FIRST AID FOR THE®

INTERNAL MEDICINE BOARDS

FOURTH EDITION

Concise summaries of **high-yield topics** facilitate last-minute review

Hundreds of full-color clinical images and tables

Mnemonics and **clinical pearls** improve exam-day recall

Proven strategies for passing the internal medicine boards

Mc Graw Hill Education

Tao Le • Thomas E. Baudendistel
Peter V. Chin-Hong • Cindy J. Lai

FIRST AID FOR THE® Internal Medicine Boards

Fourth Edition

TAO LE, MD, MHS
Assistant Clinical Professor of Medicine and Pediatrics
Chief, Section of Allergy and Immunology
Department of Medicine
University of Louisville
Louisville, Kentucky

PETER V. CHIN-HONG, MD, MAS
Professor of Medicine
Director, Transplant and Immunocompromised Host Infectious Diseases Program
University of California, San Francisco
San Francisco, California

THOMAS E. BAUDENDISTEL, MD, FACP
Program Director, Internal Medicine Residency
Kaiser Permanente
Oakland, California

CINDY J. LAI, MD
Professor of Medicine
Director, Medical Student Clinical Education
Department of Medicine
University of California, San Francisco
San Francisco, California

Mc Graw Hill Education

New York / Chicago / San Francisco / Athens / London / Madrid / Mexico City
Milan / New Delhi / Singapore / Sydney / Toronto

ISBN: 978-1-25-983504-9
MHID: 1-25-983504-9.

The material in this eBook also appears in the print version of this title: ISBN: 978-1-25-983503-2,
MHID: 1-25-983503-0.

eBook conversion by codeMantra
Version 1.0

NOTICE

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or com plete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Asthma

Asthma is a **chronic inflammatory disorder** of the airway resulting in **airway hyperresponsiveness, airflow limitation,** and **respiratory symptoms.** Often begins in childhood, but may have adult onset. **Atopy** is a strong identifiable **risk factor** for the development of asthma. Subtypes include exercise-induced, occupational, aspirin-sensitive, and cough-variant asthma.

Symptoms/Exam

- Symptoms include **dyspnea** (at rest or with exertion), **cough, wheezing,** mucus hypersecretion, chest tightness, and nocturnal awakenings with respiratory symptoms.
- Symptoms may have identifiable **triggers** (eg, exercise, exposure to cat dander, NSAIDs, cold exposure).
- **Acute exacerbations: Expiratory wheezing;** a prolonged expiratory phase; ↑ respiratory rate.
- **Severe exacerbations: Pulsus paradoxus,** cyanosis, lethargy, use of accessory muscles of respiration, silent chest (absence of wheezing due to lack of air movement).
- **Chronic asthma without exacerbation:** Presents with minimal to no wheezing. Signs of allergic rhinosinusitis (boggy nasal mucosa, posterior oropharynx cobblestoning, suborbital edema) are commonly found. **Exam may be normal** between exacerbations.

Diagnosis

Diagnosed by the history and objective evidence of **obstructive lung disease.**

- **PFTs:** Show a ↓ **FEV_1/FVC ratio** with **reversible obstruction** (>12% ↑ in FEV_1 after bronchodilator use) and **normal diffusing capacity.**
- **Methacholine challenge:** Useful if baseline lung function is normal but clinical symptoms are suggestive of asthma. A ⊕ methacholine challenge test is not diagnostic of asthma, but a ⊖ test indicates that asthma is unlikely **(high sensitivity, lower specificity).**

Management

See the Hospital Medicine chapter for management of acute exacerbations.

Chronic asthma therapy (Table 1.3) is based on asthma severity. The treatment regimen should be **reviewed every 1 to 6 months,** with changes made depending on symptom severity and clinical course. Additional treatment considerations for both acute and chronic asthma include the following:

- Recognize the exacerbating effects of **environmental factors** such as allergens, air pollution, smoking, and weather (cold and humidity).
- Use potentially **exacerbating medications** (ASA, NSAIDs, β-blockers) **with caution.**
- Always consider **medication compliance and technique** as possible complicating factors in poorly controlled asthma.
- Treatment of **coexisting conditions** (eg, **rhinitis, sinusitis, GERD**) may improve asthma.
- Consider the addition of anti-IgE monoclonal antibody (omalizumab) for the treatment of **severe persistent allergic asthma.**
- Consider alternative diagnoses if a patient has adult onset asthma that is difficult to control: upper airway obstruction (upper airway wheezing), other lung disease (emphysema, chronic bronchitis, ABPA, eosinophilic granulomatosis with polyangiitis [formerly Churg-Strauss], chronic eosinophilic pneumonia, obstructive sleep apnea, restrictive lung disease, PE), cardiovascular disease (CHF), respiratory infection (pneumonia).

KEY FACT

In a patient with asthma, sinusitis, and nasal polyps, and who takes aspirin (Samter's triad), consider **aspirin exacerbated respiratory disease** as the cause of asthma. Treatment would include stopping aspirin, performing aspirin desensitization, and lifelong high-dose aspirin and leukotriene inhibitor use.

KEY FACT

In a patient with new-onset asthma late in adulthood with no obvious environmental trigger, consider 2° causes such as GERD, heart failure, allergic bronchopulmonary aspergillosis, and eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss).

KEY FACT

Monotherapy with long-acting β_2-agonists have been associated with asthma-related deaths. Never use these agents as monotherapy in severe asthma.

KEY FACT

Asthma symptoms that occur more than twice weekly generally indicate the need for inhaled corticosteroid therapy.

KEY FACT

Think of reactive airway dysfunction syndrome in a patient with symptoms of asthma following a single, large exposure to an irritant such as chlorine or mustard gas (biological warfare). Treat like asthma.

TABLE 1.3. Guidelines for the Treatment of Chronic Asthma

ASTHMA CLASSIFICATION	SYMPTOMS[a]	PULMONARY FUNCTION	RECOMMENDED TREATMENT
Mild intermittent	≤2 days/week, ≤2 nights/month	Peak expiratory flow (PEF) ≥80%	Bronchodilator two to four puffs every 4 hours as needed No daily medications necessary
Mild persistent	>2 days/week but <1 time/day or >2 nights/month	PEF ≥80%	Add low-dose inhaled corticosteroids Leukotriene modifiers, theophylline, and cromolyn may also be added
Moderate persistent	Daily symptoms or >1 night/week	PEF 60%-80%	↑ to medium-dose inhaled corticosteroids and add a long-acting inhaled β_2-agonist Leukotriene modifiers or theophylline may also be added
Severe persistent	Continuous symptoms	PEF <60%	↑ to high-dose inhaled corticosteroids plus long-acting inhaled β_2-agonists. Daily oral corticosteroids may be added if necessary (60 mg once per day)

[a] Dyspnea (at rest or with exertion), cough, wheezing, mucus hypersecretion, chest tightness, and nocturnal awakenings with respiratory symptoms.

Diagnosis

- Routine evaluation should include history and physical, CBC, ECG, CXR, UA, and coagulation studies. Consider **bronchoscopy** if there are risk factors for **cancer** (especially smoking) or to **localize source of bleeding.** Order a **chest CT if bronchiectasis or AVM** is higher on the differential.
- Additional studies, if indicated, include expectorated sputum for acid-fast bacilli and cytology, BUN/creatinine, ANA, ANCA, anti-GBM antibody, ABG, 100% O_2 to evaluate for shunt, and pulmonary arteriography.

KEY FACT

To evaluate hemoptysis, do a bronchoscopy if you are concerned about cancer. Order a chest CT if you are considering bronchiectasis or AVM.

Management

- **Supportive care:** Bed rest with supplemental O_2 and blood products if needed. **Avoid antitussives, as an effective cough is needed to clear blood from the airways.** If gas exchange becomes compromised, consider early endotracheal intubation.
- **Definitive treatment:**
  - **Non-massive hemoptysis:** Treatment is directed at the specific underlying cause (eg, antibiotics for bronchitis).
  - **Massive hemoptysis: Urgent bronchoscopy or bronchial artery angiography** may localize the site of bleeding. **Angiography plus embolization stops bleeding in >90% of cases.** Emergency surgery for massive hemoptysis is controversial and reserved for those who have failed embolization.

KEY FACT

The majority of massive bleeds derive from high-pressure bronchial artery circulation rather than from low-pressure pulmonary arteries. Angiography plus embolization stops bleeding in >90% of cases.

Obstructive Airway Disease

PREOPERATIVE PULMONARY ASSESSMENT

- The type of surgery is a very important predictor of perioperative pulmonary complications with thoracic surgeries, upper abdominal surgery, emergency surgery, neck surgery, abdominal aortic aneurysm repairs, and vascular surgeries carrying the highest risk.
- Other risk factors include age >60 years, smoking, COPD, CHF, pulmonary hypertension, poor functional status, low serum albumin, and kidney disease (BUN >30 mg/dL).
- In patients **with known lung disease,** the goal is to **optimize treatment** of underlying lung disease.
- In patients **without known lung disease,** the goal is to **identify unexplained pulmonary symptoms and perform further workup,** which involves taking a history about exercise tolerance, chronic cough, and dyspnea. Consider PFTs, CXR, and ABG if undiagnosed symptoms are worrisome enough to change management or delay surgery.

ASTHMA

See the Allergy and Immunology chapter.

CHRONIC OBSTRUCTIVE LUNG DISEASE

Progressive chronic airflow limitation that is not fully reversible, resulting from chronic bronchitis and emphysema. Represents the fourth leading cause of death in the United States. Risk factors include cigarette smoking, a positive family history, α_1-antitrypsin deficiency, and occupational or environmental exposure to smoke/dust/chemicals. Chronic bronchitis and emphysema can be distinguished as follows, although most patients have overlap:

QUESTION

A 75-year-old man has worsening dyspnea on exertion and wheezing over the past two years. He has a heavy smoking history. PFTs yield the following results: FEV_1 = 60% predicted; FEV_1/FVC = 55%; TLC by plethysmography = 55% predicted; D_{LCO} = 50% predicted. What is your interpretation?

- **Chronic bronchitis:** Chronic productive cough for 3 months over 2 consecutive years.
- **Emphysema:** Abnormal enlargement of the air spaces distal to the terminal bronchioles with wall destruction.

Symptoms/Exam

- **Acute exacerbation** is suggested by three features: **worsening dyspnea, ↑ cough, and a change in sputum volume or purulence.**
- Typically presents with chronic cough in the fourth or fifth decade of life. Dyspnea usually occurs only with moderate exercise. Chest wall hyperinflation, prolonged expiration, wheezing, and distant breath and heart sounds are also seen. Clubbing is **not** seen in COPD.
- Use of respiratory accessory muscles, cyanosis (**"blue bloater" suggests chronic bronchitis**), and pursed-lip breathing (**"pink puffer" suggests emphysema**) may be seen. Neck vein distention, a tender liver, and lower extremity edema could suggest cor pulmonale.

KEY FACT

The cardinal symptoms of COPD exacerbation are ↑ dyspnea, ↑ cough, and change in ↑ sputum volume or purulence.

Differential

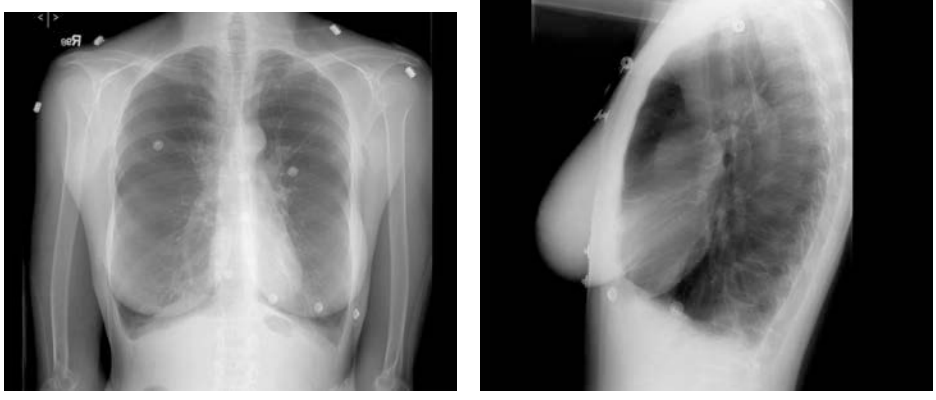
Acute bronchitis, asthma, bronchiectasis, cystic fibrosis (CF), and CHF.

Diagnosis

- Pulmonary function tests (PFTs), particularly FEV_1 (which indicates severity), are important for diagnostic confirmation and for predicting disease progression. Diagnosis is confirmed by post-bronchodilator PFTs showing an **FEV_1/FVC of <0.7** and an **FEV_1 of <80%** or lower limit of normal. **Diffusing capacity is usually ↓.**
- CXR is not required for diagnosis but may show hyperinflation with ↓ lung markings, ↑ retro-sternal airspace, and flattened diaphragms (Figure 4.4).
- Obtain an O_2 saturation and check the ABG for evidence of hypoxemia, hypercarbia, or respiratory acidosis.
- Obtain an **α_1-antitrypsin level with early-onset emphysema (fifth decade of life or earlier)** or in the setting of a suggestive family history. Associated with **basilar panlobular emphysema.**

KEY FACT

In acute exacerbations of COPD, inhaled corticosteroids are not beneficial but teaching proper use of them prior to discharge from the hospital is important. There is no advantage to IV over oral corticosteroids as long as the patient's GI absorption is not compromised.



A **B**

FIGURE 4.4. **Chronic obstructive pulmonary disease (COPD).** Posteroanterior (**A**) and lateral (**B**) CXRs show the hallmarks of COPD: hyperinflation, hyperlucency of the lung fields, and diaphragmatic flattening in a 58-year-old woman with advanced disease. (Reproduced with permission from USMLE-Rx.com.)

A ANSWER

Mixed obstructive and restrictive ventilatory pattern.

Management

- Treatment of **acute COPD** differs from that of acute asthma (Table 4.4).
- **Mild exacerbations:** Give **short-acting β_2-adrenergic** (albuterol) and **anticholinergic** (ipratropium) inhalers or nebulizers. Use as needed in all patients of all levels. These improve dyspnea and pulmonary function.
- **Moderate exacerbations:** Treat as described above. May require hospitalization. Also consider the following:
  - O_2 therapy if hypoxic.
  - Systemic oral or IV corticosteroids help ↓ the length of exacerbations and improve FEV_1.
  - Antibiotics are indicated in the setting of worsening dyspnea, cough, or sputum production.
- **Therapies for stable COPD (Table 4.5):**
  - **Smoking cessation.**
  - **Immunizations** for influenza and pneumococcus.
  - **Supplemental oxygen therapy** if indicated (see Key Fact) is the only treatment besides smoking cessation with a proven mortality benefit.
  - **β_2-adrenergic and anticholinergic agents** improve pulmonary function and ↓ dyspnea. **First-line maintenance therapy should** include **long-acting β_2-agonists** (LABA; salmeterol, formoterol) **and/or long-acting muscarinic antagonists** (LAMA; tiotropium), if short-acting agents do not control symptoms. LABAs ↓ exacerbations and hospitalizations.
  - Inhaled corticosteroids can be added to LABA for maintenance therapy in more severe COPD (FEV_1 <50%, Global Initiative for COPD [GOLD] criteria 3-4). The combination of inhaled corticosteroids and LABA is more effective in ↓ the frequency of exacerbations but may ↑ the risk of pneumonia and other adverse effects. Their long-term safety is unknown.
  - **Pulmonary rehabilitation:** Associated with improved exercise tolerance and ↓ pulmonary symptoms.
  - Azithromycin (macrolide antibiotic) or roflumilast (an oral phosophodiesterase-4 inhibitor) have been shown in patients with a history of frequent exacerbations to help with chronic control (not in acute exacerbations).
  - **Lung volume reduction surgery: ↓ hyperinflation to improve lung mechanics.** Best for patients with severe COPD who (1) do not respond to pulmonary rehabilitation and other treatments, (2) have severe emphysema in the upper lobes, and (3) are at low risk for surgery.
  - Single- or double-lung transplantation may be indicated for some patients with a low FEV_1, hypercarbia, and cor pulmonale (right heart dilation and failure due to pulmonary hypertension).

TABLE 4.4. Treatment of Acute Exacerbations of Asthma and COPD

TREATMENT	ASTHMA	COPD
Peak expiratory flow useful	Yes	No
Systemic corticosteroids	Yes	Yes
Antibiotics	No	Yes
O_2	Yes	Yes
Combination bronchodilator therapy[a]	Yes	Yes
Noninvasive mechanical ventilation	Unclear	Yes

[a]β_2-agonist and ipratropium bromide.

MNEMONIC

For the treatment of acute COPD exacerbations:

ABC-ON

Antibiotics
Bronchodilators
Corticosteroids
-
Oxygen
Noninvasive ventilation

KEY FACT

For the majority of patients, 40 mg of oral prednisone daily for 5 days is equivalent to a traditional 2-week course.

KEY FACT

General indications for long-term continuous O_2 therapy (24 hours/day):

- Pao_2 ≤55 mm Hg or O_2 saturation ≤88% at rest.

or

- Pao_2 ≤59 mm Hg or O_2 saturation ≤89% with cor pulmonale or erythrocytosis (hematocrit >55%).

KEY FACT

O_2 therapy and smoking cessation are the only interventions that ↑ life expectancy in hypoxemic COPD patients. No medication has been shown to prevent the decline of FEV_1.

QUESTION

A 45-year-old woman has had worsening asthma for 2 years despite treatment with albuterol and salmeterol/budesonide. Her cough is occasionally productive of bloody sputum. She has no fevers, chills, or night sweats. A recent CXR shows peribronchial thickening. What is the most likely etiology of her hemoptysis?

TABLE 4.5. Classification, Severity, and Treatment of Stable COPD[a]

STAGE	SPIROMETRY	TREATMENT FOR STABLE COPD
All stages	$FEV_1/FVC < 0.7$	Smoking cessation; annual influenza and pneumonia vaccinations
1 (mild)	$FEV_1 \geq 80\%$ of predicted	Short-acting bronchodilator (albuterol, ipratropium) for relief
2 (moderate)	FEV_1 50%-79% of predicted	Add long-acting β_2-agonists and/or long-acting anticholinergic bronchodilators (ie, LABA or LABA + LAMA)
3 (severe)	FEV_1 30%-49% of predicted	Combination of long-acting β_2-agonists with inhaled corticosteroid
4 (very severe)	$FEV_1 < 30\%$ of predicted or $FEV_1 < 50\%$ of predicted plus chronic respiratory failure	Also add long-term O_2 PRN; consider surgery

[a]Classification is by the GOLD criteria.

BRONCHIECTASIS

Irreversible dilatation and destruction of bronchi due to cycles of infection and inflammation, with mucopurulent sputum production. Characterized by dilated airways and focal constrictive areas.

Symptoms/Exam

- Chronic bronchiectasis presents with **chronic productive cough** with purulent, often foul-smelling sputum. Sputum volume is correlated with decline in respiratory function and quality of life. Dyspnea, wheezing, pleuritic chest pain, and hemoptysis are all possible. Patients may have a history of recurrent respiratory tract infections.
- Acute exacerbations of bronchiectasis lead to a change in sputum production, dyspnea, cough, wheezing, low-grade fever, fatigue, and decline in exercise tolerance. Changes in chest exam, PFTs, and imaging may occur.

Differential

Bronchiectasis is most commonly idiopathic, as most factors are conditions that are associated, rather than definitive. Associations include the following:

- Infections (recurrent, postinfectious), including *Pseudomonas*, *Haemophilus*, TB or other mycobacterial disease, pertussis, measles, influenza.
- Immunodeficiency, eg, common variable immune deficiency, immunoglobulin A (IgA) deficiency, HIV.
- Congenital conditions, eg, CF, 1° ciliary dyskinesia/Kartagener syndrome (autosomal recessive genetic disorder causing defects in the action of cilia in the respiratory tract).
- Autoimmune disease, eg, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjögren syndrome, relapsing polychondritis, inflammatory bowel disease (IBD).
- Hypersensitivity (ABPA).

A ANSWER

Bronchiectasis due to ABPA.

Diagnosis

- **CBC,** including differential (may see neutrophilia; eosinophilia is seen in ABPA). **CXR** shows **"tram lines" (airway dilation).** Screen for common variable immune deficiency, IgA deficiency, and ABPA (↑ serum total IgE). Check HIV.
- **HRCT** is the best diagnostic tool for mapping **airway abnormalities** (Table 4.6). Findings include airway dilation, lack of tapering of bronchi with bronchial wall dilation, airways filled with mucous.
- Other tests to consider:
  - **Spirometry** quantifies the degree of airway obstruction pre- and post-bronchodilator (obstructive pattern due to mucous filling the airways, ↓ FEV_1/FVC ratio, ↓ FEV_1, ↓ or normal FVC).
  - **Sputum sample** for bacterial, fungal, and mycobacterial cultures.
  - **Sweat chloride test for CF.**
  - **ANA, RF,** and **anti-Ro/La** if suspicious for connective tissue disease.

TABLE 4.6. Distribution of Airway Abnormalities Aids in Diagnosis

DISTRIBUTION	UNDERLYING CONDITION
Central (perihilar)	ABPA
Upper lobe	CF
Lower lobe	Idiopathic bronchiectasis

Management

- Patients with acute exacerbations have high bacterial load and inflammation. Identify and treat acute exacerbations with antibiotics for 10 to 14 days (eg, if no sputum culture data is available, a fluoroquinolone is reasonable). Also consider antibiotics based on past sputum cultures and response to selected antibiotics.
- Treatment may also include: **bronchodilators, airway clearance** (chest physiotherapy, flutter devices, percussive vests, frequencers), **mucolytic agents—hypertonic (7%) saline and DNase**—helpful in stable CF but potentially harmful in patients with non-CF bronchiectasis, and outpatient pulmonary rehabilitation. For recurrent exacerbations, consider preventive therapy with a macrolide antibiotic (eg, azithromycin). Surgical resection for massive hemoptysis or unresolving infection.

CYSTIC FIBROSIS

Caused by mutations in the CF transmembrane conductance regulator (CFTR), leading to chloride channel dysfunction. Consider especially in young adults with a history of bronchiectasis, sinus disease, infertility, or recurrent pancreatitis.

Symptoms/Exam

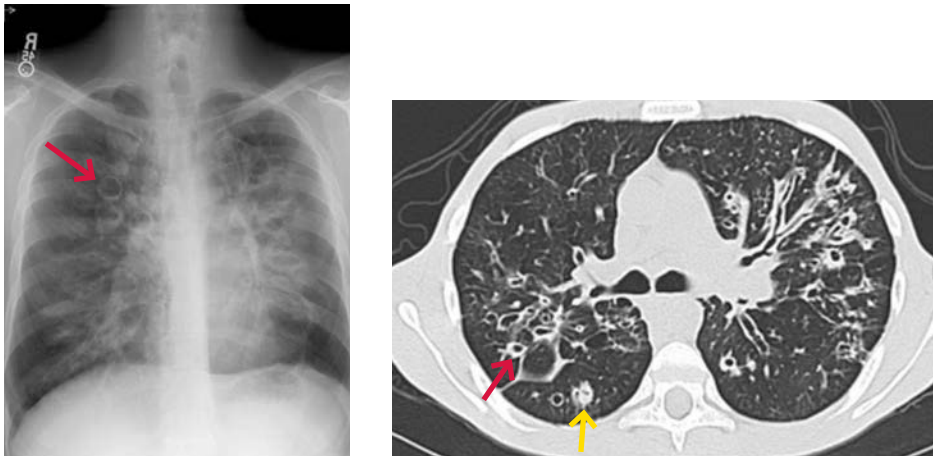
- Look for a history of failure to thrive as a child, persistent respiratory infections (*Pseudomonas*), nasal polyposis, sinusitis, intestinal obstruction, malabsorption (steatorrhea, diarrhea), recurrent pancreatitis, hepatobiliary disease, and male infertility.
- Bronchiectasis and *Staphylococcus aureus* and *Pseudomonas aeruginosa* (mucoid variant) pneumonias are common. Exam reveals an ↑ AP chest diameter, upper lung field crackles, nasal polyps, and clubbing.

Differential

Immunodeficiency, asthma, ABPA, 1° ciliary dyskinesia/Kartagener, α-1 antitrypsin deficiency, postinfectious bronchiectasis.

Diagnosis

- A **sweat chloride test** shows an elevated sweat chloride concentration. Considered the screening test of choice, but **a normal test does not rule out CF.** If the **sweat chloride test is inconclusive** but there is **high clinical suspicion** for CF, do **genotyping** for CFTR mutations and a **nasal potential difference test** (measures ion transport in the nose).
- On CXR, early CF may present as hyperinflation. More advanced disease can manifest with peribronchial cuffing, interstitial markings, and bronchiectasis (Figure 4.5).



A B

FIGURE 4.5. **Cystic fibrosis.** (**A**) Frontal CXR showing central cystic bronchiectasis (arrow) in a patient with CF. (**B**) Transaxial CT image showing cystic bronchiectasis (red arrow), with some bronchi containing impacted mucus (yellow arrow). (Reproduced with permission from USMLE-Rx.com.)

Management

- **Acute pulmonary exacerbations:** Chest physical therapy to clear lower airway secretions. Also give bronchodilators and antibiotics based on culture and sensitivities. Inhaled recombinant DNase, given to cleave extracellular DNA in viscous sputum, will improve FEV_1 and ↓ exacerbations.
- **Chronic stable CF:**
  - **Inhaled antibiotics (tobramycin/aztreonam), nebulized DNase, hypertonic (7%) saline.**
  - **Azithromycin three times per week.**
  - **Airway clearance:** Aerobic exercise, flutter devices, external percussive vests or frequencers.
  - **Pancreatic enzymes and vitamins A, D, E, and K.**
  - **Nutritional counseling.**
  - Pneumococcal and influenza vaccines.
  - **Also consider lung transplantation** for severe progressive pulmonary disease. Genetic counseling and screening of family members. New targeted therapies for CF such as ivacaftor/lumacaftor improve outcomes in populations with certain mutations.

SLEEP-DISORDERED BREATHING

An apneic period is ≥10 seconds in length. Patients with **obstructive sleep apnea (OSA) have episodic closure of the upper airway** during sleep with continued respiratory efforts. Patients with **central sleep apnea (CSA) have cessation of both airflow and respiratory efforts.** CSA is often associated with CNS disorders, respiratory muscle weakness, or cardiovascular disease (especially CHF), but it may also be idiopathic. See Table 4.7.

Obesity hypoventilation syndrome (OHS) is a condition that overlaps with OSA, and thus, often patients can have both OSA and OHS concomitantly. OHS is hypoventilation that occurs when **awake;** these patients have obesity and laboratory values consistent with hypoventilation when awake (ABG with P_{CO_2} >45 mm Hg, elevated H_{CO_3} suggesting compensatory metabolic alkalosis for chronic respiratory acidosis).

TABLE 4.7. Obstructive vs Central Sleep Apnea

	OBSTRUCTIVE SLEEP APNEA	CENTRAL SLEEP APNEA
Definition	Apnea due to transient obstruction of the upper airway, but **ventilatory effort is present**	Apnea occurs, but there is **no compensatory ventilatory effort during apneic episode.** Tachypnea can occur after the apneic episode.
Risk factors	Obesity (large neck circumference), large tonsils, upper airway soft tissue abnormalities, hypothyroidism, craniofacial abnormalities	**CHF with reduced EF** is most common. **CNS disorders,** respiratory muscle weakness, opioids/sedatives, and renal/liver failure also ↑ risk.
Treatment	Weight loss (10%-20% of weight), nasal CPAP, avoidance of alcohol and sedatives, oral devices or upper airway surgery (uvulopalatopharyngoplasty) **O_2 supplementation is not recommended as initial treatment**	Treat underlying disease; O_2 if hypoxemic; consider BiPAP or CPAP; surgery has no role. Remove culprit medications (eg, sedatives).

Symptoms/Exam

Patients may present with daytime hypersomnolence, morning headache, impaired cognition (due to small arousals during sleep), snoring, gasping or choking at night, and witnessed apneic episodes while sleeping. Patients with severe disease may have significant hypoxemia during sleep, pulmonary hypertension, systemic hypertension, heart failure, arrhythmias, and 2° erythrocytosis.

Diagnosis

Polysomnography is needed to establish the diagnosis. The sum of apneas and hypopneas per hour of sleep, apnea-hypopnea index (AHI), is used to determine severity. AHI >5 per hour during a sleep study is abnormal:

- None/minimal AHI <5 per hour.
- Mild AHI ≥5, but <15 per hour.
- Moderate AHI ≥15, but <30 per hour.
- Severe AHI ≥30 per hour.

KEY FACT

In CSA, apneic episodes are not accompanied by respiratory effort; patients may breathe faster after apneic episodes (periodic breathing = Cheyne-Stokes respiration). Polysomnography can distinguish between CSA and OSA.

Management

CPAP (continuous positive airway pressure) for OSA, and occasionally CSA. BiPAP (bilevel positive airway pressure) for OHS (hypoventilation), and occasionally OSA and CSA if CPAP fails.

Allergic Bronchopulmonary Aspergillosis

APBA is an immunologic reaction to antigens of *Aspergillus* present in the bronchial tree.

Symptoms/Exam

Asthma (may be cough variant or exercise induced); expectoration of golden brown mucous plugs; fever with acute flare. Wheezing, rales, or bronchial breath sounds; digital clubbing and cyanosis (late-stage disease).

Diagnosis

- **Essential criteria** for ABPA-S (seropositive ABPA) are as follows:
  - The presence of **asthma.**
  - ⊕ immediate **skin tests to *Aspergillus*.**
  - ↑ total serum **IgE (>1000 ng/mL).**
  - ↑ serum ***Aspergillus*-specific IgE and/or IgG.**

KEY FACT

ABPA should be considered in any patient with poorly controlled asthma or cystic fibrosis *and* elevated IgE, particularly in the presence of CXR infiltrates.

- Other features include:
  - The above plus central bronchiectasis = ABPA-CB (ABPA with central bronchiectasis).
  - Precipitating antibodies to *Aspergillus*.
  - Peripheral blood **eosinophilia** (>1000/mm^3).
  - CXR showing infiltrates—transient or fixed.
  - A sputum culture that is ⊕ for *Aspergillus* or that contains *Aspergillus* hyphae.

Management

- **Prednisone;** itraconazole may be used as an adjunctive medication.
- Chronic inhaled corticosteroids to control asthma.

Complications

Corticosteroid-dependent asthma, irreversible loss of pulmonary function, chronic bronchitis, pulmonary fibrosis, death due to respiratory failure or cor pulmonale.

Pulmonary Vascular Disease

PULMONARY EMBOLISM

See the Hospital Medicine chapter.

PULMONARY HYPERTENSION

KEY FACT

Group 1 PAH includes idiopathic and hereditary PAH, and PAH due to diseases that localize to small pulmonary arterioles. Unlike groups 2 to 5, where treatment is focused on the underlying condition, the main focus for group 1 is to treat the PAH itself.

Pulmonary hypertension is defined as a mean pulmonary artery pressure of >25 mm Hg at rest (Table 4.8).

Symptoms/Exam

Presents with progressive dyspnea on exertion. In more advanced stages, patients may have exertional dizziness, atypical chest pain, or syncope. Raynaud phenomenon may suggest an underlying collagen vascular disease. Elevated pulmonary arterial pressure and right ventricular strain on exam are associated with JVD, right ventricular heave, a right-sided S4, **a fixed/split S2, a loud P2,** and tricuspid regurgitation. Hepatomegaly, a pulsatile liver, and ascites from progressive right ventricular overload are seen in advanced disease.

TABLE 4.8. World Health Organization Classification of Pulmonary Hypertension

GROUP 1: PULMONARY ARTERIAL HYPERTENSION (PAH)	GROUP 2: PULMONARY VENOUS HYPERTENSION	GROUP 3: LUNG DISEASE OR CHRONIC HYPOXIA	GROUP 4: THROMBOTIC OR EMBOLIC DISEASE	GROUP 5: DIRECTLY AFFECTING VESSELS
Idiopathic	Left heart disease (eg, mitral valve, atrial myxoma, systolic or diastolic dysfunction)	COPD	Chronic thromboembolic disease	Sarcoidosis, vasculitis, pulmonary Langerhans cell histiocytosis
Collagen vascular disease (eg, scleroderma)		ILD		Gaucher disease, glycogen storage disease
HIV		Sleep apnea		Sickle cell disease, myeloproliferative disorders
Drugs/toxins (amphetamines, chemotherapy, cocaine)				
Portal hypertension				
Portopulmonary hypertension				