lymphocytes, eosinophils, mast cells, neutrophils, macrophages, smooth muscle cells, and epithelial cells
  - Inflammatory mediators such as IL-5, IL-4, and IL-13
- IgE plays an important role in activation and maintenance of allergic disease
  - Early-phase reaction or Type I IgE-mediated reactions occur within minutes of an allergen-related trigger
    - Cells (such as mast cells) release preformed inflammatory mediators that can lead to vasodilation, edema, bronchoconstriction, and increased airway mucus secretion
    - Early airway obstruction occurs, in addition, there is activation of leukocytes, which in turn leads to late-phase IgE-mediated reactions
  - A late-phase IgE-mediated reaction follows 2–12 h later
    - Characterized by persistent obstruction and mucus hypersecretion
    - The late reaction is the consequence of inflammatory mediators
- Respiratory infections
  - Viral respiratory infections are the most common trigger of exacerbations in children (especially those < 10 years) and have been associated with future development of asthma
  - Bronchiolitis associated with RSV and rhinovirus in early childhood increases risk of developing asthma

Table 20.2 Differential diagnosis for asthma

Red flags	Possible diagnosis
Sudden onset of symptoms, witnessed choking, localized wheezing	Foreign body aspiration
Coughing and choking when eating or drinking	Dysphagia with aspiration
Sneezing, cough, nasal congestion	Chronic upper airway cough syndrome
Poor growth and low BMI	Cystic fibrosis, immunodeficiency
Chronic rhinorrhea, recurrent sinusitis, early-onset respiratory symptoms	Cystic fibrosis, primary ciliary dyskinesia
Acute-onset dyspnea and/or stridor in teens	Vocal cord dysfunction
Chronic wet productive cough, recurrent infections	Bronchiectasis
Recurrent pneumonia	Immunodeficiency, anatomical abnormality
Chronic wet cough, difficulties feeding, early onset, noisy breathing	Vascular ring, tracheoesophageal fistula, tracheomalacia
Heart murmur, poor weight gain, cyanosis with feedings	Congenital heart disease
Prematurity, prolonged mechanical ventilation or supplemental oxygen	Bronchopulmonary dysplasia

Assessment

- There is no diagnostic test for asthma
- Diagnosis is based on constellation of clinical symptoms including presence of airflow limitation that is at least partially reversible
- Exclusion of alternative diagnoses (Table 20.2)
- Assess for associated comorbidities, including obesity, GER, rhinitis/sinusitis, depression, anxiety, sleep-disordered breathing, and allergic bronchopulmonary aspergillosis
- **Typical symptoms:**
  - Wheezing, chest tightness, shortness of breath, cough
  - Symptoms are usually worse at night and early morning
  - The more symptoms, the more likely the diagnosis
  - If cough only symptom or chronic sputum production reported, broaden your differential

- **Common triggers:**
  - Respiratory infections (especially viral infections)
  - Exercise
  - Inhaled allergens (e.g., pollen, pet exposure, dust mites, cockroaches, mold)
  - Irritants (tobacco smoke, air pollution)
  - Medications (e.g., nonsteroidal anti-inflammatory medications, beta-blockers)
  - Changes in weather
- **Physical findings and objective data:**
  - Wheezing on exam, especially on forced exhalation; signs of atopy such as allergic shiners, rhinitis, or eczema
  - PFT
    - Spirometry measurements before and after bronchodilator recommended in the assessment of patients ≥ 5 years/o
      - Look for obstruction on spirometry
      - Use bronchodilator response to assess reversibility
      - Decline in lung function (FEV1 and FEV1/FVC ratio) can usually be seen in those with symptoms starting < 3 years and is noted by 6 years
  - Exercise challenge can be used to evaluate for exercise-induced asthma
    - Baseline spirometry obtained prior to treadmill challenge
    - Spirometry obtained after exercise to document drop in pulmonary function
  - CXR
    - May show hyperinflation, peribronchial wall thickening, atelectasis
    - Most helpful to evaluate for differential causes of symptoms
  - Allergy testing
    - Skin testing or serum testing may help in identifying sensitization to inhaled perennial allergens

Asthma classification

- Severity is best assessed prior to initial controller therapy (Table 20.3)
- Assess components of severity: impairment and risk

Table 20.3 Asthma classification

Severity	Daytime symptoms/ SABA use Nighttime symptoms	Activity limitation Pulmonary function
Intermittent		
0–4 years	≤ 2 days/week 0 nights/month	None
5–11 years	≤ 2 days/week ≤ 2 nights/month	None FEV1 > 80%; FEV1/FVC > 85%
12–19 years	≤ 2 days/week ≤ 2 nights/month	None FEV1 > 80%; FEV1/FVC > 85%
Mild persistent		
0–4 years	3–6 days/week 1–2 nights/month	Minor limitation
5–11 years	3–6 days/week 3–4 nights/month	Minor limitation FEV1 > 80%; FEV1/FVC > 80%
12–19 years	3–6 days/week 3–4 nights/month	Minor limitation FEV1 > 80%; FEV1/FVC > 85%
Moderate persistent		
0–4 years	Daily 3–4 nights/month	Some limitation
5–11 years	Daily > 1 night/week	Some limitation FEV1 60–80%; FEV1/FVC 75–80%
12–19 years	Daily > 1 night/week	Some limitation FEV1 60–80%; FEV1/FVC 80–85%
Severe persistent		
0–4 years	Daily > 1 night/week	Extremely limited
5–11 years	Throughout the day Often	Extremely limited FEV1 < 60%; FEV1/FVC < 75%
12–19 years	Throughout the day Often	Extremely limited FEV1 < 60%; FEV1/FVC < 80%

SABA short-acting beta-2 agonist, *FEV1* forced expiration volume in 1 s, *FVC* forced vital capacity

  - **Impairment:** Relates to the frequency and intensity of symptoms, how the disease affects day-to-day function
  - **Risk** estimates likelihood of exacerbations or having reduced lung function

Exercise-Induced Asthma (EIA)

- Clinical presentation of EIA

  - Shortness of breath, coughing, wheezing, chest tightness, or pain associated with physical activity. Can present in isolation or associated with symptoms of poorly controlled asthma
  - Symptoms present during or minutes after exertion, peak after 5–10 min of exercise, and improve within 20–30 min
  - Usually self-limited but may result in a severe asthma attack
- Management of EIA
  - Warm-up period 15 min prior to exercise and wearing scarf/mask may reduce symptoms
  - In 80% of patients, short-acting beta-agonists (SABAs) before exercise prevent symptoms for about 2–3 h
  - Montelukast can lead to decrease in bronchospasm in about 50% of patients, but onset of action is several hours after administration

Management of asthma

Assessment and monitoring:

- After initial diagnosis: Review response to therapy, reassess severity and control, adjust therapy to reduce impairment and risk
- Periodic reassessment recommended due to variable nature of asthma
- Annual increase in asthma exacerbations seen in September
- Reassess patients every 2–6 weeks initially to gain disease control and then every 1–6 months
- Assess frequency of daytime symptoms, nighttime symptoms, and reliever use over the past month
- Can use asthma control tools such as the Asthma Control Test (ACT) or Asthma Control Questionnaire (ACQ) as part of assessment
- Evaluate technique and compliance with controller therapy
- PFT at initial assessment, after treatment and stabilization of symptoms, during periods of uncontrolled symptoms, and at least every 1–2 years
- Increased risk of exacerbation *if 1 or more*:
  - Uncontrolled asthma symptoms, increased use of SABA, inadequate dose or use of ICS, < 60% FEV1, psychological and/or socioeconomic barriers, comorbidities, eosinophilia, exposure to known triggers, history of pediatric intensive care unit or intubation, ≥ 1 severe exacerbation in the last year
- Consider step-down in therapy if asthma under good control for at least 3 months

Education:

- Self-management education (patient and families) key in individual asthma control and improve outcomes
- Provide asthma action plan that provides guidance in daily management as well as plan of care for worsening symptoms

Control environmental factors and comorbidities:

- Assess for allergen exposures either by skin testing or serum testing and correlate with medical and exposure history
- Patients should reduce exposure to allergens, irritants, and pollution to which they are sensitized or have a reaction
- Assess for and control comorbidities associated with increased risk for poor control: Obesity, allergic rhinitis/sinusitis, allergic bronchopulmonary aspergillosis, OSA, depression, and other psychosocial factors.

Medications:

- Initial treatment based on severity category (Table 20.4)
- On reassessment of asthma control, adjust therapy regardless of initial severity classification.

Beta-2 agonists

- Relieve airway constriction by binding to receptors on airway smooth muscle
- Frequent use can signal poor asthma control

Table 20.4 Asthma: Initial controller therapy

≥ 6 years	Preferred initial therapy	≤ 5 years	Preferred initial therapy
Intermittent asthma symptoms	**Step 1** SABA as needed	Infrequent viral wheezing and no symptoms in between episodes	**Step 1** SABA as needed Consider intermittent ICS
Persistent symptoms or high-risk factor for exacerbations	**Step 2** Low-dose ICS	Uncontrolled asthma symptoms, > 3 exacerbations/y or consider trial in those with frequent wheezing (every 6–8 weeks)	**Step 2** Daily low-dose ICS
Asthma symptoms/SABA use > 2X/week	**Step 2** Low-dose ICS Consider LRTA	Uncontrolled asthma on low-dose ICS	**Step 3** Double low-dose ICS
Asthma symptoms most days or waking > 1X/week	**Step 3** Medium-/high-dose ICS or if ≥ 12 years, low-dose ICS/LABA	Uncontrolled asthma on double low dose	**Step 4** Refer to specialist Add LTRA Add intermittent ICS or increased ICS frequency
Severe initial presentation (uncontrolled asthma or acute exacerbation)	**Step 4** Short OCS course AND High-dose ICS or if ≥ 12 years, moderate dose ICS/LABA		
Uncontrolled asthma after initial therapy	Step up therapy or use adjunct therapies **Step 3**: Can add LTRA to low-dose ICS **Step 4**: Can add ipratropium (if > 12 years) to ICS or add LTRA to high-dose ICS **Step 5**: Refer to specialist for add-on therapy (e.g., tiotropium, anti-IgE, anti-IL-5, low-dose OCS)		

Adapted with modifications from Global Initiative for Asthma Report [1]
SABA short-acting beta-2 agonist, *ICS* inhaled corticosteroid, *LRTA* leukotriene receptor antagonist, *LABA* long-acting beta-2 agonist, *OCS* oral corticosteroid

- Short-acting beta-2 agonists (SABA)
  - Onset of action is within 15 min, but of relatively short duration (3–4 h)
- Long-acting beta-2 agonists (LABA)
  - Effects can last at least 12 h
  - Used in combination with ICS
- Adverse effects
  - Agitation, irritability, tremors, tachycardia, insomnia, arrhythmias; higher doses used during acute asthma exacerbations can lead to hypokalemia or hypoglycemia

Inhaled corticosteroids

- Most potent and effective medication for long-term control of asthma
- Decrease airway inflammation and bronchial hyperresponsiveness, relieve asthma symptoms, and improve lung function
- Patients should rinse and spit out after inhalation
- Adverse effects
  - Oral thrush, oral absorption, and higher-dose ICS use may lead to decrease in growth velocity and adrenal suppression

Leukotriene receptor antagonists

- Block leukotriene, which acts as a potent mediator leading to bronchoconstriction, vascular permeability, and increased mucus production and activates inflammatory cells
- Usually an add-on therapy and not preferred treatment option in mild persistent asthma
- Adverse effects
  - Generally, well tolerated, but associated with upper respiratory tract infection, fever, headache, sore throat, behavior/mood-related changes

Acute asthma exacerbations

- Patients present with acute or subacute worsening from baseline symptoms and/or pulmonary function
- Brief initial assessment should concentrate on time of onset and possible triggers, severity compared to previous exacerbations, recent use of asthma medications, and associated cardiorespiratory process
- Severe exacerbation presentation: shortness of breath, inability to speak in full sentences, sitting hunched, agitated, accessory muscle use, tachypnea and tachycardia, pulsus paradoxus > 20 mmHg, SpO2 < 92% (after an hour of therapy is a good predictor for hospitalization needs), PEF < 40% baseline
- Life-threatening exacerbations can present with silent chest, drowsiness, or confusion
- CXR not recommended routinely, but patient can present with atelectasis, which needs to be clinically differentiated from pneumonia
- Therapy for acute exacerbations:
  - Oxygen as needed to keep SpO2 > 90%
  - Three SABA treatments spaced every 20–30 min
  - Adding high doses of ipratropium bromide leads to decreased rate of hospitalization
  - Systemic corticosteroids to patients with moderate to severe exacerbations or with poor initial response to SABA

PNEUMONIA

Background

- Lower respiratory tract infection with fever and respiratory symptoms with parenchymal involvement on exam or by CXR findings
- *Streptococcus pneumoniae* is the most common bacterial cause in children older than 1 week of age
- Viruses account for 14–35% of cases
- Complicated pneumonia with empyema and necrosis
- Community-associated methicillin-resistant *Staphylococcus aureus*

Most common causes of pneumonia by age group

- Neonates (0–3 m)
  - Group B strep and Gram-negative bacteria
  - Early and late onset
  - Early onset—first 3 days of life with respiratory distress
- Three weeks to 3 months
  - Chlamydia trachomatis
    - Interstitial infiltrate on CXR
  - RSV and parainfluenza
    - Bronchiolitis or pneumonia
  - *Streptococcus pneumoniae*
    - Major cause of pneumonia through childhood
  - Bordetella pertussis
    - Tracheobronchitis with severe paroxysm, usually no fever
- Three months to 5 years
  - Most common etiology—viruses (RSV, parainfluenza, human metapneumovirus, influenza, and rhinovirus)
  - Strep pneumonia—most treatable pathogen
  - Mycoplasma pneumoniae
    - Increased incidence in children approaching school age
- Five years to adolescence

  - Most common cause
    - Atypical organisms such as *Mycoplasma* and *Chlamydophila pneumoniae*
      - *Mycoplasma*—leading cause of pneumonia in school-age children and young adults

Most common causes of pneumonia by geographic location

- Histoplasmosis
  - Ohio and Mississippi River Valleys and Caribbean
- Coccidioidomycosis
  - California, Arizona, and New Mexico
- Blastomycosis
  - Ohio, Mississippi River Valleys; Great Lakes states
- *Legionella*
  - Infected water worldwide
- Avian influenza
  - Southeast Asia

Pneumonia via animal vectors

- Tularemia
  - Rabbits and ticks
- Psittacosis
  - Birds and parakeets
- Q fever
  - Sheep, cows, and goats

Pneumonia with associated exanthems

- Varicella
  - Human to human airborne droplets
- Measles
  - Human to human droplets

Clinical presentation

- Nonspecific signs and symptoms
- Cough and fever—hallmark symptoms
- Tachypnea is the most sensitive and specific sign of pneumonia
- Most children with cough and fever do not have pneumonia
- Tachypnea, retractions, wheezing, nasal flaring, grunting, apnea, and abdominal pain may be presenting or associated symptoms
- Grunting may be a sign of impending respiratory failure in younger patients/infants
- Findings on exam may be dullness to percussion, crackles, decreased breath sounds, and bronchial breaths
- In the absence of fever, tachypnea, increased work of breathing, or auscultatory abnormalities, bacterial pneumonia is unlikely

Diagnosis

- Clinical diagnosis as above
- Rapid influenza test may help to identify the cause of fever and to reduce unnecessary use of antibiotics
- CBC, chemistry, or serology will not help in identifying etiology or aid in management
- Blood culture rarely helpful (only 10% of the time organism is recovered)
- ESR and C-reactive protein (CRP) may be elevated but are not specific
- Tuberculin test if there are TB risk factors or TB is being considered
- CXR (Fig. 20.3)

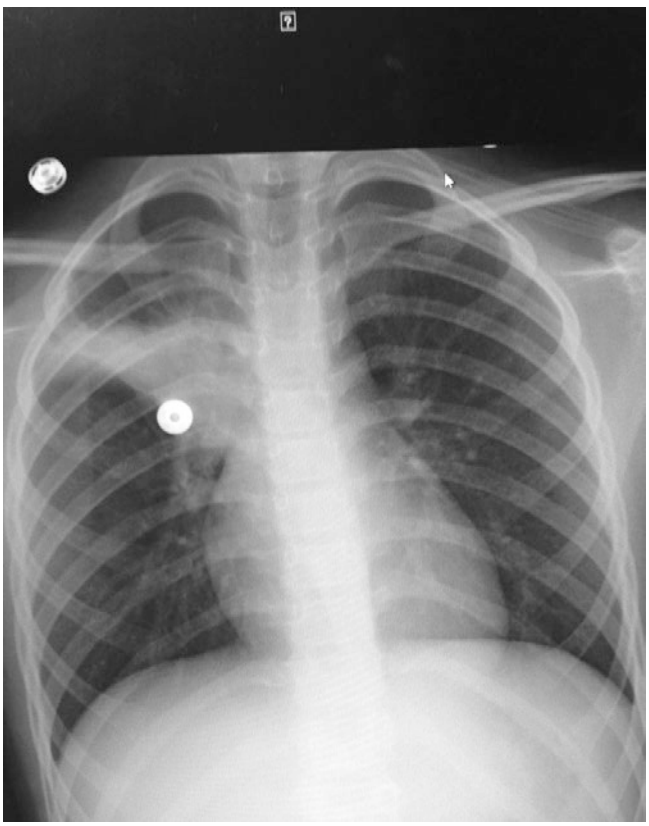

Fig. 20.3 A 9-year-old female presents with cough and fever. Chest radiograph shows right upper lobe infiltrate.

- A CXR will not change clinical management for patients being treated as outpatient
- Afebrile children do not need a CXR
- CXR always lags behind clinical response. No need to obtain to confirm response to antibiotics
- Obtain a CXR if:
  - Complicated pneumonia is being considered
  - Clinical deterioration
  - Prolonged fever with no obvious source of infection
  - Abdominal pain with normal appendix

Management

- National guideline for antibiotic initiation with community-acquired pneumonia:
  - High-dose amoxicillin (80–90 mg/kg/day) for uncomplicated cases being treated as outpatient
  - Augmentin or cefuroxime as outpatient, if resistant
  - School age or > 5 years of age azithromycin to cover for *Mycoplasma*
- Indication for hospitalization: Suspected sepsis, severe dehydration, toxic appearance, hypoxemia (SpO2 < 90%), unresponsive to outpatient therapy, inability to drink
  - Intravenous fluids and O2, if needed, and antibiotics
  - Consider blood culture, CXR, chemistry profiles, and CBC
  - If inpatient: Cefuroxime, ceftriaxone, or cefotaxime are the antibiotics of choice
  - Adolescents: Fluoroquinolones (levofloxacin, gatifloxacin, moxifloxacin) may be used for atypical pneumonia
  - If *Staphylococcus* is considered, add clindamycin or vancomycin
  - Uncomplicated pneumonia responds to antibiotics in 48–96 h
  - If no response or persistent pneumonia
    - Repeat CXR
    - Consider empyema, bacterial resistance, and nonbacterial pneumonia (FB, CF, pulmonary sequestration, bronchiolitis obliterans, aspiration, and hypersensitivity pneumonitis)

BRONCHIECTASIS

Background

- Destruction of the airway wall (bronchi and bronchioles) leads to loss of integrity of the muscular and elastic layers of the bronchial wall, results leading to dilated and collapsible airway

Clinical presentation

- Productive cough is most common symptom
- Dyspnea, rhinosinusitis, and hemoptysis are less common
- Crackles, wheezing, and rhonchi are often heard; digital clubbing may be present

Differential diagnosis

- CF is the most common cause of bronchiectasis in pediatric patients in the USA.
- Impaired mucociliary clearance (CF and ciliary dyskinesia)
- Infections (*Mycobacterium tuberculosis*, *Pseudomonas*, adenovirus)
- Immunodeficiency syndromes
- Immune-mediated (connective tissue diseases), allergic bronchopulmonary aspergillosis (ABPA), inflammatory bowel disease (IBD)
- Airway injury (chronic aspiration, inhalation of toxic fumes, hot gases)
- Congenital or connective tissue abnormalities (yellow nail, Marfan syndrome, alpha-1 antitrypsin deficiency, airway cartilage deficiency, tracheobronchomegaly, Young syndrome)
- Obstructed airways (retained FB, intraluminal masses, extraluminal compression)

Evaluation

- PFT may show obstruction, restriction, or both, depending on etiology and severity
- CXR may reveal airway dilation, increased pulmonary markings with "tram tracking" (thickening of the bronchial walls), and areas of atelectasis
- High-resolution CT scan is the gold standard and reveals detailed anatomy of the bronchial tree
- There is a lack of airway tapering with luminal dilation, bronchial wall thickening, honeycombing, and mucous plugging

Management and prognosis

- Determining the primary cause is of critical importance and is best done with direction from pediatric pulmonologist
- Evaluation may include swallow study, sweat chloride testing, and bronchoscopy
- Mucus clearance should be enhanced with hypertonic saline nebulization, inhaled mucolytics, and chest physiotherapy
- ICS can reduce airflow obstruction
- Chronic macrolide therapy has been found to be as beneficial as anti-inflammatory drugs
- Culture should be obtained
- Aggressive treatment of *Pseudomonas* and *Staphylococcal* infections is indicated, but antimicrobial therapy should be targeted to specific pathogens
- If bronchiectasis is localized and severe, lobectomy is a last resort in cases without systemic etiology

CYSTIC FIBROSIS

Background

- Autosomal recessive inheritance pattern due to a mutation on the long arm of chromosome 7
- Highest incidence in Caucasians, highly prevalent in Latinos and African Americans. Less frequently seen in Asians and Native Americans
- CF transmembrane regulator (CFTR) dysfunction/absence leads to:
  - Excessive reabsorption of sodium and deficient chloride secretion
  - Passive movement of water is decreased, and airway secretions are dehydrated with very low surface liquid layer
  - Cilia become compressed, inhibiting ciliary clearance and cough clearance
  - Bacteria thrive, and the immune function at the airway surface is also abnormal
  - Repeated bacterial infection leads to airway damage and bronchiectasis in the lung
    - CFTR dysfunction leads to dysfunction in other organ systems:
      - Organ systems primarily involved: respiratory, GI, genitourinary, and integumentary (sweat glands)
- There are > 1700 mutations in the CFTR protein
- Different classes of mutations result in different levels of CFTR function/production, thus variable clinical presentation
- The most prevalent mutation is F508 deletion (F508del), associated with both pulmonary disease and pancreatic insufficiency
  - 85% of the US population have one copy

Clinical presentation

- ***Pulmonary manifestations***
  - Cough is most common and consistent symptom. Often productive but can also be dry
  - Increased anteroposterior (AP) diameter of the chest due to hyperinflation associated with airway obstruction
  - Hyperresonance, diffuse or localized crackles
  - Nasal obstruction, nasal polyps, recurrent sinusitis
  - Clubbing
  - In advanced disease: Cyanosis, exercise intolerance, shortness of breath, growth failure, respiratory failure, and death

  - Common bacterial pathogens include *Staphylococcus aureus and Pseudomonas aeruginosa*
  - Multidrug-resistant organisms are becoming more common (MRSA, *Stenotrophomonas maltophilia, and Burkholderia cepacia* complex).
- ***Gastrointestinal manifestations***
  - *Meconium ileus* is seen in up to 20% of newborns with CF
  - Characterized by abdominal distention, emesis, and failure to pass meconium in the first 24–48 h
  - Abdominal radiograph (KUB) shows air fluid level with ground glass-appearing material in the central abdomen
  - Gastrografin enema diagnostic and therapeutic
  - Can give hyperosmolar contrast as well
  - May need to consider surgery if medical management fails
  - **Pancreatic-insufficient** (PI) patients will progress to complete or almost complete disruption of pancreatic acini and replacement with fibrous tissue. Lack of endogenous digestive enzymes causes fat malabsorption
    - Symptoms: Frequent, loose, foul smelling, and greasy stools, flatus, and poor weight gain
    - PI also associated with fat-soluble vitamins (ADEK) deficiency
      - Deficiencies can cause night blindness, decreased bone density, and neurologic dysfunction (neuropathy, dementia)
- ***Genitourinary manifestations***
  - Pubertal development is often delayed, particularly if nutrition is poor
  - Females have decreased fertility related to thick cervical mucus
  - Many females with CF carry pregnancies to term, without detriment to lung function
  - > 95% of males are infertile due to absence or atretic vas deferens
- ***Integumentary manifestations***
  - Excessive salt loss in sweat predisposes children to hyponatremia, particularly when hot or exercising
  - Hypochloremic alkalosis and dehydration, especially in hot environments, can be deadly in infants

Complications

- ***Distal intestinal obstruction syndrome (DIOS)***
  - More commonly seen with poor enzyme adherence, also in those with a history of meconium ileus
  - Fecal material accumulates in the terminal portion of the ileum and cecum
  - Osmotic agents such as polyethylene glycol (MiraLAX®) are helpful
  - Can also give enemas and other stool softeners as an adjunct
  - If severe or complete obstruction, can require Gastrografin enema to relieve obstruction
- ***Rectal prolapse***
  - Due to combination of intestinal disease and poor supporting musculature from poor nutrition
  - Evidence of recurrent rectal prolapse in otherwise healthy children is an indication for sweat chloride testing to assess for CF
- ***Nasal polyps***
  - Most prevalent in teens and young adults
  - Local steroids and nasal rinses can be of benefit for symptom control
  - If there are nasal obstructive symptoms such as chronic rhinorrhea, snoring, and sinus pain or pressure, surgical intervention is warranted
  - Even with surgical resection, polyps are likely to return
- ***CF-related liver disease***
  - Found in 2–3% of cases
  - More common in those with severe mutations with little CFTR function
  - Mainstay of treatment is to prevent ongoing liver damage and associated complications of portal hypertension and cirrhosis

- ***CF-related diabetes***
  - Most common comorbidity
  - Affects 20% of adolescents and up to 40% of adults
  - Shares features of both Type I and Type II diabetes but is a distinct entity
  - Primarily caused by insulin insufficiency, but fluctuating insulin levels also play a part
  - Often clinically silent, screen with oral glucose tolerance test (OGTT) annually after age 10 years

Diagnosis

- ***Newborn screening:***
  - US states use different methods of testing
  - In most states, initial testing uses immunoreactive trypsinogen testing and, if elevated, limited DNA testing
  - Confirmatory sweat testing is recommended
  - Newborn screening can miss positive cases, especially pancreatic sufficient or those with less common mutations. CF must be a consideration if there are clinical features
- ***Sweat chloride*** is abnormal if > 40 in infant less than 6 months, and > 60 in those older than 6 months
  - Pilocarpine iontophoresis is used to stimulate sweating
  - Positive results should be confirmed with genetic testing
  - Negative results with high clinical suspicion should also have genetic testing
  - False-positive sweat chloride can occur:
    - If testing is completed on skin affected by eczema or contaminated with lotion
    - Hypothyroidism
    - Skin disorders
    - Untreated adrenal insufficiency
    - Nephrogenic diabetes insipidus
    - Hypoparathyroidism
    - Severe malnutrition
- ***DNA testing*** can confirm and, when sequencing is sent, will identify > 95%
- ***Pancreatic function testing***
  - Pancreatic fecal elastase preferred
  - Can assess fecal fat but much less accurate

Management per CF Foundation Guidelines

- ***Centers of care:*** Care is managed in a network of multidisciplinary centers.
- ***Visits:*** Infants seen monthly for follow-up until age 1 and then quarterly
- ***Imaging:***
  - CXR done annually, generally demonstrating mucous plugging and central and upper lobe bronchiectasis
  - May need CXR to evaluate more closely for bronchiectasis
- ***PFT*** via spirometry assessed quarterly starting at age 5 years
  - Initially obstructive process, and then with increasing lung damage, a restrictive process is noted
- ***Microbiology***
  - Sputum cultures to be assessed a minimum 3 times per year
  - First common bacteria noted is *Staphylococcus aureus*
  - *Pseudomonas* is next commonly seen and treated to eradicate due to potential for colonization and hastening lung damage
  - Also, commonly seen: MRSA, *Stenotrophomonas maltophilia*
  - Low prevalence but primarily seen in CF: *Burkholderia cepacia*

Primary goals of management

- Maintain lung function as close to normal as possible.
- Mainstay therapies include *hydration of airway surface layer* with hypertonic saline, *liquefying mucus* with use of dornase alfa, and *clearance of airways* using various ACTs
- Prevent infections by limiting exposure to other CF patients and other reservoirs of

infection (freshwater lakes, humidifiers, hot tubs)
- Treat infections when present with directed antimicrobial therapy
- Ensure adequate nutrition through high-calorie diet, appropriate enzyme supplementation, and close monitoring of growth

Managing complications
- Mild acute exacerbation treatment
  - Increased inhaled bronchodilator therapies and mucolytics
  - Increased ACTs
  - Usually oral antimicrobials
- Moderate and severe pulmonary exacerbations
  - Usually require hospital admission for IV antibiotics
  - Aggressive respiratory therapies
  - May require additional nutritional intervention to maintain adequate growth during illness

Standard therapies for treatment in CF
- Pancreatic enzyme replacement orally
- Multivitamins (particularly fat-soluble vitamins)
- Bronchodilators
- Hydrating agents (7% hypertonic saline)
- Mucolytics (dornase alfa)
- Antibiotics (inhaled, oral, or IV)
- ACT/chest physiotherapy (CPT)
  - Oscillating chest compression vest
  - PEP (positive expiratory pressure) devices
  - Autogenic drainage
  - Directed coughing, huff coughing
- Anti-inflammatory agents
  - Azithromycin
- Insulin for CF-related diabetes
- CFTR modulator drugs to improve ion transport
  - Ivacaftor; ivacaftor/lumacaftor; ivacaftor/tezacaftor
- Lung transplant indicated for severe and end-stage lung disease
- Surgical intervention required
  - Meconium ileus
  - Intussusception
  - Gastrostomy tube placement
  - Rectal prolapse

CF care across the life span
- Transition to adult care is a requirement of all accredited CF centers
  - There is often formal preparation for patients 18–21 transitioning to adult care
- Median survival is currently 37 years
- Infants now born with CF and who are cared for in an accredited CF center will likely survive beyond age 50

PRIMARY CILIARY DYSKINESIA

Background
- Autosomal recessive disorder with extensive genetic heterogeneity
- Characterized by dysmotile, immotile, or absent cilia
- The ciliary defects lead to abnormal mucociliary clearance

Clinical presentation
- Symptoms in organs where ciliary motility is important for normal function
  - Neonatal respiratory distress or neonatal pneumonia (frequently misdiagnosed as transient tachypnea)
  - Recurrent pneumonias and bronchiectasis
  - Recurrent wheezing frequently diagnosed as asthma
  - Chronic persistent rhinosinusitis
  - Nasal polyps and recurrent otitis media; recurrent otitis media may begin in neonates
  - Men are infertile and women have decreased fertility

Diagnostic evaluation
- Gold standard: Cilia from nose or trachea by brushings or mucosal biopsy for evaluation of

ciliary abnormalities on electron microscopy (absent, abnormal dynein arms, radial spokes, doublet arrangements)
- Genetic testing—need two mutations in a single gene for diagnosis. Problematic due to heterogeneity, and inability to identify two mutations does not rule out diagnosis
- CT scan
  - Sinuses: Paranasal sinuses involvement
  - Chest: Bronchiectasis

Management
- ACT, antibiotics for infections documented on culture with sensitivities, ENT evaluation for surgery if needed

EXTRAPULMONARY RESPIRATORY CONDITIONS

Pleural Effusion

Background
- > 10 mL fluid in the thoracic cavity
- Due to excessive filtration or defective absorption
- Normal fluid balance
  - 0.1–0.2 mL/kg of sterile colorless fluid
  - Ninety percent filters from arterial capillaries, reabsorbed at venous capillaries
  - About 10% returned via lymphatic
  - Normal pleural fluid (0.3 mL/kg)
- Etiologies
  - Pneumonia is the most common
  - Neonatal period: Chylous effusion most common
  - Others: Malignancy, renal disease, trauma, congestive heart failure, and systemic diseases

Clinical presentation
- Suspect in any child with worsening pneumonia
- Respiratory distress, tachypnea, cough, chest pain with pleural inflammation
- Decreased to absent breath sounds, pleural rub with smaller collection of fluid
- Egophony
- Dullness to percussion
- Midline shift

Diagnosis and management
- Transudate: Clear or straw colored; low protein and lactate dehydrogenase (LDH)
- Exudate: Straw colored or cloudy
  - Pleural fluid/serum protein ≥ 0.5
  - Pleural fluid/serum LDH ≥ 0.6
  - Pleural fluid LDH > 2/3 of the upper limit of normal for serum LDH
- Appearance:
  - Purulent fluid—infection
  - Thin white milky fluid—chyle
  - Blood—trauma or malignancy
- CXR—opacification of thorax, blunted costophrenic angles (Fig. 20.4)
  - Decubitus views helpful if fluid is free-flowing

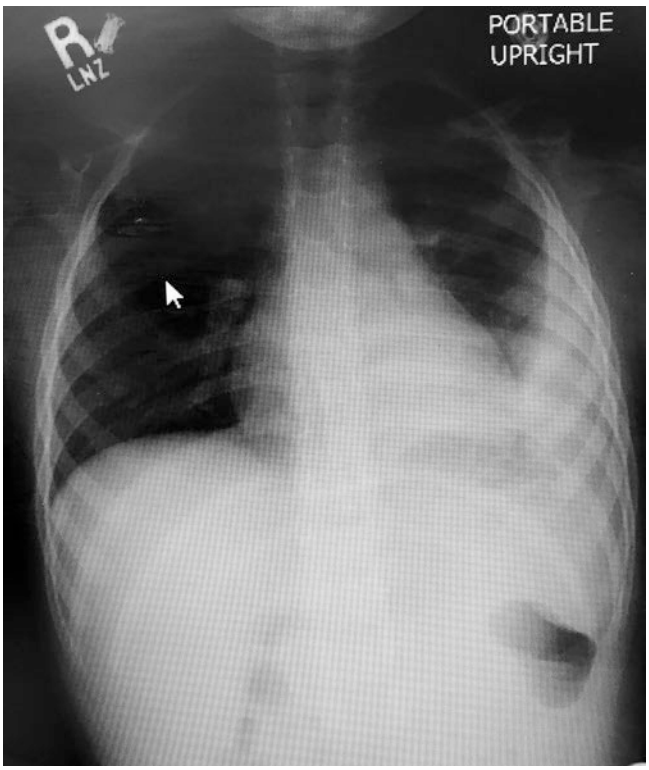

Fig. 20.4 Chest radiograph of a 2-year-old child with left pleural effusion

- Ultrasound helpful to evaluate for loculations
- CT scan for complicated effusions/empyema to define pulmonary and fluid characteristics
- Thoracentesis
  - Routine thoracentesis not recommended
  - Perform thoracentesis to relieve dyspnea for large effusions, worsening symptoms, sepsis, or a lack of improvement in symptoms despite administration of broad-spectrum antibiotics for diagnostic purposes
- Oxygen for hypoxemia
- Consultation with experts as needed

Pneumothorax

Causes

- **Primary spontaneous pneumothorax**
  - Occurs without trauma or underlying cause
  - More frequently in tall, thin males, likely related to subpleural blebs
  - Family history is positive in many patients
  - Usually occurs at rest, but can be precipitated by air travel in an unpressurized cabin, weight lifting, and Valsalva maneuver
- **Secondary pneumothorax**
  - Related to an underlying lung issue (asthma, CF, necrotizing pneumonia, interstitial lung disease)
  - Trauma (blunt trauma)
  - Loud music (air pressure)
  - Catamenial pneumothorax (unusual condition associated with menses due to passage of intra-abdominal air through a diaphragmatic defect)

Clinical presentation

- Onset is abrupt, and the severity depends on degree of lung collapse
- In simple pneumothorax, the lung collapses up to 30%
- In a tension pneumothorax, patient will be hypoxemic, dyspneic, and possibly cyanotic
- Point of maximal impulse shifts due to displacement of intrathoracic organs to the opposite side

Diagnosis

- CXR
  - Upright, if possible
  - Expiratory films accentuate the contrast between lung markings and the clear area of the pneumothorax
- Recurrence rate is high after primary spontaneous pneumothorax

Management

- Small pneumothorax $< 5\%$ may resolve spontaneously
- If $> 5\%$ of pneumothorax or collapse, or if recurrent or under tension, a chest tube for drainage is necessary
- Pneumothoraces complicating CF frequently recur, and definitive treatment may be justified with the first episode
- One means of definitive therapy is sclerosing with doxycycline (chemical pleurodesis)
- Video-assisted thoracic surgery is preferred therapy for blebectomy, pleural stripping, pleural brushing, and instillation of sclerosing agents over open thoracotomy
- Extensive pleural adhesion and aggressive pleural stripping may interfere with lung transplant potential in the future, an issue that must be discussed with the family

Pneumomediastinum

Background

- Can be traumatic or spontaneous
- Spontaneous pneumomediastinum occurs when air leaks through small alveolar rupture to the surrounding bronchovascular sheath
- Less commonly, occurs with air escaping from the upper respiratory tract, intrathoracic airways, or esophageal rupture
- Triggers: (Most common) asthma exacerbation and lower respiratory infection; (less common) Valsalva/strenuous lifting and vomiting

Clinical presentation

- Chest pain, dyspnea, cough, neck pain, dysphagia, odynophagia

Management

- Usually resolves by itself

THORACIC DEFORMITIES

Background

- Thoracic deformities affect rib cage, spine, and respiratory muscles
- Abnormalities can result in restrictive disease due to reduced compliance of chest wall and increased workload/fatigue of respiratory muscles

Pectus Excavatum (Funnel Chest) (Fig. 20.5)

Background

- 1/400 births, more common in males, rare in African Americans
- Can be isolated, familial, or associated with connective tissue diseases (e.g., Marfan or Ehlers-Danlos syndrome), neuromuscular disease (e.g., spinal muscular atrophy)
- Incidence: > 90% of congenital wall anomalies

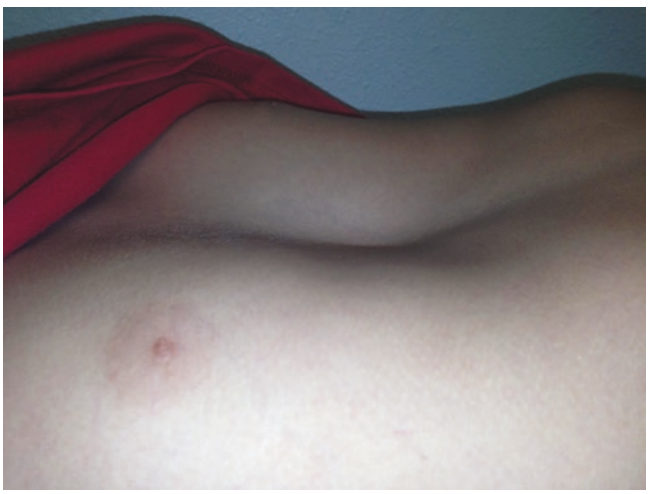

Fig. 20.5 Pectus excavatum. A 12-year-old healthy boy with funnel-shaped chest

Clinical presentation

- Often noted at birth, may be not associated with any symptoms
- Range from asymptomatic to increasing symptoms in more severe cases
  - Exercise intolerance
  - Fatigue
  - Chest pain
  - Palpitations
  - Recurrent chest infections
  - Wheezing
  - Stridor
  - Cough
  - Tall and thin
- Children may experience significant psychological stress because of cosmetic appearance

Evaluation

- CXR; increased AP diameter
- CT for Haller index (HI); if significant, should be repaired
  - HI = lateral internal rib cage dimension/AP internal sternum to vertebrae dimension
  - Normal value HI: 2.5
  - Surgical repair if HI > 3.25 and/or cardiopulmonary involvement
- ECG commonly abnormal; right axis deviation
- Echo may demonstrate cardiac compression and mitral valve prolapse

Management

- Based on severity of deformity and physiologic compromise
- Mild: Observation and physical therapy to maintain posture
- Corrective surgery if significant physiologic compromise (Nuss or Ravitch procedure)

Pectus Carinatum (Pigeon Chest)

Background

- Anterior displacement of midsternum and adjacent costal cartilage
- Rare: 1/1500 of chest wall deformities
- Associated with mild to moderate scoliosis, mitral valve prolapse, and coarctation of aorta

Clinical presentation

- Rarely causes limitations
- Physical appearance most common complaint
- HI less than two is significant

Management

- Surgery for cosmetic and psychological stress

Scoliosis

Background

- Cobb angle = angle from most tilted vertebrae above and below the apex of the curve
- Scoliosis defined as lateral curvature of the spine with Cobb angle > 10°
- Curvatures > 50° more likely to be progressive
- Extreme curvatures can lead to respiratory compromise due to restrictive chest wall disease

Management

- Observe for progression
- Bracing
- Spinal fusion for curves > 40°–45°

PULMONARY HYPERTENSION

Background

- Mean pulmonary artery pressure of 25 mm Hg or more at rest
- Can be caused by left heart disease, lung disease (including BPD), thromboembolic disease, autoimmune disease, variety of other disease or idiopathic

Clinical presentation

- Exertional dyspnea, progressive fatigue in older child
- Infants less specific: Poor appetite, failure to thrive, diaphoresis, tachypnea, tachycardia, and irritability
- Syncope, presyncope, and chest pain are features of more advanced disease; hemoptysis late and sometimes fatal symptom

Management

- Outcome in pediatrics has improved
- Should be seen by specialist (cardiology or pulmonology)
- Patients may require a combination of therapies, and some patients require surgery (septostomy)

Cor pulmonale

- Right ventricular (RV) hypertrophy leading to RV failure caused by increased afterload caused by pulmonary hypertension
- Can be caused by chronic lung disease, bronchopulmonary dysplasia, cystic fibrosis, arterial hypertension, neuromuscular disease

OBSTRUCTIVE SLEEP APNEA (OSA)

Background

- OSA and primary snoring are part of a spectrum of sleep-disordered breathing
  - **Primary snoring** = Incidence 12–20%; no discrete obstructive events or gas exchange abnormalities
  - **OSA** = Prevalence 2–4% in healthy children; obstructive apnea and hypopneas often seen with arousals, disturbed sleep, and gas exchange abnormalities
- The disorder can occur at any age but is most common in the preschool age group (2–6 years) and adolescents
- A higher prevalence has been reported in African American and obese children

Risk factors and associated conditions

- Adenotonsillar hypertrophy
- Obesity
- Craniofacial abnormalities (such as midface hypoplasia and micrognathia)
- Hypotonia (e.g., Down syndrome)
- Neuromuscular disease
- Cerebral palsy

Clinical presentation

- All children should be screened for snoring
- Signs and symptoms that may signal OSA
  - Snoring
  - Gasping during sleep
  - Enuresis (especially if secondary)
  - Restless sleeper
  - Unusual positioning during sleep (hyperextended neck, sleeping propped up)
  - Cyanosis
  - Sweating during sleep
  - Morning headaches
  - Daytime sleepiness in older children
  - ADHD-like symptoms, including hyperactivity and/or inattention, difficulty concentrating
  - Adenoidal facies as well as signs of atopy or nasal congestion
  - Chronic mouth breathing with chronic nasal congestion
  - Tonsillar hypertrophy
  - Obesity
  - Failure to thrive
  - Unexplained hypertension

Management

- History and physical exam cannot distinguish between primary snoring and OSA
- Polysomnography diagnostic test of choice
- Complex, high-risk patients (e.g., craniofacial disorders, genetic syndromes, neuromuscular disorders, severe OSA) should be referred to specialist
- Patients with neuromuscular disease may desaturate during sleep but appear well awake
  - Overnight saturation monitoring may be a helpful screening tool for sleep-disordered breathing in these patients
- Adenotonsillectomy is first-line therapy and curative in about 80% of children with OSA
- Noninvasive positive airway pressure is an option for poor surgical candidates or those with residual OSA after surgery
- High-risk patients should be monitored as inpatients postoperatively
- Patients should be re-evaluated postoperative to determine if additional treatment is required

ACUTE LIFE-THREATENING EVENT (ALTE)/BRIEF RESOLVED UNEXPLAINED EVENT (BRUE)

Background

- Common associations with ALTE
  - GER disorder most common association for awake ALTE
    - Prevalence of GER in infants with ALTE as high as 70%
    - Highly symptomatic infants may benefit from therapy with antacids, positional changes, and thickened feedings
  - Neurologic
    - Seizures second most common association
    - High index of suspicion of child abuse important
    - Up to 10% presenting ALTE associated with child abuse
  - Viral respiratory infections
    - RSV most commonly associated ALTE
    - More common in < 2 months, lower birthweight, history of prematurity
- BRUE now preferred term to more subjective ALTE, but terms frequently used interchangeably
- BRUE
  - < 1 year of age
  - Sudden, brief, and resolved episode with ≥ 1 of the following:
    - Cyanosis or pallor
    - Absent, decreased, or irregular breathing
    - Change in tone

    - Altered responsiveness
  - Unexplained after adequate history and physical
- Presence of BRUE does not predict SIDS

Management

- Low-risk BRUE: Patients > 2 months, older preterm infant (> 32 weeks and postconceptual age > 45 weeks), event < 1 min, no previous events, no need CPR, negative history and exam
  - Management of low-risk BRUE
    - No need for admission
    - Workup considered even in low-risk BRUE
      - Pertussis testing as infants may present with few symptoms
      - Pulse oximetry monitoring in the emergency department
      - ECG due to severe outcome associated with channelopathies
  - Has good negative predictive value
  - Observation, further testing, and treatment as supported by history and exam

SUDDEN INFANT DEATH SYNDROME (SIDS)

- Factors associated with triple risk model of SIDS:
  - Critical period in development
    - Risk peaks at 2–4 months with most deaths having occurred by 6 months
    - Male predominance
  - Infant vulnerability
    - Brain stem dysfunction
    - Genetic predisposition
    - Defects in arousal
    - Prematurity, low birthweight
    - Poor prenatal care
  - Environmental factors
    - Prone sleep position
    - Tobacco smoke exposure
    - Soft bedding
    - Co-sleeping
    - Overheating
    - Young maternal age
- Increased risk in siblings, but risk of second child death < 1%
- National recommendation on SIDS prevention
  - "Back to sleep": Supine position. "Tummy to play": Awake and monitored
    - Marked decline in SIDS rate following mass education of this public policy
  - Firm mattress
  - Cool ambient air
  - No soft object or loose bedding
  - No co-sleeping
  - Encourage breastfeeding
  - No smoking
  - Sleep in parents' room for 1st year, but on separate surfaces
  - Pacifiers
    - Use pacifier once breastfeeding has been established
    - Offer pacifier at bedtime or nap time

PEARLS AND PITFALLS

Diagnostic Testing for Respiratory Conditions

Interpretation of spirometry

- Obstruction: N ↓ FVC, ↓ FEV1, ↓ FEV1/FVC, ↓ FEF 25–75
- Restriction: ↓ FVC, ↓ FEV1, N FEV1/FVC, ↓ FEF 25–75

Blood gas analysis

- Arterial blood gas analysis (see Table 20.1)
- In capillary blood gases, values are comparable to arterial pH and pCO2, but pO2 measurement in CBG is less reliable.

Chest imaging

- Imaging in suspected FB:
  - Get inspiratory and expiratory or bilateral decubitus views. May be able to see asym-

metric hyperinflation in side with foreign body.
– Most foreign bodies are not seen, as they are radiolucent.

General Signs and Symptoms

Stridor/wheezing

- **In**spiratory—**Ex**trathoracic swelling or obstruction will lead to airway collapse on inspiration. Example: Laryngomalacia
- **Ex**piratory—**In**trathoracic swelling or obstruction will lead to airway collapse on expiration. Example: Tracheomalacia
- **Biphasic stridor—indicates fixed airflow obstruction—subglottic space obstruction**
- **Laryngomalacia:** Most common cause of stridor in infants, accounts for up to 75% of all causes of stridor
- **Choanal atresia:** Infant/newborn in respiratory distress with inability to pass a 6F catheter into oropharynx through nose
- **Left vocal cord paralysis:** Associated with trauma to the recurrent laryngeal nerve at birth or surgical trauma
- **Subglottic hemangioma:** 50% accompanied by cutaneous hemangiomas of head and neck. Inspiratory or biphasic stridor, which worsens as hemangiomas enlarge
- **Viral croup:** Course of viral croup in infants younger than 1 year of age is prolonged. Symptoms often improve during the day with recurrence of symptoms in the early hours of the morning.
- **Epiglottitis:** Stridor is not a prominent feature.

Cough

- Nocturnal cough is rare in normal children
- Associations: Brassy (tracheal irritation, tracheomalacia); barky (croup); honking (habit cough); staccato (chlamydia, mycoplasma); paroxysmal/whoop (pertussis, CF, FB)

Exercise intolerance

- Vocal cord dysfunction: More common in adolescent females. May mimic EIA—need to consider if not responding to EIA treatment

Hemoptysis

- Differentiating from hematemesis (vomiting blood) and epistaxis (nasal bleeding) can be tricky.
- Most common reason for symptom usually not true hemoptysis, but bleeding from upper airway (e.g., nasal bleeding)

Congenital airway and pulmonary malformations

- With symptoms and presenting during infancy, most will require surgical intervention.

Acute bronchiolitis

- Most common lower respiratory tract infection in < 2 years
- Etiology: RSV > 50%
- Apnea may be more prominent than wheezing in infants < 2 months or former preterm infants.
- Peak symptomatology at days 3–4 of illness ("day of illness")
- "Day of illness": Important variable for providing anticipatory guidance in outpatient management and making decisions regarding admission/discharge
- Routine use of bronchodilators or systemic steroids in management NOT recommended

Asthma

- Asthma symptoms are more common in boys before puberty, but more severe in girls after puberty.
- **Early-phase reaction or Type I IgE-mediated reactions** occur within minutes of an allergen-related trigger.

- **A late-phase IgE-mediated reaction** follows 2–12 h later.
- Viral respiratory infections (such as RSV and rhinovirus) have been associated with future development of asthma and are the most common trigger of exacerbations in young children.
- All that wheezes is not asthma! Think about the differential if diagnosis not clear.
- If cough is the only symptom or chronic sputum production is reported, broaden your differential.
- ICS are the most potent and effective medication for long-term control of asthma.
- EIA: In 80% patients, SABA before exercise prevents symptoms for about 2–3 h.
- Acute asthma exacerbation: SpO2 < 92% after an hour of therapy is a good predictor for hospitalization need.

Pneumonia

- *Streptococcus pneumoniae* is the most common bacterial cause in children older than 1 week of age.
- Viruses account for 14–35% of cases.
- For school-age children needing inpatient therapy: Cefuroxime, ceftriaxone, and cefotaxime are the antibiotics of choice.

Bronchiectasis/cystic fibrosis

- CF is the most common cause of bronchiectasis in pediatric patients in the USA.
- CFTR dysfunction/absence leads to thick secretions, impaired mucociliary clearance, recurrent inflammation, and infection, leading to development of bronchiectasis.
- All US states have newborn screening, but results are not 100% sensitive.
- Diagnostic tests include sweat testing and DNA testing.
- Patients should be managed by a multidisciplinary team at a CF care center.
- Pneumothorax/pneumomediastinum
  - Pneumothorax > 5% hemithorax will require chest tube drainage, but pneumomediastinum usually resolves spontaneously.

Thoracic cage deformities

- Pectus excavatum: > 90% of congenital wall anomalies
- Scoliosis: Curvatures > 50° more likely to be progressive. Extreme curvatures can lead to respiratory compromise due to restrictive chest wall disease.

OSA

- Higher prevalence in African Americans and obese children
- Polysomnography diagnostic test of choice
- Adenotonsillectomy is first-line therapy and curative in about 80% of children with OSA.

SIDS

- Peaks at 2–4 months of age, male predominance
- "Back to sleep" supine position for sleep led to marked decline in SIDS rate

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