SECTION 8

PULMONARY MEDICINE

CHAPTER 66

EVALUATION OF CHRONIC COUGH

1. **EPIDEMIOLOGY**
   - Nearly all adult cases of chronic cough in nonsmokers who are not taking an ACEI can be attributed to the "Pathologic Triad of Chronic Cough" (asthma, GERD, upper airway cough syndrome [UACS; previously known as postnasal drip syndrome]).
   - ACEI cough is idiosyncratic, occurrence is higher in female than males
2. **PATHOPHYSIOLOGY**
   - Afferent (sensory) limb: chemical or mechanical stimulation of receptors on pharynx, larynx, airways, external auditory meatus, esophagus stimulates vagus and superior laryngeal nerves
   - Receptors upregulated in chronic cough
   - CNS: cough center in nucleus tractus solitarius
   - Efferent (motor) limb: expiratory and bronchial muscle contraction against adducted vocal cords increases positive intrathoracic pressure
3. **DEFINITION**
   - Subacute cough lasts between 3 and 8 weeks
   - Chronic cough duration is at least 8 weeks
4. **DIFFERENTIAL DIAGNOSIS**
   - Respiratory tract infection (viral or bacterial)
   - Asthma
   - Upper airway cough syndrome (postnasal drip syndrome)
   - CHF
   - Pertussis
   - COPD
   - GERD
   - Bronchiectasis
   - Eosinophilic bronchitis
   - Pulmonary tuberculosis
   - Interstitial lung disease
   - Bronchogenic carcinoma
   - Medication-induced cough
5. **EVALUATION AND TREATMENT OF THE COMMON CAUSES OF CHRONIC COUGH**
   - Upper airway cough syndrome: rhinitis, sinusitis, or postnasal drip syndrome
   - Presentation: symptoms of rhinitis, frequent throat clearing, itchy throat or palate, although some are asymptomatic; exam may reveal edematous nasal turbinates and a glistening "cobblestone" appearance of the oropharynx
     - Empiric trial of an oral antihistamine
     - Nasal corticosteroids × 3–4 weeks
     - Ipratropium nasal spray can be added for refractory cough
     - Consider empiric antibiotics if coronal CT scan of sinuses suggests sinusitis

- Cough-variant asthma: atopic history or family history of eczema, allergies, or asthma; history of cough triggers (e.g., exercise, cold exposure, environmental allergens, or animal dander); only manifestation of asthma in up to 55% of pts
  - Test with routine spirometry, and, if normal, a methacholine challenge test; if both are normal, they effectively rule out cough-variant asthma
  - Consider an empiric trial of inhaled steroids and albuterol for 6–8 weeks
  - Leukotriene receptor antagonists can be added for refractory symptoms
- Gastroesophageal reflux (GERD): history of heartburn, dyspepsia, or sour taste in the mouth exacerbated by meals and supine position; also, may have frequent throat clearing, morning hoarseness, and a globus sensation
- Up to 75% of patients with GERD-induced cough have no reflux symptoms
  - Nonpharmacologic interventions: diet high in protein; avoid bedtime snacks, fatty foods, chocolate, excess alcohol, caffeine, mints, and citrus fruits; smoking cessation and elevate head of the bed 6 inches
  - Empiric trial of proton pump inhibitor or moderate–high dose H_2-blockers for 4–6 months; extend therapy for 3 months past resolution of symptoms
  - Metoclopramide 10 mg PO after meals and at bedtime can be added for refractory cough
  - Insufficient data to support Nissen fundoplication for refractory cases
  - Esophageal pH probe testing usually not necessary but solidifies diagnosis

6. EVALUATION OF LESS COMMON CAUSES OF CHRONIC COUGH

- Initial studies and interventions to consider
  - Chest X-ray, place a PPD test, and stop ACEI therapy
  - Investigate for toxic occupational exposures and counsel to stop smoking
  - Pulmonary function tests to assess for chronic bronchitis or cough asthma
  - Coronal CT scan of paranasal sinuses to rule out chronic sinusitis
  - Induced sputum for eosinophils greater than 3% and normal methacholine challenge test indicate eosinophilic bronchitis; treat with inhaled steroids × 14 days
- Second-tier diagnostic studies
  - High-resolution CT scan of chest to evaluate for interstitial lung disease or bronchiectasis if chest X-ray abnormal and high clinical suspicion
  - Bronchoscopy indicated if high suspicion for lung cancer or foreign body
- See **Figure 66.1**

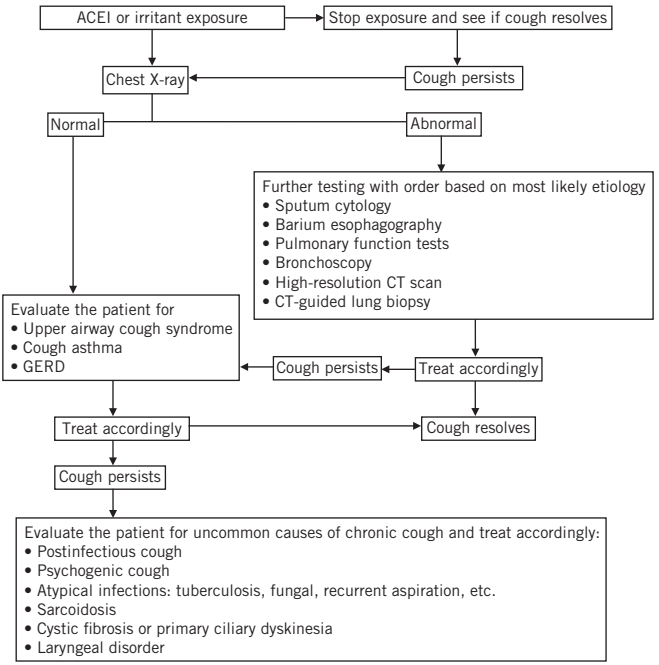


FIGURE 66.1. Evaluation of Chronic Cough in Immunocompetent Patients

Source: Adapted from *Chest,* 1998; 114 (Suppl 2 Managing): 166S.

REFERENCES

Am Fam Physician, 2011;84(8):887–92; *Chest,* 1998;114(2 Suppl Managing):133S–81S; *Eur Respir J,* 2004; 24(3):481–92; *Otolaryngol Head Neck Surg,* 2006;134(4):693–700; *Ann Allergy Asthma Immunol,* 2007;98(4):305–13; Chest, 2006;129:59–94; *Thorax,* 2004;59(4):342–6; *Am Fam Physician,* 2004;69(9):2159–66; *Am J Respir Crit Care Med,* 2011;183(6):708–15.

CHAPTER 67

EVALUATION OF DYSPNEA

1. PATHOPHYSIOLOGY

- Afferent (sensory) limb: feedback from peripheral receptors to sensory cortex
  - Decreased PaO_2, increased $PaCO_2$, decreased pH all stimulate chemoreceptors in carotid bodies and medulla
  - Bronchospasm stimulates mechanoreceptors in lung
  - Interstitial fluid, increased PA pressure triggers pressure receptors in pulmonary vasculature
  - Exercise stimulates metaboreceptors in skeletal muscle
- Efferent (motor) limb: feed-forward from motor cortex to ventilatory muscles
- CNS: respiratory center in medulla
- Mismatch between feedback and feed-forward signals increase dyspnea

2. ETIOLOGIES

- Common etiologies
  - Asthma: intermittent breathlessness, certain triggers, allergic rhinitis, prolonged expiration, wheezing
  - COPD: history of smoking, barrel chest, prolonged expiration, wheezing
  - CHF: history of HTN, CAD, or DM; orthopnea, paroxysmal nocturnal dyspnea, pedal edema, JVD, bibasilar rales, wheezing, S3 gallop
  - Anxiety: history of anxiety, PTSD, OCD, panic disorder; sighing breathing
  - GERD: postprandial dyspnea
- Hemoptysis suggests cancer, pneumonia, bronchiectasis, arteriovenous malformation
- Recurrent pneumonia suggests lung cancer, bronchiectasis, aspiration
- Drug exposure: β blockers can exacerbate reactive airway disease; amiodarone and nitrofurantoin can cause pneumonitis; methotrexate can cause lung fibrosis
- Immunosuppression: consider opportunistic infections including PCP, tuberculosis, legionella, cytomegalovirus, aspergillus, and coccidiomycosis

3. DIFFERENTIAL DIAGNOSIS

- Panic attack
- Pneumonia
- COPD
- Interstitial lung disease
- Asthma
- Pneumothorax
- Pulmonary embolus
- CHF
- Acute myocardial infarction
- Arrhythmia
- Metabolic acidosis
- Cyanide toxicity
- Methemoglobinemia
- Carbon monoxide poisoning
- Conversion disorders
- Malingering

4. WORKUP

- Initial testing
  - CBC, chemistry panel, chest radiograph, ECG, spirometry, pulse oximetry
  - Treat common causes (asthma, COPD, CHF, pleural effusion, anemia) accordingly
- Secondary testing
  - Echocardiogram, BNP, pulmonary function testing, arterial blood gas, Holter monitor, ventilation-perfusion scan, high-resolution CT scan, myocardial perfusion cardiac study
  - Treat cause accordingly (pericardial disease, CHF, valvular heart disease, CAD, arrhythmia, restrictive lung disease, interstitial lung disease, chronic PE)
- Tertiary testing
  - Cardiac catheterization, cardiopulmonary exercise testing, bronchoscopy, esophageal pH testing, open lung biopsy
  - Treat cause accordingly (GERD, CAD, deconditioning, pulmonary hypertension, psychogenic dyspnea)

5. TREATMENT

- Treat accordingly based on etiology of dyspnea

REFERENCE

Am Fam Physician, 2005;71(8):1529–37.

CHAPTER 68

EVALUATION OF HEMOPTYSIS

1. EPIDEMIOLOGY

- United States: bronchitis 50%, primary lung cancer 23%, bronchogenic carcinoma 5–44% (20% develop hemoptysis at some point, but only 7% at initial diagnosis), idiopathic 7–34%
- Worldwide: Tb is the most common cause with prevalence of 2 billion people
- Massive hemoptysis, whether in developed or developing countries, is attributed to Tb, mycetoma, or lung abscess

2. PATHOPHYSIOLOGY

- Anatomic approach
- Alveolar (diffuse alveolar hemorrhage): capillaries overloaded by pulmonary circulation (low pressure)
- Inflammatory: small-vessel vasculitis (granulomatosis with polyangiitis [formerly known as Wegener's granulomatosis], microscopic polyangiitis, SLE, Goodpasture's syndrome, post-BMT)
- Noninflammatory: inhalational injury (burns, cocaine, toxins)
- Small and medium airways: bronchial vessels from systemic circulation (high pressure)
- Infectious: bronchitis, bronchiectasis, pneumonia (especially cavitary), tuberculosis, lung abscess, paragonimiasis
- Noninfectious: inhalation, trauma, foreign body, lung cancer (especially in proximal airways, which leads to erosion into hilar vessels), metastases
- Pulmonary vessels: increased LA pressure from CHF, MR with focal regurgitant jet, AVMs, PE
- Pulmonary hypertension

3. CLINICAL PRESENTATION

- Hemoptysis: spitting of blood from lungs or bronchi
- Historical clues
  - Fever, productive cough suggests upper respiratory infection, pneumonia
  - Dyspnea on exertion with orthopnea suggests CHF
  - Pleuritic chest pain suggests pulmonary embolus
  - Anticoagulant use suggests medication effect
  - History of breast, colon, or renal cancer suggests metastatic disease
  - History of chronic lung disease suggests bronchiectasis or lung abscess
  - HIV or immunosuppression suggests neoplasia, TB, or Kaposi's sarcoma
  - Tobacco use suggests bronchitis, lung cancer, or pneumonia
  - Weight loss suggests emphysema, lung cancer, tuberculosis, bronchiectasis, lung abscess, or HIV

- See **Table 68.1**

TABLE 68.1. Causes of Hemoptysis

Category	Causes
Infectious	Bronchitis, pneumonia (viral, bacterial, fungal), bronchiectasis, aspergillosis, tuberculosis
Malignancy	Primary lung cancer or lung metastases
Cardiovascular	PE, pulmonary artery rupture, CHF, mitral stenosis
Vasculitis	Granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis) or Goodpasture's syndrome
Miscellaneous	Chest trauma, foreign body, anticoagulation, epistaxis, bronchovascular fistula, pulmonary arteriovenous malformation

Source: Information from *Arch Intern Med*, 1991; 151(12): 2449–51 and *Chest*, 1997; 112(2): 440–4.

4. EVALUATION OF HEMOPTYSIS

- Labs: CBC, chemistry panel, PT, PTT, urinalysis, and oximetry
- Chest X-ray and high-resolution CT scan of the chest (tracheal or proximal bronchial lesions missed by CXR)
- Tests to consider: sputum culture, PPD, sputum for AFB, coccidioidomycosis titer, and antineutrophil cytoplasmic and antiglomerular basement membrane antibodies
- Fiberoptic bronchoscopy indicated for unexplained hemoptysis

5. MANAGEMENT OF MASSIVE HEMOPTYSIS

- See **Figure 68.1**
- Intubation (preferably selective intubation of normal lung) and mechanical ventilation with the affected lung kept dependent in the lateral decubitus position
- Transfuse platelets or fresh frozen plasma for thrombocytopenia or a coagulopathy
- Pulmonary angiogram and selective embolization of the bronchial artery
- Lobectomy or pneumonectomy in refractory cases

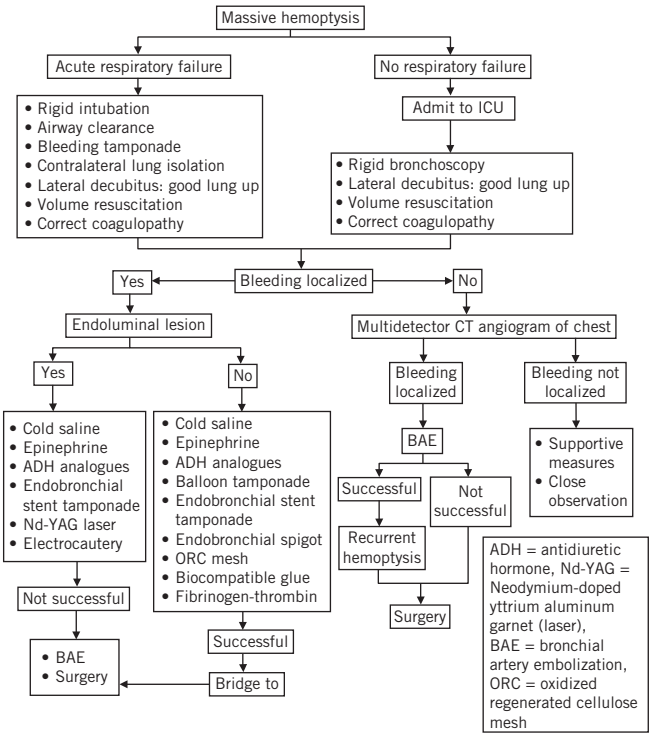


FIGURE 68.1. Management of Massive Hemoptysis

Source: Adapted from Respiration, 2010; 80(1): 38–58.

6. COMPLICATIONS

- Exsanguination
- Hemorrhagic shock
- Asphyxiation
- Respiratory failure

REFERENCES

Respiration, 2010;80(1):38–58; *Am Fam Physician*, 2005;72(7):1253–60; *Chest*, 2008;133(1):212–9; *Curr Opin Pulm Med*, 2008;14(3):195–202; *Clin Chest Med*, 1994;15(1):147–67.

CHAPTER 69

EVALUATION OF PLEURAL EFFUSIONS

1. EPIDEMIOLOGY

- United States: 1.5 million cases annually; mostly due to CHF, bacterial PNA, malignancy, and PE
- Worldwide: 320/100,000

2. PATHOPHYSIOLOGY

- Increased fluid entering pleural space (from interstitium, capillaries in parietal pleura, or holes in diaphragm) or decreased drainage of pleural space by lymphatics in parietal pleura leads to effusion
- Transudate: due to systemic process
  - Left-sided CHF: fluid accumulates in lung interstitium faster than the ability of lymphatics to drain pleural space, leading to bilateral effusion
  - Hepatic hydrothorax: cirrhotic ascites enter pleural space via holes in diaphragm, which leads to right-sided (90%) or bilateral (10%) effusion
- Exudate: due to local process
  - Bacterial pneumonia: parapneumonic effusion or empyema (frankly purulent)
  - Cancer: most commonly lung, breast, lymphoma; also mesothelioma
  - Pulmonary embolism
  - Viral infection
  - Tuberculosis: hypersensitivity reaction to TB antigen
  - Chylothorax: damaged thoracic duct from trauma or mediastinal tumors
  - Hemothorax: trauma or malignancy

3. CLINICAL PRESENTATION

- Dyspnea, cough, and pleuritic chest pain are common
- Historical clues
  - Trauma history suggests hemothorax
  - Cancer history suggests malignant effusion
  - Recent abdominal surgical procedures suggest postoperative effusion, subphrenic abscess, pulmonary embolism
  - Alcohol abuse or pancreatic disease suggests pancreatic effusion
  - Chronic hemodialysis suggests heart failure or uremic pleuritis
  - Cirrhosis suggests hepatic hydrothorax, spontaneous bacterial empyema
  - Cardiac surgery suggests Dressler's syndrome
  - Esophageal procedure suggests esophageal perforation
  - Asbestos exposure suggests mesothelioma, benign asbestos effusion
  - Childbirth suggests postpartum pleural effusion
  - HIV infection suggests pneumonia, TB, lymphoma, Kaposi's sarcoma
  - Rheumatoid arthritis suggests rheumatoid pleuritis
  - Lupus suggests lupus pleuritis, pneumonia, pulmonary embolism
- Signs
  - Ascites: hepatic hydrothorax, ovarian cancer, Meigs' syndrome
  - Dyspnea on exertion, orthopnea, peripheral edema: CHF
  - Pericardial friction rub, pericarditis
  - Unilateral leg swelling: PE
  - Yellowish nails, lymphedema: yellow nail syndrome
  - Fever: pneumonia, empyema, tuberculosis

- See **Tables 69.1** through **69.3**

TABLE 69.1. Classification of Pleural Effusions

Test	Transudate	Exudate*
PF NT-proBNP†	1300 pg/mL or greater	Less than 1300 pg/mL
Serum-PF albumin gradient†	Greater than 1.2 g/dL	Up to 1.2 g/dL
Serum-PF protein gradient†	3.1 mg/dL or greater	Less than 3.1 mg/dL
PF protein/serum protein	Up to 0.5	Greater than 0.5
PF LDH (international units)	Up to 200	Greater than ⅔ upper limit of labs normal range (or greater than 200)
PF LDH/serum LDH	Up to 0.6	Greater than 0.6

PF = pleural fluid, NT = N-terminal (as in NT-pro-BNP), BNP = B-type natriuretic peptide, LDH = lactate dehydrogenase
* Light's criteria: only one test needs to be abnormal to classify effusion as an exudate; 80–85% accurate for exudates:
  - PF glucose less than 60 suggests cancer, tuberculosis, empyema, or effusion from lupus or RA
  - Bloody effusion suggests CA, tuberculosis, PE, or trauma
  - PF lymphocytosis greater than 50%: 90–96% from CA or tuberculosis
  - PF pH less than 7.2: empyema, malignancy, RA, or SLE
† Useful to diagnose transudative effusions after patient has received diuretics

Source: Adapted from ***NEJM***, 2002; 346(25): 1971–7, *Curr Opin Pulm Med*, 2011; 17(4): 215–9, and *Med Clin N Amer*, 2011; 95(6): 1055–70.

TABLE 69.2. Causes of Transudative Effusions

• Constrictive pericarditis • Urinothorax	• Hepatic hydrothorax • Heart failure*	• Nephrotic syndrome • Peritoneal dialysis	• Severe hypoalbuminemia* • Superior vena cava syndrome

* Most common causes of transudative pleural effusions

Source: Adapted from ***NEJM***, 2002; 346(25): 1971–7.

TABLE 69.3. Evaluation of Exudative Effusions

Diagnosis	PF Appearance	Diagnostic PF Testing
Empyema	Purulent	PF pH less than 7.2*, increased WBC†, glc less than 40 mg/dL, positive culture
Malignant	+/– Bloody	Positive pleural fluid cytology (60% of time)
Chylothorax	Milky	Triglycerides greater than 110 mg/dL
Pancreatitis	–	High amylase
Uremia	–	Blood urea nitrogen (usually greater than 100 mg/dL)
Sarcoidosis	–	High angiotensin converting enzyme level
Lupus pleuritis	–	PF antinuclear antibody (ANA) greater than or equal to 1:160
Rheumatoid lung	Yellow-green	Characteristic cytology, glucose less than 30 mg/dL
Ovarian hyper-stimulation syn.		Fertility medication use
Meigs' syndrome	–	Ascites and ovarian fibroma present
Amebic abscess	Anchovy paste	Elevated amebic titers and liver abscess present
Pulmonary embolus	Bloody	Positive CT pulmonary angiogram or V/Q scan
Tuberculosis	Bloody	Positive AFB on pleural biopsy and less than 5% mesothelial cells in pleural fluid AFB RNA by PCR (40–80% sensitive); adenosine deaminase greater than 40 units/L (93% sensitive/90% specific)
Mesothelioma	–	PF mesothelin greater than 20 nmol/L (+LR = 7.1/–LR = 0.32)

PF = pleural fluid, glc = glucose, ANA = antinuclear antibody, CT = computed tomograpy, V/Q = ventilation/perfusion, AFB = acid fast bacili, LR = likelihood ratio

* Fluid for pleural fluid pH should be collected in a lithium heparin tube and kept on ice

† Increased WBC = pleural fluid white blood count greater than 25,000 cell/μL (collect in a purple top tube)

- Pleural fluid lymphocytosis greater than 50%: 90–96% secondary to either malignancy or tuberculosis
- Pleural fluid pH less than 7.2: empyema, malignancy, tuberculosis, ruptured esophagus, urinothorax, lupus pleuritis, or rheumatoid lung
- Bloody effusion: trauma, malignancy, pulmonary embolus, tuberculosis, or traumatic tap
- **Any significant parapneumonic effusion should be aspirated and analyzed.**

Source: Adapted from *AFP*, 2006; 73(7): 1211–20.

4. COMPLICATIONS

- Trapped lung (formation of a restrictive, fibrous pleural peel around the visceral pleura)
- Empyema
- Severe sepsis

REFERENCES

Am Fam Physician, 2006;73(7):1211–20; *N Engl J Med,* 2002;346(25):1971–7; *Curr Opin Pulm Med,* 2011;17(4):215–9; *Med Clin North Am,* 2011;95(6):1055–70.

CHAPTER 70

ASTHMA EXACERBATION

1. EPIDEMIOLOGY

- Prevalence in United States is around 8% of population (9% for kids younger than 18 yo)
- Mortality is 2/100,000/year
- Most common reason for exacerbation is inadequate medical therapy combined with noncompliance
- Predominantly in boys during childhood: male-to-female ratio of 2:1 until puberty, then it becomes 1:1; 50% of these children have symptom resolution by early adulthood; boys are more likely to have symptom resolution than girls
- Most adult-onset asthma is diagnosed over age 40 yo in women
- United States spends about 14 billion dollars per year on asthma, about 25% of which is on asthma exacerbations

2. PATHOPHYSIOLOGY

- Exposure to allergens causes inflammation driven by mast cells, dendritic cells, and eosinophils, which activate inflammatory mediators leading to simultaneous inflammation and repair in airways
- Epithelial damage
- Subepithelial fibrosis results in basement membrane thickening
- Smooth muscle hypertrophy results in airway hyperresponsiveness, which enables reversible obstruction
- Increased vascular flow leads to airway edema
- Goblet cell and submucosal gland hypertrophy $\rightarrow$ mucus hypersecretion

3. CLINICAL PRESENTATION

- Signs: use of accessory muscles, chest wall retractions, tachypnea, cyanosis, hypoxia
- Mild: dyspnea with activity
- Moderate: dyspnea that prevents usual activity
- Severe: dyspnea at rest, interferes with conversation

4. DIAGNOSIS

- Reversible airflow obstruction on spirometry confirms asthma diagnosis
  - FEV_1 less than 80% predicted or FEV_1/FVC less than 70%
  - FEV_1 increases to 12% or more and 200 mL or FVC increases to 12% or more after inhaled β_2-agonist
  - Bronchoprovocation test with inhaled methacholine can diagnose hyperbronchial responsiveness, which is suggestive of asthma
    - Consider this test if spirometry is normal and clinical history very suggestive of asthma

5. DIFFERENTIAL DIAGNOSIS

- COPD
- Churg-Strauss syndrome
- Eosinophilic pneumonia
- CHF
- Vocal cord paralysis
- Vocal cord dysfunction
- Foreign body aspiration
- Laryngotracheal masses

- Tracheomalacia
- Angioedema
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Cystic fibrosis
- Bronchiolitis obliterans
- Conversion disorders
- Munchausen syndrome
- Malingering

6. EVALUATION

- Pulmonary function testing
- Consider allergen skin testing if exogenous trigger suspected
- See **Tables 70.1** through **70.3**

TABLE 70.1. Classification of Asthma Severity*

Class	Days with Symptoms	Nights with Symptoms	PEF or FEV1††	SABA Use for Symptoms
Mild intermittent	2 or fewer/week	2 or fewer/month	80% or more	2 days or fewer/week
Mild persistent	3–6/week	3–4/month	80% or more	More than 2 days/week
Moderate persistent	Daily	More than 1/week	More than 60% up to 80%	Daily
Severe persistent	Daily	Most nights	Up to 60%	Several times/day

PEF = peak expiratory flow, variability = daily variability over 1–2 weeks, FEV1 = Forced expiratory volume in 1 second, SABA = short-acting β_2-agonist
* Same criteria used for children under 5 although spirometry not possible
† % personal best for PEF, % predicted for FEV1; may not correlate with symptoms

Source: Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. *Expert Panel Report 3: guidelines for the diagnosis and management of asthma.* Summary report 2007: 344 available at www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm.

TABLE 70.2. Predicted PEF (Liters/Min) for Nonsmoking Patients

	Women (height in inches)					Men (height in inches)					Children	
Age (years)	55	60	65	70	75	60	65	70	75	80	Height (inches)	PEF (L/min)
20	390	423	460	496	529	554	602	649	693	740	44	160
30	380	413	448	483	516	532	577	622	664	710	48	214
40	370	402	436	470	502	509	552	596	636	680	52	267
50	360	391	424	457	488	486	527	569	607	649	56	320
60	350	380	412	445	475	463	502	542	578	618	60	373
70	340	369	400	432	461	440	477	515	550	587	64	427

Source: Adapted from *Am Rev Resp Dis*, 1963; 88: 644–51.

TABLE 70.3. Risk Factors for Death in Asthmatics

Sudden, severe attacks	Prior intubation/ICU stay	2 or more ER/hospitalizations/year
Hospital/ER in last month	Recent systemic steroids	More than 2 albuterol canisters/ month
Cardiac problems	Illicit drug use	Low socioeconomic class
Psychosocial problems	Lack of asthma action plan	Denial of asthma diagnosis

Source: Adapted from *Proc Amer Thor Society,* 2009; 6(4): 357–66.

7. TREATMENT

Trigger Avoidance/Control

- Possible triggers: smoke, allergens, medications (β blocker, aspirin, NSAIDs)
- Exercise-induced: starts during and peaks 5–10 minutes after exercise
  - Inhaled β_2 agonist or mast cell stabilizer for prophylaxis
- Allergic rhinitis: control with intranasal steroids, allergen avoidance
- Gastroesophageal reflux: raise head of bed, avoid bedtime snack, medications

Stepwise Approach to Stable Asthma Management

- Gain control early with oral steroids or high-dose inhaled steroids
- Step down therapy every 1–2 months to least medications necessary
- Never use salmeterol or formoterol **alone without** an inhaled steroid
- Consider anti-IgE therapy if severe allergic asthma with elevated serum IgE
- See **Tables 70.4** and **70.5** and **Figure 70.1**

TABLE 70.4. Management of Stable Asthma

Class	Preferred Meds	Additional Medications
Mild intermittent	SA β_2-agonist* prn	–
Mild persistent	Low-dose inhaled steroids (see Table 70.5) and SA β_2-agonist* prn	Mast cell stabilizers (children) or leukotriene receptor blockers
Moderate persistent	LA β_2-agonists **and** low–medium dose inhaled steroids	Leukotriene receptor blockers or zileuton with or without theophylline SR‡
Severe persistent	High dose inhaled steroids (See Table 70.5) **AND** LA β_2-agonists†	Oral steroids with or without omalizumab if elevated serum IgE level

* SA = short-acting β_2-agonists: albuterol and levalbuterol used for breakthrough symptoms in all classes
† LA = long-acting β_2-agonists: salmeterol and formoterol
‡ Theophylline SR titrated to level 5–15 mcg/mL

TABLE 70.5. Inhaled Steroids: Recommended Daily Doses for Adults*

Drug	Form	Adult Daily Doses		
		Low	Medium	High
Beclomethasone MDI	40 mcg/puff	2–6	6–12	More than 12
	80 mcg/puff	1–3	3–6	More than 6
Budesonide DPI	180 mcg/dose	1–3	3–7	More than 7
	Soln for nebs	–	–	–
Ciclesonide MDI	80 mcg/puff	1–3	4–6	More than 7
	160 mcg/puff	1–2	3–4	More than 6
Flunisolide MDI	250 mcg/puff	2–4	4–8	More than 8
	80 mcg/puff	2–6	6–15	More than 15
Fluticasone MDI	110 mcg/puff	1–2	2–4	More than 4
	220 mcg/puff	1	2	More than 2
	44 mcg/dose	2–6	6–12	More than 12
Fluticasone DPI	100 mcg/dose	1–3	3–6	More than 6
	250 mcg/dose	1	2	More than 2
Mometasone DPI	220 mcg/dose	1	2	More than 2
	110 mcg/dose	1–2	3–4	More than 4
Triamcinolone MDI	75 mcg/puff	4–8	8–12	More than 12

* MDI = metered dose inhaler, DPI = dry powder inhaler; all doses in puffs (MDI) or inhalations (DPI)

Sources: Adapted from Hamilton RJ, ed. *Tarascon Pocket Pharmacopoeia, 2012.* Burlington, MA: Jones and Bartlett Publishing.

Initial Assessment of Severity in Acute Asthma Exacerbations in Adults			
Symptoms	Mild	Moderate	Severe
Speaking in	Sentences	Phrases	Words
Heart rate	Less than 100 beats/min	100–120 beats/min	More than 120 beats/min
PEF/FEV_1 (% predicted)	Greater than 70%	40–70%	Less than 40% (esp. Less than 25%)
Room air pulse oximetry	Greater than 95%	91–95%	or less 90%
Mental status	Alert	Drowsy	Lethargic/obtunded
$PaCO_2$ (mmHg)	Less than 40	40–50	Greater than 50t

Inpatient treatment of moderate–severe asthma exacerbations
- Oxygen to keep SaO_2 above 90%
- Albuterol 2.5 mg Neb q1 h until stable, then q 2 h/q 1 h prn x 24 h, then q 4 h/q 2 h prn
  - Consider 2.5 mg Neb q 20 min x 3 **or** 10 mg continuous over 1 h for severe asthma
  - Albuterol and levalbuterol are equally efficacious
- Ipratropium 0.5 mg Neb q 20 min x 3 for severe asthma, then q 4 h/q 2 h prn, then q 6 h
- Methylprednisolone 60 mg IV q 6 h until bronchospasm controlled, then prednisone 1 mg/kg PO daily to complete 10–14 days of therapy, then taper
- Consider magnesium 2 g IV over 20 minutes for severe asthma exacerbations
- Empiric antibiotics for pneumonia or bronchitis **only** if purulent sputum production

Good response after 1–2 h
- Continue current therapy on wards
- Serial PEF and oximetry monitoring
- Smoking cessation counseling, if applicable, and patient education

Partial/poor response after 1–2 h
- Consider noninvasive positive pressure ventilation in ICU
- Continue q 1 h nebulizer treatments

PEF = peak expiratory flow rate, FEV_1 = forced expiratory volume at 1 second, $PaCO_2$ = partial pressure of carbon dioxide, SaO_2 = arterial oxygen saturation, ICU = intensive care unit, ABG = arterial blood gas, cmH_2O = centimeters of water

Reassess after 1–2 h
- ABG
- Serial PEF and oximetry monitoring
- Consider IV aminophylline only for severe, refractory asthma (high risk of toxicity)
- Consider intubation for: persistent $PaCO_2$ Greater than 50 with respiratory acidosis, worsening mental status, hemodynamic instability, or progressive deterioration despite maximal medical therapy
  - Propofol and ketamine will bronchodilate
  - Maximize expiratory time
  - Keep plateau at 30 cmH_2O

FIGURE 70.1. Management of Acute Asthma Exacerbations

Source: Information from: *Allergy*, 2008; 63(8): 997–1004, *Curr Opin Pulm Med*, 2008; 14(1): 13–23, *Curr Opin Crit Care*, 2011; 17(4): 335–41, and *Proc Amer Thor Soc*, 2009; 6(4): 357–66.

8. COMPLICATIONS

- Pneumothorax
- Respiratory failure

REFERENCES

Allergy, 2008;63(8):997–1004; *Curr Opin Pulm Med,* 2008;14(1):13–23; *Curr Opin Crit Care,* 2011;17(4):335–41; *Proc Am Thorac Soc,* 2009;6(4):357–66; *Am Fam Physician,* 2005;71(8):1529–37; *Am Fam Physician,* 2011;84(1):40–7; *Am Fam Physician,* 2009;79(9):761–7; *Curr Opin Crit Care,* 2011;17(4):335–41.

CHAPTER 71

CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION

1. EPIDEMIOLOGY

- Fourth leading cause of death in the United States
- Prevalence is 20% in the United States
- Cigarette smoking is implicated in 90% of cases
- 75% of patients have serious chronic dyspnea and nearly 25% have profound total body pain
- 60 yo smoker with chronic bronchitis has a 10-year mortality of 60%, which is 4 times higher than age-matched nonsmoking asthmatics
- Inpatient mortality is 11%, 6-month mortality is 33%, and 1-year mortality is 43%
- Those who survived first hospitalization have a 50% chance of rehospitalization within 6 months
- Initial hospitalization: 93% are male, mean age is 63.5 yo, less than 1% never smoked, mean FEV_1 is 47%, and 50% are admitted to the ICU

2. PATHOPHYSIOLOGY

- Large airways: mucus and goblet cell hyperplasia increase mucus, which leads to cough then chronic bronchitis
- Small airways: irreversible airway obstruction (decreased FEV_1) with compensatory hyperinflation (increased residual volume)
- Initially, air trapping maintains airflow (increased lung volume increases elastic recoil, increased airway diameter decreases airway resistance)
- Hyperinflation flattens diaphragm decreases inspiratory capacity
- Decreased abdominal pressure transmitted to diaphragm
- Shorter, less effective diaphragmatic muscle fibers
- Due to Laplace's law, need to increase tension to produce a given pressure
- Lung parenchyma: with chronic inflammation, elastase activity exceeds antielastase activity, leading to degradation of extracellular matrix, cell death, and patchy enlarged air spaces (i.e., emphysema)
- FEV_1 less than 50% predicted associated with hypoxemia
- FEV_1 less than 25% predicted associated with hypercapnia

3. CLINICAL PRESENTATION

- Acute change from baseline dyspnea, cough, or sputum production
- Other symptoms: chest tightness; tachycardia; decreased exercise tolerance; confusion; depression; insomnia; change to color, volume, or tenacity of sputum; dyspnea; tachypnea; wheezing; fever; fatigue; malaise
- Physical findings
  - Cardiac impulse palpable below the xiphoid [LR+ 7.4, LR– NS]
  - Hoover sign: hands placed on costal margin, with fingers touching at xiphoid process—with normal respiration, the hands will separate; in COPD, the hyperexpansion prevents further excursion and the hands come closer together [LR+ 4.2, LR– 0.5]
  - Accessory (scalene/sternocleidomastoid) muscle use [LR+ 3.3, LR– 0.7]
  - Decreased breath sounds [LR+ 3.2, LR– 0.5]
  - Wheeze [LR+ 2.8, LR– 0.8]
  - Barrel chest [LR+ 1.5, LR– 0.6]

4. DIAGNOSIS

- **Spirometry**: airflow obstruction that is not fully reversible
  - FEV_1/FVC less than 70% predicted and postbronchodilator FEV_1 less than 80%
- **Diagnosis of COPD exacerbations**: increase in dyspnea, cough, sputum volume, or purulence

5. DIFFERENTIAL DIAGNOSIS

- Asthma
- CHF
- Angioedema
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Cystic fibrosis
- Bronchiolitis obliterans
- Conversion disorders
- Munchausen syndrome
- Malingering
- Interstitial lung disease

6. EVALUATION

- Baseline pulmonary function test, pulse oximetry, chest X-ray
- Labs: α-1 antitrypsin

Evaluation of COPD Exacerbations

- Assess with chest X-ray, sputum culture, oximetry, or arterial blood gas
- Admit for moderate–severe exacerbations: respiratory acidosis, need for ventilation, PEF less than 100 L/min, FEV_1 less than 1 L or less than 40% predicted, or serious comorbidities
- See **Table 71.1**

TABLE 71.1. Management of Stable COPD by Stage

Stage*	Spirometry	Therapy
All	No smoking! Influenza, pneumococcal vaccines, and exercise	
0 (at risk)	Normal	
I (mild)	$FEV_1/FVC<70\%$ $FEV_1 \geq 80\%$ predicted	Short-acting or long-acting β_2-agonist or anticholinergic (AC) agent† prn
II (moderate)	$FEV_1/FVC<70\%$ $50\% \leq FEV_1<80\%$	Scheduled long-acting β_2-agonist or AC agent† and pulmonary rehabilitation‡
III (severe)	$FEV_1/FVC<70\%$ $30\% \leq FEV_1 <50\%$	Add inhaled steroids to scheduled long-acting bronchodilators (especially if greater than or equal to 1 exac./yr)
IV (very severe)	$FEV_1<30\%$ or $<50\%$ + chronic respiratory failure	As for Stage III; oxygen§ (improves survival!); consider bullectomy/transplantǁ; Consider roflumilast¶

* FEV_1 used to stratify severity
BODE index (body mass index, airway obstruction, dyspnea, exercise capacity on 6 min. walk) better to assess risk of death: see http://content.nejm.org/cgi/reprint/350/10/1005.pdf
† Bronchodilators (anticholinergics > β_2-agonists » methylxanthines): use combination therapy if monotherapy inadequate; long-acting anticholinergic (tiotropium) and β_2-agonist (e.g., salmeterol or formoterol) are preferred over short-acting anticholinergic (ipratropium) or β_2-agonist (e.g., albuterol)
‡ Aerobic exercise, good nutrition and education
§ $PaO_2 \leq 55$ mmHg/O_2 sat $\leq 88\%$ ($PaO_2 \leq 60$ mmHg if pulmonary hypertension, polycythemia, or cor pulmonale)
ǁ Bullectomy or lung-volume reduction surgery best for upper lobe emphysema and low exercise capacity; lung transplantation indicated for idiopathic emphysema or α-1 antitrypsin deficiency
¶ Roflumilast 500 mcg PO daily (PDE_4 inhibitor) decreases COPD exacerbations

Source: Adapted from the GOLD initiative 2010 executive summary available at www.goldcopd.org/uploads/users/files/GOLDReport_April112011.pdf

7. TREATMENT OF ACUTE COPD EXACERBATIONS

- Albuterol 2.5 mg and ipratropium 0.5 mg nebulized q 2–4 h
- Antibiotics × 5–10 days for severe exacerbations or presence of purulent sputum
  - Uncomplicated exacerbation if age 65 yo or younger, FEV_1 50% or more, and fewer than 4 exacerbations/year
    - New macrolide, doxycycline, or 2nd–3rd generation cephalosporin
  - Complicated exacerbation if age older than 65 yo, FEV_1 less than 50%, more than 4 exacerbations/year, or use of antibiotics in the last 3 months
    - Use amoxicillin-clavulanate or a respiratory quinolone
  - Risk for pseudomonas if recurrent antibiotic use, recurrent steroid courses, or if bronchiectasis is present; use an antipseudomonal quinolone
- Systemic steroids with methylprednisolone 30–40 mg/day (or prednisone 40–60 mg PO daily) × 7–10 days if FEV_1 is less than 50% predicted, **or** if $PaCO_2$ is greater than 45 and pH is less than 7.35 with or without steroid taper
- Oxygen if hypoxia to maintain SaO_2 is 88–90% or PaO_2 is 55 mmHg or higher
- Noninvasive positive-pressure ventilation if acute respiratory acidosis (pH 7.35 or less, $PaCO_2$ 45 mmHg or higher) and no contraindications to its use
- Indications for ICU admission: $PaCO_2$ greater than 60 mmHg and pH less than 7.25, depressed level of consciousness, unstable medical comorbidities, hemodynamic or rhythm instability, and need for invasive mechanical ventilation
- Indications for mechanical ventilation: severe respiratory acidosis refractory to noninvasive ventilation, respiratory arrest, hemodynamic instability, or obtundation

8. COMPLICATIONS

- Progressive dyspnea
- Respiratory failure
- Frequent/recurrent pulmonary infections
- Pulmonary hypertension results in cor pulmonale
- Depression

REFERENCES

GOLD initiative at www.goldcopd.com; *Am J Med*, 2006;119:S46; *Am J Med*, 2007;120(8 Suppl 1):S4–13; *Ann Fam Med*, 2006;4(3):253–62; *Lancet*, 2004;364(9437):883–95; *Chest*, 2008;133(3):756–66; *Am Fam Physician*, 2010;81(5):607–13.

CHAPTER 72

PERIOPERATIVE PULMONARY EVALUATION AND MANAGEMENT

1. PREOPERATIVE RISK STRATIFICATION

- Few patients have an absolute pulmonary contraindication to surgery
- Preoperative spirometry should *not* be used to prevent surgery but rather as a tool to optimize preoperative lung function; appropriate if the patient has
  - Asthma or COPD and airflow obstruction that has not been optimized
  - Unexplained dyspnea or cough and will undergo major surgery (as below)
  - Patient will be undergoing lung resection surgery
- Indications for an arterial blood gas: resting hypoxia, risk for chronic hypercapnia, or anticipated lung resection surgery

2. PERIOPERATIVE PULMONARY MANAGEMENT TABLES

TABLE 72.1. Risk Factors for Perioperative Pulmonary Complications*

• Age older than 60 years • Smoking within 8 weeks of surgery • Poor general health (ASA 3 or more)† • Emergency surgery • Thoracic, abdominal aortic aneurysm, neurosurgery, head and neck or upper abdominal surgery • Surgery lasting more than 3 hours • General anesthesia • Long-acting neuromuscular blockade	• COPD • CHF • Elevated arterial carbon dioxide pressure ($PaCO_2$ 45 mmHg) • Functional dependence for ADLs • Impaired sensorium • Malnourished (albumin less than 3.5 g/dL) • Renal failure (blood urea nitrogen [BUN] 21 mg/dL or higher) • Transfusion more than 4 units of blood

Note: Obesity alone or asthma does not appear to increase risk
ASA = aspirin, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, ADL = activities of daily living, BUN = blood urea nitrogen
* Perioperative pulmonary complications include atelectasis, pneumonia, or respiratory failure
† American Society of Anesthesiologists Classification at www.asahq.org/clinical/physicalstatus.htm

Source: Adapted from *Ann Intern Med*, 2006; 144(8): 575–80.

TABLE 72.2. Postoperative Respiratory Failure Index

Factor	Score	Factor	Score
Type of surgery		Albumin less than 3 g/dL	9
AAA repair	27	BUN greater than 30 mg/dL	8
Thoracic surgery	21	History of COPD	6
Neurosurgery, upper abdomen, or peripheral vascular surgery	14	Partially or fully dependent functional status	7
Neck surgery	11	Age 70 yo or older	6
Emergency surgery	11	Age 60–69 yo	4

Class	Points	Incidence of Postoperative Respiratory Failure
1	10 or fewer	0.5%
2	11–19	1.8%
3	20–27	4.2%
4	28–40	10.1%
5	More than 40	26.6%

Source: Adapted from *Ann Intern Med*, 2006;144:575.

3. INTERVENTIONS TO REDUCE PERIOPERATIVE RISK

- Smoking cessation: beneficial if patient quits 8 or more weeks prior to surgery
- Inhaled tiotropium 1 puff daily for COPD with or without β_2 agonists for wheezing
- Oral or inhaled steroids and inhaled tiotropium if COPD or asthma and pulmonary function not optimal (no increase in risk of infections, but potential for adrenal suppression if 20 mg/day or more of prednisone for at least 3 weeks)
- Defer elective surgery for acute exacerbations of pulmonary disease
- Consider shorter procedures (under 3 hours), laparoscopic approach, and spinal/epidural or regional anesthesia rather than general anesthesia for high-risk patients
- Avoid long-acting neuromuscular blockers (e.g., pancuronium)
- Postoperative lung expansion maneuvers and early mobilization recommended
- Consider postoperative epidural analgesia for thoracic or upper abdominal surgery

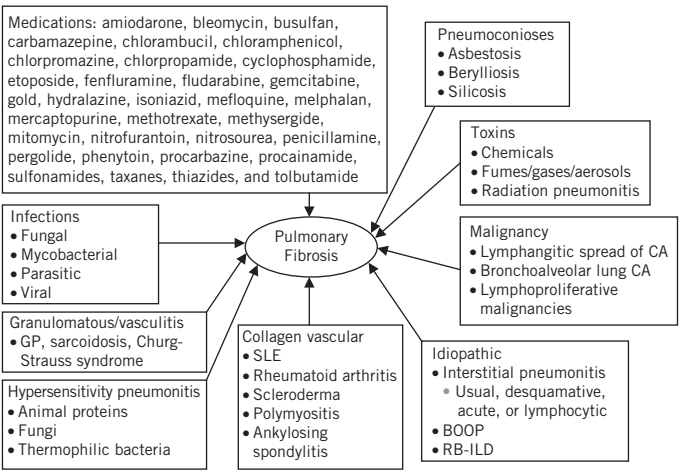
REFERENCES

Ann Intern Med, 2006;144(8):575–80; *Anesth Clin N Amer*, 2004;22:77; *Ann Surg*, 2000;232(2):242–53.

CHAPTER 73

DIFFUSE INTERSTITIAL LUNG DISEASE

1. **EPIDEMIOLOGY**
   - 75% of IPF are older than 60 yo at diagnosis
   - Almost all patients with lymphangioleiomyomatosis (LAM) are women
2. **PATHOPHYSIOLOGY**
   - Predominant histopathological patterns
     - Granulomatous: T cells, macrophages, and epitheloid cells organized into granulomas
       - Known cause: hypersensitivity pneumonitis
       - Unknown cause: sarcoidosis, granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis), Churg-Strauss
     - Inflammatory/fibrotic: epithelial injury induces alveolar inflammation; interstitial and vascular inflammation leads to interstitial fibrosis, irreversible scarring, and impaired gas exchange
     - Known cause: asbestos, inhalation, medications (nitrofurantoin, amiodarone), chemotherapy (bleomycin), radiation, aspiration, post-ARDS, desquamative interstitial pneumonia, Langerhans cell granulomatosis
     - Unknown cause: idiopathic pulmonary fibrosis (usual interstitial pneumonia), diffuse alveolar damage, cryptogenic organizing pneumonia, nonspecific interstitial pneumonia, rheumatologic diseases, Goodpasture's syndrome, pulmonary alveolar proteinosis, eosinophilic pneumonia, lymphangioleiomyomatosis, amyloidosis, genetic diseases, graft-versus-host, etc.
3. **CLINICAL PRESENTATION**
   - Progressive dyspnea and cough
   - Acuity of onset ranges from years (UIP) to days/weeks (AIP)
   - Signs: crackles, inspiratory squeaks; rarely cor pulmonale
4. **DIAGNOSIS**
   - Definitive diagnosis is via a tissue biopsy
   - History: occupational/environmental exposures, travel, meds, medical comorbidities
5. **DIFFERENTIAL DIAGNOSIS**
   - CHF
   - Fungal pneumonia
   - Miliary tuberculosis
   - Pulmonary hypertension
   - Interstitial spread of cancer
6. **EVALUATION**
   - Chest X-ray and arterial blood gas
   - High-resolution chest CT: reticulonodular infiltrates, interstitial infiltrates, "ground glass" opacities, or honeycombing
   - Pulmonary function testing reveals a pattern of restrictive lung disease with a decline in lung volumes and diffusion capacity
   - Labs: CBCD, chemistry panel, angiotensin converting enzyme, ANA, RF, antineutrophil cytoplasmic antibody, antiglomerular basement membrane antibody, anti-ScL-70, HIV, ESR, CK, HLA-B27, aldolase levels, and coccidioidomycosis titers
   - Induced sputa or bronchoalveolar lavage for cytology and AFB or fungi
   - Open lung biopsy
   - See **Figure 73.1**



GP = granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis), SLE = systemic lupus erythematosus, BOOP = bronchiolitis obliterans with organizing pneumonia, RB-ILD = respiratory bronchiolitis-interstitial lung disease, CA = cancer

FIGURE 73.1. Causes of Diffuse Interstitial Lung Disease

Source: Adapted from *South Med J*, 2007; 100(6): 579–87.

7. TREATMENT OF DIFFUSE INTERSTITIAL LUNG DISEASE (DILD)

- Targeted therapy of any underlying disease that has been identified
- Avoidance of offending medication(s) or occupational exposures if relevant
- Supplemental O_2 to keep PaO_2 above 55 mmHg; pneumococcal and influenza vaccines
- Idiopathic interstitial pneumonitis: prednisone 0.5–1 mg/kg/day often, with cyclophosphamide 2 mg/kg PO daily OR azathioprine 2 mg/kg PO daily
- Refer appropriate patients for lung transplantation

8. COMPLICATIONS

- Pulmonary hypertension
- Cor pulmonale
- Respiratory failure

REFERENCES

South Med J, 2007;100(6):579–87; *Chest*, 2006;129(Suppl 1):180S–5S; *Curr Opin Pulm Med*, 2008;14(5):427–33; *Thorax*, 2008;63(Suppl 5):v1–58.

CHAPTER 74

PULMONARY HYPERTENSION

1. EPIDEMIOLOGY

- Uncommon; incidence 2.4–7.6 cases per million, prevalence of 15–50 cases per million
- Poor prognosis with 15% mortality within 1 year
- Male to female ratio is 1:2; mean age of onset is around 37 yo; idiopathic type is most common at 39%, 70% arise from a germline mutation in BMPR2 gene
- Drug-induced PAH is primarily related to anorexigen (diet pill), 10%; other drugs such as amphetamines and L tryptophan are also associated with its development
- 25–50% of patients suffer from Eisenmenger syndrome
- 4% or patients with PE go on to develop PAH
- 4% PE patients go on to develop PAH

2. CLINICAL PRESENTATION

- Early phases are asymptomatic
- Presenting symptoms are dyspnea on exertion, fatigue, chest pain, palpitations, and edema
- Signs: R parasternal lift, accentuated second heart sound, pansystolic murmur (tricuspid regurgitation), third heart sound, diastolic murmur (pulmonary valve insufficiency), peripheral edema
- Risk factors are congenital heart disease, connective tissue disease, portal hypertension, sickle cell disease, thyroid disease, and HIV

3. DEFINITION

- Mean pulmonary artery pressure is greater than 25 mmHg (rest)
- Pulmonary arterial hypertension (PAH): above and normal PCWP or normal LVEDP
- See **Table 74.1**

TABLE 74.1. Classification of Pulmonary Hypertension (PHTN)

Subtypes of PHTN	Causes
Pulmonary arterial hypertension (PAH)	• Idiopathic • Familial • Associated with a connective tissue disease • Associated with HIV infection • Portopulmonary hypertension • Drug-induced or toxin-induced • Pulmonary veno-occlusive disease • Pulmonary capillary hemangiomatosis
PHTN with left heart disease	• Chronic CHF, moderate–severe MS or MR
Secondary to chronic hypoxia	• COPD, DILD, OSA, obesity-hypoventilation syncope, neuromuscular disorders, intracardiac right-to-left shunts
Recurrent pulmonary emboli	• Recurrent PE or tumor emboli
Miscellaneous	• Sarcoidosis, Langerhans cell histiocytosis, schistosomiasis, and lymphangiomatosis

Source: Adapted from *J Am Coll Cardiol*, 2004(12 Suppl S); 43: 5S–12S.

4. EVALUATION OF PULMONARY HYPERTENSION

- ECG: right axis deviation, right atrial abnormality, and right ventricular hypertrophy
- Chest X-ray: enlarged right atrium and ventricle, dilated pulmonary arteries, and "pruning" of the peripheral pulmonary vasculature
- Pulmonary function test: screen for underlying obstructive or restrictive lung disease
- Nocturnal polysomnogram: evaluate for obstructive or central sleep apnea
- Arterial blood gas: screen for resting hypoxia or hypercarbia
- V/Q scan superior to CT pulmonary angiogram to screen for recurrent PE
- Echocardiogram: evaluate left ventricular systolic and diastolic function, valve abnormalities, chamber sizes, and noninvasive estimate of pulmonary pressures
- Right heart catheterization: confirms diagnosis of pulmonary arterial hypertension
- Labs: CBCD, chemistry panel, ANA, RF, anti-Scl-70, anticentromere, HIV, and ESR
- 6-minute walk test to determine functional capacity

5. TREATMENT

- Supplemental oxygen to keep SaO_2 90% or more
- Interventions: influenza and pneumococcal vaccinations; smoking cessation; chronic anticoagulation; and *avoid* decongestants, pregnancy, NSAIDs, and air travel
- Consider cautious diuresis and/or digoxin therapy for right ventricular dysfunction
- Pulmonary vasoreactivity as determined by inhaled nitric oxide testing during right heart catheterization can benefit from nifedipine ER, amlodipine, or diltiazem therapy
- Initial medication therapy for functional classes 2–3 and good hemodynamic profile
  - Endothelin receptor antagonists: bosentan or ambrisentan
  - Phosphodiesterase-5 inhibitors: sildenafil
- Initial medication therapy for functional classes 3–4 with poor hemodynamic profile
  - Prostanoid therapy: epoprostenol IV or inhaled iloprost or treprostinil SQ or IV

6. COMPLICATIONS

- Cor pulmonale
- Hypoxemia
- Cardiac arrhythmias
- Hemoptysis

REFERENCES

Am J Med Sci, 2008;335(1):40–5; *Circulation,* 2008;118(21):2190–9; *Crit Care Med,* 2007;35(9):2037–50; *Expert Opin Pharmacother,* 2008;9(1):65–81.