

RESPIROLOGY

Dr. C. Chan and Dr. N. Lazar
Adrienne Chan and Gloria Rambaldini, editors
Deborah Cheng, associate editor

PULMONARY PHYSIOLOGY	2	DISEASES OF THE MEDIASTINUM	28
APPROACH TO THE RESPIRATORY	3	AND PLEURA	
PATIENT		Mediastinal Disease	
History and Differential Diagnosis of Symptoms in		Pleural Effusions	
Respiratory Disease		Empyema	
Physical Exam and Differential Diagnosis of Signs in		Pneumothorax	
Respiratory Disease		Asbestos-Related Pleural Disease	
Investigations and their Interpretation		PULMONARY INFECTIONS.	31
Pulmonary Function Tests (PFTs)		Pneumonia	
Arterial Blood Gases (ABGs)		Lung Abscess	
DISEASES OF AIRWAY OBSTRUCTION	12	Fungal Infections	
Asthma		Mycobacteria	
Chronic Obstructive Pulmonary Disease (COPD)		NEOPLASMS	38
Bronchiectasis		Approach to the Solitary Pulmonary Nodule	
Cystic Fibrosis (CF)		Benign	
INTERSTITIAL LUNG DISEASE	18	Malignant	
Unknown Etiologic Agents		RESPIRATORY FAILURE	42
Idiopathic Pulmonary Fibrosis		Hypoxemic Respiratory Failure	
Sarcoidosis		Hypercapnic Respiratory Failure	
Pulmonary Infiltrates with Eosinophilia		Acute Respiratory Distress Syndrome (ARDS)	
(PIE Syndrome)		Mechanical Ventilation	
Associated with Collagen Vascular Disease		SLEEP-RELATED BREATHING	44
Cryptogenic Organizing Pneumonia (Bronchiolitis)		DISORDERS	
Obliterans with Organizing Pneumonia – BOOP)			
Known Etiologic Agents			
Hypersensitivity Pneumonitis			
Pneumoconioses			
PULMONARY VASCULAR DISEASE.	23		
Pulmonary Vasculitis			
Pulmonary Hypertension			
Pulmonary Emboli (PE)			

Ventilation (Alveolar)

- ❑ the prime determinant of arterial $p\text{CO}_2$
- ❑ hypoventilation results in hypercapnia

Control of Ventilation

- ❑ respiratory control centre (medulla and pons)
 - receives input from respiratory sensors and controls output to respiratory effectors
- ❑ respiratory sensors
 - chemoreceptors (responds to levels of O_2 , CO_2 , and H^+)
 - central (medulla): increased H^+ / increased $p\text{CO}_2$ stimulates ventilation
 - peripheral (carotid body, aortic arch): decreased $p\text{O}_2$ stimulates ventilation
 - mechanoreceptors: stretch in airway smooth muscles inhibits inflation
- ❑ respiratory effectors (muscles of respiration)
 - inspiration: diaphragm, external intercostal and scalene muscles, sternomastoids
 - expiration: abdominal wall and internal intercostal muscles

Perfusion

- ❑ two separate blood supplies to the lungs
 - pulmonary
 - bronchial (systemic)

Control of Perfusion

- ❑ in response to decreased $p\text{O}_2$ or increased $p\text{CO}_2$, the pulmonary vessels constrict to decrease Q in order to maintain a 1:1 V/Q ratio

Imbalances in V/Q Ratio

- ❑ $V > Q$ → dead space ventilation that does not contribute to gas exchange
- ❑ $V < Q$ → hypoxemia that can be corrected with supplemental O_2
- ❑ Q but no V → shunt (i.e. blood bypasses the alveoli, resulting in hypoxemia that cannot be corrected with supplemental O_2)

Oxygenation

- ❑ occurs by diffusion through alveolar-capillary membrane to form oxygenated Hb within the red blood cell
- ❑ normal $\text{PaO}_2 = 80\text{-}100$ mm Hg (O_2 sat = 98%)
- ❑ normal $\text{PaCO}_2 = 35\text{-}45$ mm Hg

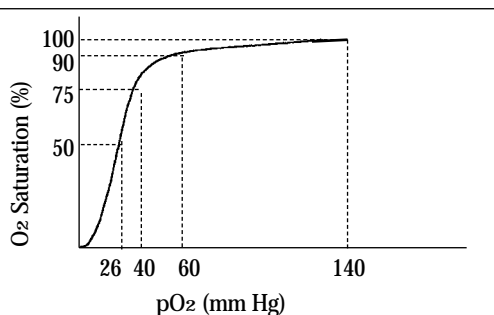


Figure 1. O_2 -Hb Association Curve

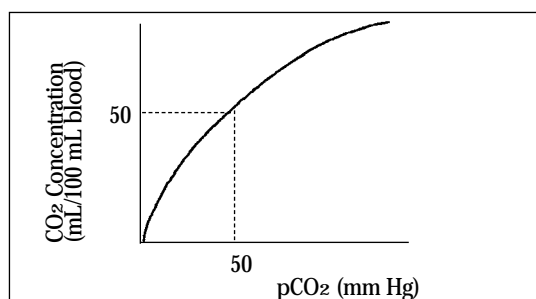


Figure 2. CO_2 -Hb Association Curve

Clinical Pearl

- ❑ Bohr Effect is a shift in the O_2 -Hb curve to the right due to an increase in H^+ , $p\text{CO}_2$, temperature, or 2,3-diphosphoglycerate. This shift facilitates O_2 unloading in peripheral capillaries

Lung Compensation in Hypoxemia and Hypercapnia

- ❑ hypoxemic: failure in oxygenation of end-organs ($\text{PaO}_2 < 60$ mm Hg)
- ❑ hypercapnic: failure in ventilation ($\text{PaCO}_2 > 50$ mm Hg and respiratory acidosis)
- ❑ in hypoxemic disease states due to V/Q mismatch, normal lung areas cannot compensate for areas of the lung with a low V/Q (increasing minute ventilation cannot compensate due to the sigmoid shape of O_2 -Hb association curve) (see Figure 1)
- ❑ the lungs can compensate for hypercapnia by hyperventilation, due to the relatively linear shape of the CO_2 -Hb association curve (see Figure 2)

APPROACH TO THE RESPIRATORY PATIENT

HISTORY AND DIFFERENTIAL DIAGNOSIS OF SYMPTOMS IN RESPIRATORY DISEASE

- ❑ dyspnea/SOB
 - PND/orthopnea: SOB when recumbent in CHF, asthma, COPD, or GERD
 - trepopnea: SOB when right or LLDB in CHF, cardiac mass
 - platypnea: SOB when upright in post-pneumonectomy, neurologic disease, cirrhosis, hypovolemia
 - episodic: in bronchospasm, transient pulmonary edema
 - DDX of dyspnea (see Table 1)
- ❑ cough
 - productive: bronchiectasis, bronchitis, abscess, bacterial pneumonia, TB
 - nonproductive: viral infections, interstitial lung disease, anxiety, allergy
 - wheezy: suggests bronchospasm, asthma, allergy
 - nocturnal: asthma, CHF, postnasal drip, GERD, or aspiration
 - barking: epiglottal disease (croup)
 - positional: abscess, tumour
 - DDX of cough (see Table 2)
- ❑ sputum
 - mucoid: asthma, tumour, TB, emphysema
 - purulent green: bacterial pneumonia, bronchiectasis, chronic bronchitis
 - purulent rusty: pneumococcal pneumonia
 - frothy pink: pulmonary edema
 - red currant jelly: *Klebsiella pneumoniae*
 - foul odour: abscess (anaerobic pathogens)
- ❑ hemoptysis

hemoptysis	vs.	hematemesis
• cough		• nausea/vomiting
• sputum present		• no sputum
• stable bubbles		• no stable bubbles
• alkaline pH		• acid pH
• alveolar macrophages		• no alveolar macrophages
• DDX of hemoptysis (see Table 3)		
- ❑ chest pain
 - due to parietal pleura, chest wall, diaphragm, or mediastinal involvement
 - pleuritic: sharp knife-like pain worse with deep inspiration or coughing
 - DDX of chest pain (see Table 4)

Table 1. Differential Diagnosis of Dyspnea

Respiratory
 Airway disease
 asthma
 COPD
 upper airway obstruction
 Parenchymal lung disease
 ARDS
 pneumonia
 interstitial lung disease
 Pulmonary vascular disease
 PE
 pulmonary HTN
 pulmonary vasculitis
 Pleural disease
 pneumothorax
 pleural effusion
 Neuromuscular and chest wall disorders
 polymyositis, myasthenia gravis,
 Guillain-Barré syndrome
 kyphoscoliosis
 C-spine injury
 Cardiovascular
 Elevated pulmonary venous pressure
 LVF
 mitral stenosis
 Decreased cardiac output
 Severe anemia
 Anxiety/psychosomatic

Table 2. Differential Diagnosis of Cough

Airway irritants
 inhaled smoke, dusts, fumes
 aspiration
 gastric contents
 oral secretions
 foreign body
 postnasal drip
 Airway disease
 URTI including postnasal drip and sinusitis
 acute or chronic bronchitis
 bronchiectasis
 neoplasm
 external compression by node or mass lesion
 asthma
 COPD
 Parenchymal disease
 pneumonia
 lung abscess
 interstitial lung disease
 CHF
 Drug-induced

Table 3. Differential Diagnosis of Hemoptysis

Airway disease
 acute or chronic bronchitis
 bronchiectasis
 bronchogenic CA
 bronchial carcinoid tumour
 Parenchymal disease
 TB
 lung abscess
 pneumonia
 miscellaneous
 Goodpasture's syndrome
 idiopathic pulmonary hemosiderosis
 Vascular disease
 PE
 elevated pulmonary venous pressure
 LVF
 mitral stenosis
 vascular malformation
 Miscellaneous
 impaired coagulation
 pulmonary endometriosis

Table 4. Differential Diagnosis of Chest Pain

Nonpleuritic	Pleuritic
Pulmonary neoplastic pneumonia PE Cardiac MI ischemia myocarditis/pericarditis Esophageal spasm esophagitis ulceration achalasia neoplasm Mediastinal lymphoma thymoma Subdiaphragmatic PUD gastritis biliary colic pancreatic Vascular dissecting aortic aneurysm MSK costochondritis skin breast ribs	Pulmonary pneumothorax hemothorax PE pneumonia bronchiectasis neoplasm TB empyema Cardiac pericarditis Dressler's syndrome GI pancreatitis MSK costochondritis fractured rib myositis herpes zoster

Reproduced with permission SE Weinberger, *Principles of Pulmonary Medicine*, 2nd edition, 1992

PHYSICAL EXAM AND DIFFERENTIAL DIAGNOSIS OF SIGNS IN RESPIRATORY DISEASE

Inspection

- face
 - nasal flaring, pursed lip breathing
 - pallor: anemia
 - central cyanosis: inadequate SaO₂
- posture
 - orthopnea, platypnea, trepopnea
- accessory muscle use
- chest shape
 - horizontal ribs: emphysema
 - barrel chest (increased AP diameter): advanced COPD
 - kyphosis/scoliosis: restricts chest expansion
 - pectus excavatum (sternal depression): restricts chest expansion
 - flail chest: multiple rib fractures
- hands
 - clubbing (base angle of nail obliterated, increased sponginess of nail bed): for DDx see Table 5
 - peripheral cyanosis: excessive O₂ extraction
- respiratory rate and patterns (see Table 6)
 - apnea (complete cessation of airflow lasting at least 10 seconds)
 - hypopnea (a decrease in airflow by at least 50% lasting at least 10 seconds)




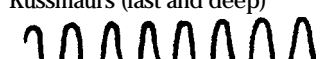
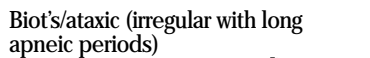
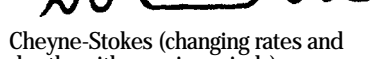

Clinical Pearl

- Central cyanosis is not detectable until the SaO₂ is < 85%. It is also marked in polycythemia and less readily detectable in anemia

Table 5. Differential Diagnosis of Clubbing

<p>Pulmonary</p> <ul style="list-style-type: none"> CF pulmonary fibrosis chronic infections lung CA (primary or mets) mesothelioma A-V fistula bronchiectasis <p>Cardiac</p> <ul style="list-style-type: none"> cyanotic congenital heart disease infective endocarditis <p>Gastrointestinal</p> <ul style="list-style-type: none"> IBD chronic infections laxative abuse polyposis malignant tumours cirrhosis HCC 	<p>Mediastinal</p> <ul style="list-style-type: none"> esophageal CA thymoma achalasia <p>Other</p> <ul style="list-style-type: none"> Graves' disease thalassemia other malignancies primary hypertrophic osteoarthropathy
---	---

Table 6. Respiration Patterns in Normal and Disease States

Respiration Pattern	Causes
normal inspiration and expiration 	
obstructive (prolonged expiration) 	asthma, COPD
bradypnea (abnormal slowness of breathing) 	drug-induced respiratory depression diabetic coma increased ICP
Kussmaul's (fast and deep) 	metabolic acidosis exercise anxiety
Biot's/ataxic (irregular with long apneic periods) 	drug-induced respiratory depression increased ICP brain damage, especially medullary
Cheyne-Stokes (changing rates and depths with apneic periods) 	drug-induced respiratory depression brain damage (especially cerebral) CHF uremia
apneustic (prolonged inspiratory pause) 	pontine lesion

Palpation

- chest wall tenderness: MSK disease
- asymmetrical chest excursion
 - pleural effusion, lobar pneumonia, pulmonary fibrosis, bronchial obstruction, pleuritic pain with splinting, pneumothorax
- tactile fremitus
 - increased: consolidation (pneumonia)
 - decreased:

unilateral	vs.	bilateral
• pneumothorax		• COPD
• pleural effusion		• pleural effusion
• bronchial obstruction		• chest wall thickening (fat, muscle)
• pleural thickening		
- trachea
 - deviated: contralateral pneumothorax/pleural effusion, ipsilateral atelectasis
 - decreased mobility: mediastinal fixation (neoplasm, TB)

Percussion

- dull: pneumonia, pleural effusion, atelectasis, hemothorax, empyema, tumour
- hyperresonant: emphysema, pneumothorax, asthma
- diaphragmatic excursion (normal diaphragmatic movement 4-5 cm from inspiration to expiration)

Auscultation

Vesicular	Bronchial
<ul style="list-style-type: none"> • soft • low-pitched • inspiratory >> expiratory phase • normal over most of peripheral lung 	<ul style="list-style-type: none"> • loud • high-pitched • expiratory > inspiratory phase • normal over manubrium but represents consolidation elsewhere
Decreased air entry	Crackles (Rales/Crepitations)
<ul style="list-style-type: none"> • asthma • emphysema • pneumothorax • pleural effusion • atelectasis • ARDS 	<ul style="list-style-type: none"> • bronchitis • respiratory infections, pneumonia • pulmonary edema • interstitial fibrosis • CHF • excess airway secretions
Wheeze (Rhonchi)	Pleural rub
<ul style="list-style-type: none"> • asthma • bronchitis • pulmonary edema • CHF • foreign body • CF • aspiration • tumour, vascular ring • rapid airflow through obstructed airway 	<ul style="list-style-type: none"> • pneumonia • pleural effusion • pulmonary infarction
	Voice sounds
	<ul style="list-style-type: none"> • egophony (e to a) • whispering pectoriloquy • bronchophony • all are due to consolidation

INVESTIGATIONS AND THEIR INTERPRETATIONS

PULMONARY FUNCTION TESTS (PFTs)

- ❑ useful in differentiating the pattern of lung disease (obstructive vs. restrictive) (see Table 8)
- ❑ assesses lung volumes, flow rates, and diffusion capacity (see Figures 3 and 4)

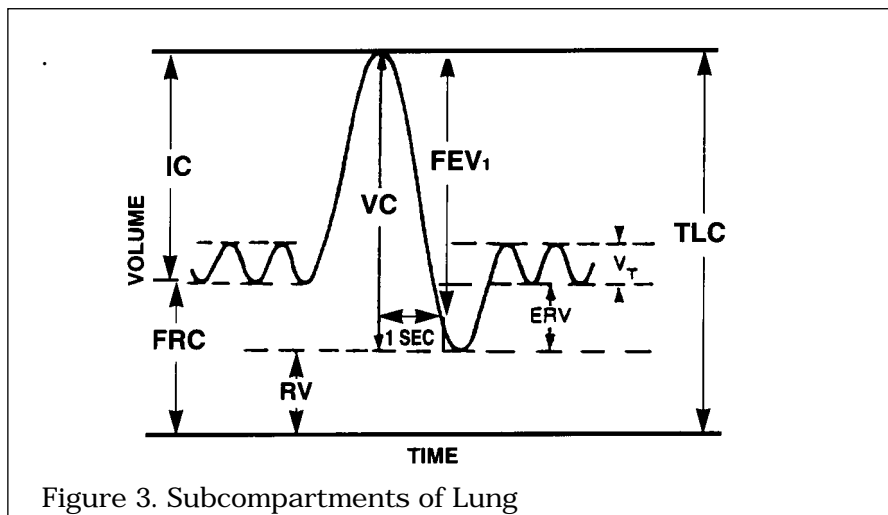


Figure 3. Subcompartments of Lung

Reproduced with permission from SE Weinberger, *Principles of Pulmonary Medicine*, 2nd edition, 1992

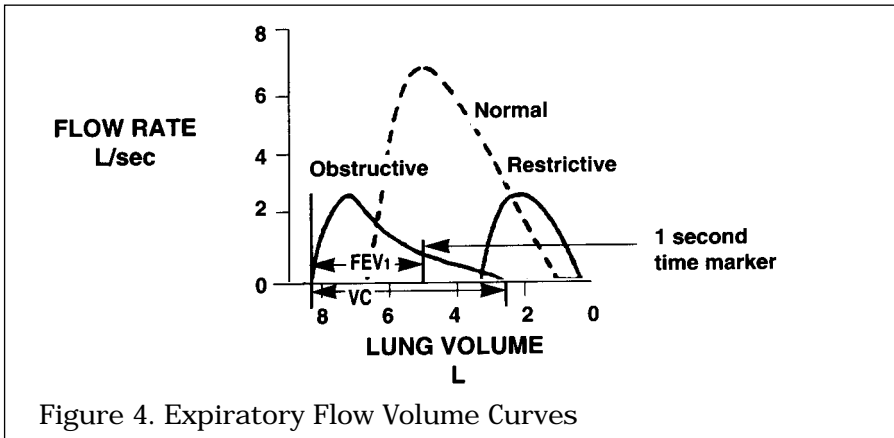


Figure 4. Expiratory Flow Volume Curves

Obstructive Lung Disease

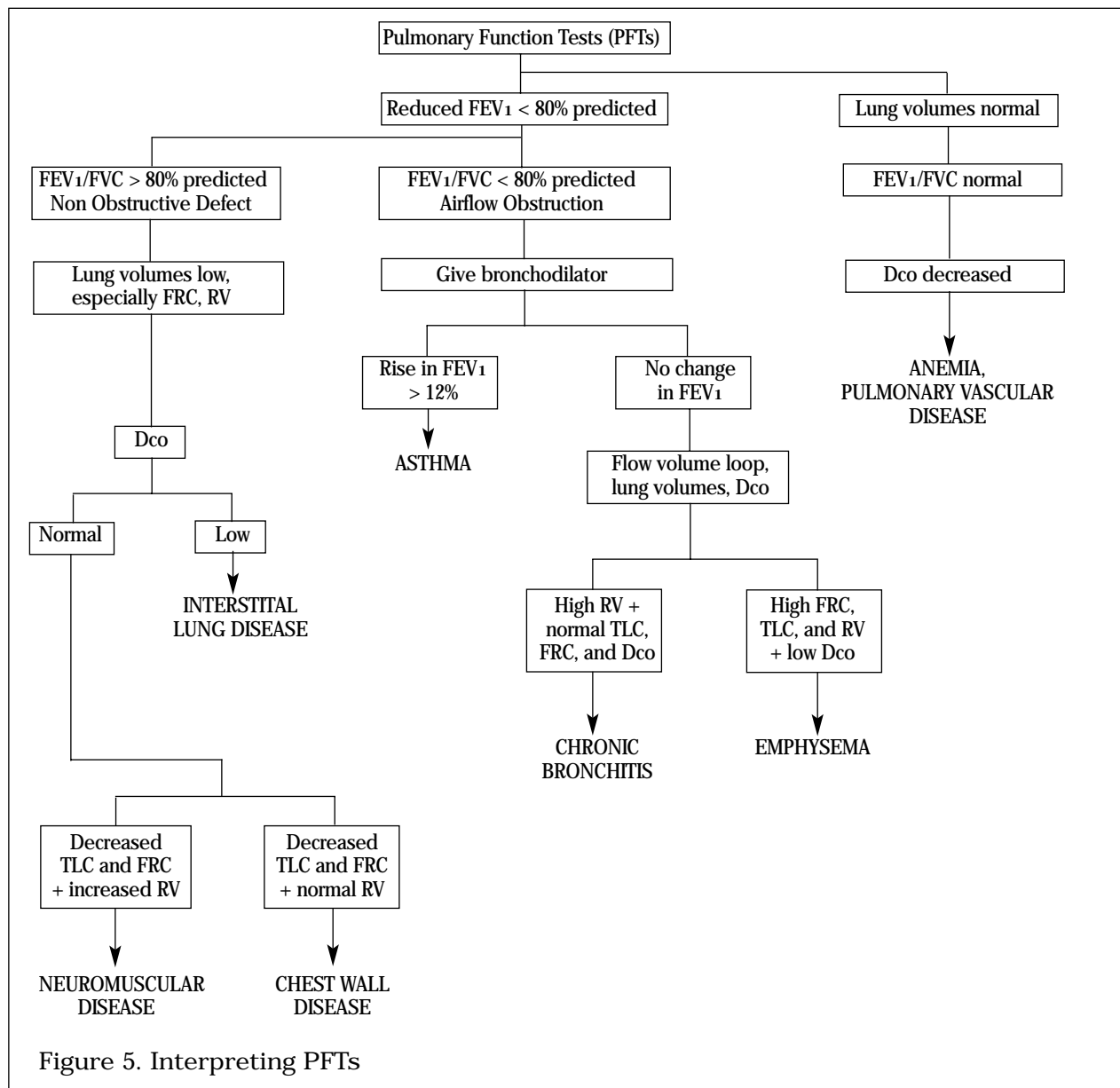
- ❑ characterized by obstructed airflow, decreased flow rates (most marked during expiration), air trapping (increased RV/TLC), and hyperinflation (increased FRC, TLC)
- ❑ DDx includes asthma, COPD, CF, bronchiectasis

Restrictive Lung Disease

- ❑ characterized by decreased lung compliance and lung volumes
- ❑ DDx includes interstitial lung, neuromuscular, or chest wall disease

Table 8. Comparison of Lung Flow and Volume Parameters in Obstructive vs. Restrictive Lung Disease

		Obstructive	Restrictive
Flow Rates (i.e. Lung Mechanics)	FEV ₁ FVC FEV ₁ /FVC FEF ₂₅₋₇₅ =MMFR	↓ ↓ ↓ ↓	↓ or N ↓ ↑ or N ↑ or N
Lung Volumes	TLC FRC VC RV RV/TLC	↑ or N ↑ or N ↓ or N ↑↑ ↑	↓ ↓ ↓ ↓ N
Diffusing Capacity	Dco	↓ or N	↓ or N



- ❑ normal values for FEV₁ are approximately +/- 20% of the predicted values (for age, sex and height); race may affect predicted values

Clinical Pearl

- ❑ Dco decreases with: 1) decreased surface area, 2) decreased hemoglobin, 3) interstitial lung disease, and 4) pulmonary vascular disease

ARTERIAL BLOOD GASES (ABGs)

- ❑ provides information on acid-base and oxygenation status

Approach to Acid-Base Status

1. What is the pH? acidemic (pH < 7.35), alkalemic (pH > 7.45), or normal (pH 7.35-7.45)
2. What is the primary disturbance?
 - metabolic: change in HCO₃⁻ and pH in same direction
 - respiratory: change in PaCO₂ and pH in opposite direction

3. Has there been appropriate compensation? (see Table 9)
- metabolic compensation occurs over 2-3 days reflecting altered renal HCO_3^- production/excretion
 - respiratory compensation through ventilation control of PaCO_2 occurs immediately
 - inadequate compensation may indicate a second acid-base disorder

Disturbance	PaCO_2	HCO_3^-
Respiratory Acidosis		
Acute	10	1
Chronic	10	3
Respiratory Alkalosis		
Acute	10	2
Chronic	10	4
Metabolic Acidosis	1	1
Metabolic Alkalosis	3	10

4. If there is metabolic acidosis, what is the anion gap and osmolar gap? (see Nephrology Notes)
- anion gap = $[\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$; normal = 10-15 mmol/L
 - osmolar gap = measured osmolarity - calculated osmolarity
= measured - $(2[\text{Na}^+] + \text{glucose} + \text{urea})$; normal = 10

Differential Diagnosis of Respiratory Acidosis

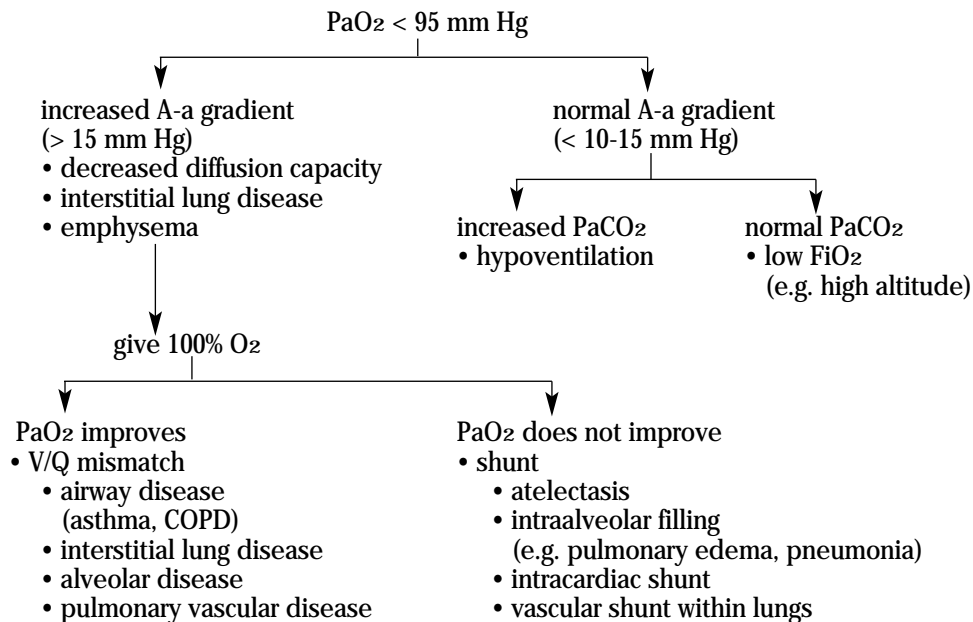
- characterized by increased PaCO_2 secondary to hypoventilation
- respiratory centre depression
 - drugs (anesthesia, sedatives)
 - trauma
 - increased ICP
 - post-encephalitis
 - stroke
 - sleep-disordered breathing (sleep apnea, obesity)
 - supplemental O_2 in chronic CO_2 retainers
- neuromuscular disorders
 - myasthenia gravis
 - Guillain-Barré syndrome
 - poliomyelitis
 - muscular dystrophies
 - myopathies
 - chest wall disease (obesity, kyphoscoliosis)
- airway obstruction (asthma, foreign body)
- parenchymal disease
 - COPD
 - pulmonary edema
 - pneumothorax
 - pneumonia
 - pneumoconiosis
 - ARDS
- mechanical hypoventilation

Differential Diagnosis of Respiratory Alkalosis

- characterized by decreased PaCO₂ secondary to hyperventilation
- hypoxemia
 - pulmonary disease (pneumonia, edema, PE, interstitial fibrosis)
 - anemia
 - heart failure
 - high altitude
- respiratory centre stimulation
 - CNS disorders
 - hepatic failure
 - gram-negative sepsis
 - drugs (ASA, progesterone, theophylline, catecholamines, psychotropics)
 - pregnancy
 - anxiety
 - pain
- mechanical hyperventilation

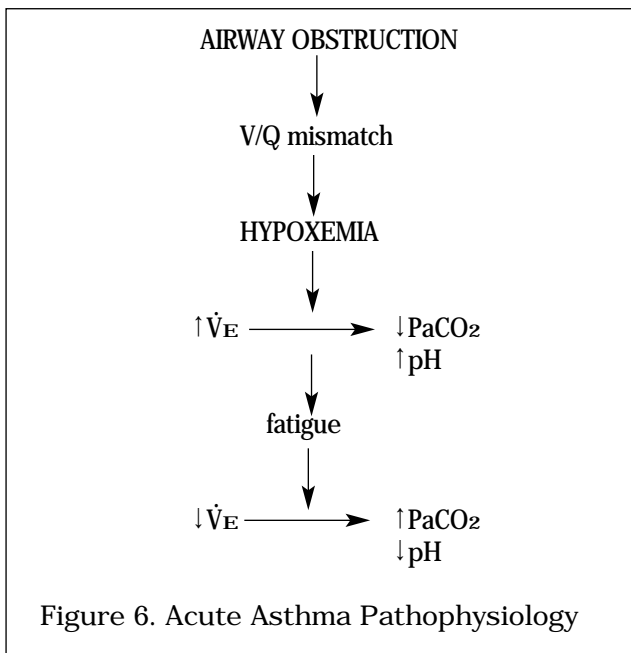
Approach to Oxygenation Status

1. What is the PaO₂? (normal = 95-100 mm Hg)
2. What is the AaDO₂? (normal < 15 mm Hg)
 - $AaDO_2 = PAO_2 - PaO_2$
 - $= [FiO_2(Patm - PH_2O) - PaCO_2/RQ] - PaO_2$
 - On room air: FiO₂ = 0.21, Patm = 760 mm Hg, PH₂O = 47 mm Hg, RQ = 0.8
 —> $AaDO_2 = [150 - 1.25(PaCO_2)] - PaO_2$
 - the normal AaDO₂ increases with age
3. What is the cause of the hypoxemia?



ASTHMA

- ❑ characteristics
 - inflammation of the airways, infiltration of inflammatory cells (eosinophils, lymphocytes), development of edema
 - hyperactive airway smooth muscle with reversible airflow limitation (bronchoconstriction)
 - results in airway obstruction (see Figure 6)
- ❑ common (7-10% of adults), especially in children (10-15%)
- ❑ most children with asthma improve significantly in adolescence
- ❑ asthma triad: asthma, ASA/NSAID sensitivity, nasal polyps
- ❑ often family history of atopy (asthma, allergic rhinitis, eczema)
- ❑ triggers
 - URTIs
 - allergens (pet dander, house dusts, molds)
 - irritants (cigarette smoke, air pollution)
 - drugs (NSAIDs, β -blockers)
 - preservatives (sulphites, MSG)
 - non-specific (emotion/anxiety, cold air, exercise, gastroesophageal reflux)
 - often no identifiable trigger



Symptoms

- ❑ SOB, wheezing, cough (especially nocturnal), chest tightness

Signs

- ❑ tachypnea
- ❑ wheezing
- ❑ respiratory distress
 - accessory muscle use, tracheal tug, nasal flare, intercostal muscle indrawing, pulsus paradoxus, inability to speak (indicates severe asthma)
- ❑ life threatening episode
 - silent chest, fatigue, cyanosis, diminished respiratory effort and/or level of consciousness

Profile of Patients at Risk for Severe Asthma

- ❑ previous non-fatal episodes
 - intubation

- ICU admission
- frequent ER visits
- loss of consciousness during asthma attack
- ❑ ominous symptoms and signs
 - night-time symptoms
 - limited activities of daily living
 - use of β_2 -agonist > 3 times per day
 - FEV₁ or PEF < 60%

Clinical Pearl

- ❑ The best predictor of a potential life-threatening attack is an excess consumption of short-acting β_2 -agonists

Investigations

- ❑ O₂ saturation
- ❑ PFTs (may not be possible during severe attack)
 - spirometry demonstrates variable airflow obstruction (decreased FEV₁/FVC, FEV₁ variable or improves > 12% after bronchodilator; FVC also decreases due to gas trapping)
 - lung volumes normal or slightly increased
 - Dco normal
 - provocation testing: asthmatics will readily bronchoconstrict after inhaling low doses of methacholine, histamine, or even saline (= airway hypersensitivity)
- ❑ ABGs
 - decreased PaO₂ during attack (V/Q mismatch)
 - decreased PaCO₂ in mild asthma due to hyperventilation
 - normal or increased PaCO₂ ominous as patient is no longer able to hyperventilate (worsened airway obstruction or respiratory muscle fatigue)

Treatment

- ❑ 3 components of treatment
 - short-term relief with bronchodilators (β_2 agonists, theophylline (not used as first-line), anticholinergics)
 - long-term prevention with anti-inflammatory meds (inhaled corticosteroids, cromolyn, nedocromil, or oral LRA)
 - asthma education
 - characteristics of the disease
 - causal factors
 - objectives of treatment, including side effect profiles
 - lifestyle modifications
- ❑ medication plan
 - mild asthma (minimal symptoms, normal flow rates)
 - inhaled β_2 -agonist (e.g. salbutamol 2 puffs QID PRN)
 - +/- low-dose inhaled steroids (< 800 ug/d)
 - moderate asthma (< 12 puffs of β_2 -agonist/wk, > 3 hr relief, FEV₁ > 60%)
 - high-dose inhaled steroids (> 800 ug/d)
 - β_2 -agonist PRN
 - +/- long-acting β_2 -agonist
 - +/- theophylline
 - +/- LRA
 - severe asthma (unable to do daily activities or does not meet criteria for moderate asthma)
 - oral steroids (e.g. prednisone 0.5 mg/kg po)
 - β_2 -agonist
 - +/- anticholinergic (e.g. ipratropium bromide)
 - +/- LRA

Clinical Pearl

- ❑ Remember to step-down therapy to lowest doses which control symptoms/signs of bronchoconstriction
- ❑ management of life-threatening episode
 - supportive therapy: sit up, O₂ by mask, cardiac monitoring, oximetry, IV fluids
 - continuous β_2 -agonist and anticholinergics given by nebulizer or meter dose inhaler
 - methylprednisolone 125 mg IV in ER, 1-2 mg/kg/day in divided doses
 - intubation if decreasing LOC, exhaustion, cyanosis, acidemia, silent chest

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

- ❑ characterized by irreversible/minimally reversible airflow obstruction
- ❑ includes chronic bronchitis and emphysema; usually coexist to variable degrees in most patients

Emphysema

- ❑ anatomical definition: dilatation and destruction of air spaces distal to the terminal bronchiole without obvious fibrosis
- ❑ decreased elastic recoil of lung parenchyma causes decreased expiratory driving pressure, airway collapse, and air trapping
- ❑ 2 types
 - centriacinar (respiratory bronchioles predominantly affected)
 - typical form seen in smokers
 - primarily affects upper lung zones
 - panacinar (respiratory bronchioles, alveolar ducts, and alveolar sacs affected)
 - responsible for less than 1% of emphysema cases
 - primarily affects lower lobes
 - think of α -1-antitrypsin deficiency (normal (MM), heterozygote (MZ), homozygote (ZZ))
 - ZZ can develop emphysema in their thirties, especially smokers

Clinical Presentation: Pink Puffer (Type A)

- ❑ PaO₂ normal or mildly decreased (i.e. "pink")
- ❑ do not get significant V/Q mismatch because destruction of alveolar walls destroys alveolar capillaries as well
- ❑ major symptom is dyspnea and increased minute ventilation (i.e. "puffer")
- ❑ other clinical features
 - exertional dyspnea with minimal cough
 - tachypnea
 - hyperinflation/barrel chest
 - may use accessory muscles of respiration
 - hyperresonant on percussion (absent cardiac dullness)
 - decreased diaphragmatic excursion
 - decreased breath sounds
 - thin (anorexia, increased work of breathing)
 - pneumothorax due to formation of bullae
 - more work of breathing than Type B
- ❑ investigations
 - CXR
 - hyperinflation (more than 6 anterior ribs seen above diaphragm in midclavicular line)
 - flat hemidiaphragm (seen on lateral film)

- increased AP diameter, increased retrosternal airspace
- bullae
- reduced peripheral vascular markings
- small heart
- ABGs
 - PaO₂ and PaCO₂ are normal or mildly decreased
- PFTs
 - decreased FVC, FEV₁, FEV₁/FVC, and FEF₂₅₋₇₅
 - increased lung volumes/air trapping (RV, TLC, RV/TLC)
 - decreased Dco
 - prolonged FVC (bedside test where stethoscope placed over trachea; prolonged if expiration > 5 seconds)

Chronic Bronchitis

- clinical diagnosis defined as chronic cough and sputum production on most days for at least 3 consecutive months in 2 successive years
- obstruction due to narrowing of the airway lumen by mucosal thickening and excess mucus
- usually due to smoking but air pollution increasingly important
- exacerbations due to respiratory tract infections (typically viral), air pollution, bronchospasm, mucus plugging, and CHF
- some have features of asthma and chronic bronchitis (asthmatic bronchitis)

Clinical Presentation: Blue Bloater (Type B)

- often cyanotic due to hypoxemia (i.e. "blue")
- V/Q mismatch significant
- frequently obese and may have peripheral edema from RVF (cor pulmonale) (i.e. "bloater")
- clinical features
 - chronic productive cough is major symptom
 - dyspnea is mild and starts after the cough
 - sputum often purulent
 - crackles, wheezes
 - hemoptysis
- hypoxemia leads to secondary polycythemia and to pulmonary vasoconstriction causing pulmonary HTN and eventually cor pulmonale
- normal lung compliance
- investigations
 - CXR (see Colour Atlas K11, K12)
 - normal or increased bronchovascular markings
 - enlarged heart with cor pulmonale
 - ABGs
 - decreased PaO₂ due to V/Q mismatch
 - normal or increased PaCO₂ due to abnormal central CNS respiratory drive and increased work of breathing
 - exacerbations can cause progression into a hypercapnic/hypoxemic type of respiratory failure (noted by a change in arterial pH)
 - PFTs
 - decreased FVC, FEV₁, FEV₁/FVC, and FEF₂₅₋₇₅
 - normal TLC
 - increased RV/TLC
 - Dco may be normal
 - prolonged FVC

Treatment of COPD

Maintenance Therapy

- smoking cessation (FEV₁ declines slower in nonsmokers)
- immunization with influenza vaccine and Pneumovax
- adequate nutrition and exercise conditioning
- rehabilitation: chest physio, general conditioning to improve exercise tolerance
- elimination of occupational and environmental respiratory allergens/irritants
- prompt treatment of respiratory infections
- bronchodilators
 - quaternary anticholinergic i.e. ipratropium bromide (Atrovent) has fewer CV side effects and longer duration of action
 - sympathomimetic i.e. β_2 -agonist may be added to regimen (synergy)
- theophylline may be useful in select population
- corticosteroids may be useful in patients with severe but stable COPD who are symptomatic with maximum bronchodilation; patients need oral steroid trial to assess efficacy
- home O₂: see below for indications
- α -1-antitrypsin replacement for documented deficiency (evidence is lacking and treatment is very expensive)
- lung transplant, volume reduction surgery

Acute Exacerbations

- defined as increase in dyspnea, effort intolerance, change in cough/volume of sputum
- assess ABCs, consider assisted ventilation if decreasing LOC or poor ABGs
- supplemental O₂ (controlled FiO₂)
- 1st line: sympathomimetics (rapid onset of action and have minimal side effects with inhalation therapy)
- anticholinergics are used concurrently with β_2 -agonist
- theophylline: 3rd line agent used to augment respiratory muscle contractility (important side effects including cardiac arrhythmias)
- corticosteroids have been shown to accelerate recovery from acute exacerbation
- antibiotics often used to treat precipitating infection

Indications for Home O₂

- PaO₂ < 55 mm Hg or PaO₂ < 60 mm Hg with erythrocytosis (Hct > 55%) or cor pulmonale
- hypoxemia must persist after 3 weeks of maximal therapy in an otherwise stable patient
- PaO₂ maintained between 65-80 mm Hg during wakeful rest and increased by 1 L/minute during exercise or sleep as determined by oximetry

Prognosis in COPD

- factors
 - severity of airflow limitation
 - development of complicating factors such as hypoxemia or cor pulmonale
- average decline in FEV₁
 - 25 mL/year in normal healthy people
 - 75 mL/year for COPD (this rate approaches the normal rate with cessation of smoking)
- 5-year survival
 - FEV₁ < 1 L = 50%
 - FEV₁ < 0.75 L = 33%

BRONCHIECTASIS

- an irreversible dilatation of airways due to inflammatory destruction of airway walls resulting in persistently infected mucus
- once bronchiectasis is established *Pseudomonas aeruginosa* is the most common pathogen

Etiology

- obstruction
 - tumours
 - foreign bodies
 - thick mucus
 - infection superimposed on obstruction may contribute to airway destruction
- post-infection (results in dilatation of bronchial walls)
 - TB
 - measles
 - pertussis
 - pneumonia
 - allergic bronchopulmonary aspergillosis
- impaired defences (leads to interference of drainage, chronic infections, and inflammation)
 - hypogammaglobulinemia
 - CF
 - defective leukocyte function
 - ciliary dysfunction (Kartagener's syndrome: triad of bronchiectasis, sinusitis, and situs inversus)

Clinical Presentation

- chronic cough
- purulent sputum (but 10-20% have a dry cough)
- hemoptysis which may be massive
- recurrent pneumonia
- clubbing
- local crackles (inspiratory and expiratory)
- wheezes

Diagnosis

- PFTs
 - often demonstrate obstructive pattern but may be normal
- CXR (see Colour Atlas K2)
 - often nonspecific abnormalities in the involved area ("tram tracking" - parallel narrow lines radiating from hilum due to thickened bronchi)
- thoracic CT diagnostic ("signet ring" - dilated bronchi with thickened walls)

Treatment

- postural drainage/physiotherapy
- antibiotics
- vaccination: influenza and Pneumovax
- bronchodilators
- surgical excision only for localized disease refractory to medical treatment

CYSTIC FIBROSIS (CF)

- C1- transport dysfunction: thick secretions from exocrine glands (lung, pancreas, skin, gonads) and blockage of secretory ducts
- results in severe lung disease and pancreatic insufficiency
- clinical presentation and treatment (see Pediatrics Notes)

Investigations

- sweat chloride test
 - increased concentrations of sodium, chloride, and potassium
 - > 60 mmol/L is diagnostic in children
 - heterozygotes have normal sweat tests (and no symptoms)
- PFTs
 - characteristic of obstructive airway disease
 - early on, only small airways will be affected
 - later on, characteristic of obstructive disease with airflow limitation, hyperinflation, decreased Dco
- ABGs
 - hypoxemia, hypercapnia later in disease with eventual respiratory failure and cor pulmonale
- CXR
 - hyperinflation, increased pulmonary markings, bronchiectasis

Prognosis

- median survival age is 31 years for male and 30.5 for females
- death usually due to lung disease (pneumonia, respiratory failure, cor pulmonale)

INTERSTITIAL LUNG DISEASE

Pathophysiology

- inflammatory process in the alveolar walls --> thickening and destruction of pulmonary vessels and fibrosis of interstitium leading to
 - decreased lung compliance
 - decreased lung volumes
 - impaired diffusion
 - hypoxemia without hypercarbia (V/Q mismatch) due to vasoconstriction and fibrosis
 - pulmonary HTN and subsequent cor pulmonale secondary to hypoxemia and blood vessel destruction

Due to Unknown Etiologic Agents (65%)

- idiopathic pulmonary fibrosis
- sarcoidosis
- PIE syndrome
- associated with collagen vascular disease
- cryptogenic organizing pneumonia (bronchiolitis obliterans +/- organizing pneumonia)

Due to Known Etiologic Agents (35%)

- hypersensitivity pneumonitis
- pneumoconioses
- drug-induced (chemotherapeutic, cytotoxic)
- radiation-induced

Clinical Presentation

- SOB, especially on exertion with decreasing SaO₂
- dry crackles
- +/- dry cough
- clubbing
- features of cor pulmonale

Investigations

- CXR (see Colour Atlas K1)
 - decreased lung volumes, reticulonodular pattern, Kerley B lines, hilar/medistinal adenopathy, lytic bone lesions
 - DDx of interstitial CXR pattern: pulmonary fibrosis, pulmonary edema (CHF), PCP, TB, sarcoidosis, pneumoconiosis, lymphangitic carcinomatosis
- PFTs
 - restrictive pattern (decreased lung volumes and compliance)
 - normal FEV₁/FVC (> 70-80%)
 - FEF₂₅₋₇₅ may be decreased due to lower lung volumes
 - flow rates are actually normal or supernormal when corrected for absolute lung volume
 - Dco decreased due to less surface area for gas exchange
- ABGs
 - hypoxemia and normal or decreased PaCO₂

Clinical Pearl

- The CXR can be normal in up to 15% of patients with interstitial lung disease

UNKNOWN ETIOLOGIC AGENTS

IDIOPATHIC PULMONARY FIBROSIS

- a diagnosis of exclusion
- also known as cryptogenic fibrosing alveolitis or usual interstitial pneumonitis
- commonly presents between ages 40-75
- additional clinical features
 - fatigue
 - anorexia
 - arthralgia
 - weight loss
 - cyanosis
 - clubbing
- lab tests (nonspecific)
 - ESR increased
 - hypergammaglobulinemia/hypocomplementemia < 10%
 - ANA and RF positive in 10%
- CXR
 - lower lung: reticulonodular or reticular pattern
 - generally bilateral and relatively diffuse
 - no pleural or hilar involvement
- biopsy
 - to exclude granulomas (found in sarcoidosis and hypersensitivity pneumonitis)
- treatment
 - steroids +/- immunosuppressants
 - mean lifespan of 5 years after diagnosis

SARCOIDOSIS

- multi-system disease with lung involvement in 90%
- characterized by noncaseating granulomas throughout body
- often discovered as bilateral hilar lymphadenopathy on incidental CXR
- in such patients, 2/3 are asymptomatic and 1/3 may have cough, fever, arthralgia, malaise, or erythema nodosum
- if interstitial disease also present, may have dyspnea, chest pain, nonproductive cough (crackles rare)

Clinical Pearl

- Sarcoidosis is more common in blacks and women. Sarcoid is silent on auscultation.
- as fibrosis occurs, CXR shows reticulonodular pattern especially in upper zones
- common extrapulmonary manifestations
 - eye involvement (anterior uveitis)
 - skin involvement (skin papules, erythema nodosum)
 - peripheral lymphadenopathy
 - hepatosplenomegaly
 - arthralgia
- less common extra-pulmonary manifestations involve bone, heart, CNS, and kidney
- Lofgren's syndrome = erythema nodosum, bilateral hilar lymphadenopathy, fever, and arthralgias

Laboratory Abnormalities

- hypercalcemia, hypercalciuria in 10%
- lymphopenia (decreased T cells)
- increased ESR
- hypergammaglobulinemia
- elevated ACE

Diagnosis

- biopsy
 - transbronchial or mediastinoscopic biopsy of lymph node for granulomas
 - in ~75% of cases transbronchial biopsy shows granulomas in the parenchyma even if the CXR is normal

Staging

- radiographic, based on CXR
 - Stage 0: no CXR changes
 - Stage I: bilateral hilar lymphadenopathy
 - Stage II: bilateral hilar lymphadenopathy and diffuse interstitial disease
 - Stage III: interstitial disease only (reticulonodular pattern)
 - Stage IV: pulmonary fibrosis (honeycombing)

Treatment

- 85% of stage I resolve spontaneously
- 50% of stage II resolve spontaneously
- steroids for persistent pulmonary infiltrates, PFT abnormalities, hypercalcemia, or involvement of eye, CNS, kidney, or heart

Prognosis

- approximately 10% mortality secondary to progressive fibrosis of lung parenchyma

PULMONARY INFILTRATES WITH EOSINOPHILIA (PIE SYNDROME)

- a broad group of disorders
 - peripheral eosinophilia and pulmonary infiltrates occur in five relatively well characterized disorders and may occur in patients with lymphoma, sarcoidosis, RA, or TB

Löffler's Syndrome

- transient and migrating peripheral lung infiltrates and eosinophilia
- often idiopathic but may be associated with parasitic infestation or certain drugs (ASA, MTX, imipramine, penicillins, sulfonamides, tetracyclines, INH)
- asymptomatic to mildly symptomatic (fever and cough) without auscultatory findings on examination of the chest
- CXR usually resolves spontaneously within two to six weeks or upon withdrawal of the offending drug

Chronic Eosinophilic Pneumonia

- infiltrates of eosinophils and macrophages in the interstitium and alveolar spaces
- commonly presents as fever, night sweats, cough +/- hemoptysis in a middle-aged woman (similar presentation to TB)
- 2/3 of cases have a very high eosinophil count ($> 25 \times 10^9$) and a very high ESR (100 mm/hour)
- diagnosis
 - clinical based on history, eosinophilia, and typical CXR
 - confirmed by rapid radiological and clinical response to corticosteroids, usually within 48 hours

Clinical Pearl

- The CXR in chronic eosinophilic pneumonia shows a peripheral alveolar infiltrate referred to as the "photographic negative of pulmonary edema"

Allergic Bronchopulmonary Aspergillosis

- airway colonization with *Aspergillus* causes an inflammatory reaction (not infection) which can lead to proximal bronchiectasis
- classic presentation: an asthmatic with an exacerbation of symptoms, low grade fever, migratory infiltrates on CXR and expectoration of golden brown mucus plugs (loaded with *Aspergillus mycelia*)
- diagnosis
 - positive culture
 - presence of serum precipitins of *A. fumigatus* (70% of patients)
 - elevation of specific IgE (> 1000 ng/mL)
 - positive skin test (immediate and/or delayed)
- treatment consists of blunting the immune response to the organism with corticosteroids, not eradication of *Aspergillus*
- commonly leads to remission but recurrence as corticosteroid treatment is tapered is also common

Tropical Eosinophilia

- cough, wheeze, and fever (especially at night) in someone who has recently visited the tropics
- positive filarial complement fixation test
- CXR: diffuse bilateral micronodules

Churg-Strauss Syndrome (see Pulmonary Vasculitis)

ASSOCIATED WITH COLLAGEN VASCULAR DISEASE

(see Pulmonary Vasculitis)

CRYPTOGENIC ORGANIZING PNEUMONIA
(BRONCHIOLITIS OBLITERANS WITH
ORGANIZING PNEUMONIA- BOOP)

- acute inflammation of bronchioles with granulation tissue and mononuclear cell infiltrate plugs
- idiopathic but may follow toxic fume inhalation/viral infection in children; associated with connective tissue diseases, idiopathic pulmonary fibrosis, and hypersensitivity pneumonitis
- presents over weeks to months with systemic and respiratory symptoms, may have URTI 2-4 months prior to SOB
- CXR: patchy infiltrates with alveolar pattern
- treatment: corticosteroids (responds faster and more frequently than idiopathic pulmonary fibrosis)

Clinical Pearl

- ❑ The CXR and CT often display a “ground glass” appearance

KNOWN ETIOLOGIC AGENTS

HYPERSENSITIVITY PNEUMONITIS

- ❑ also known as extrinsic allergic alveolitis
- ❑ granulomas present, airway centred
- ❑ acute +/- chronic reaction to inhaled organic antigens
- ❑ exposure usually related to occupation or hobby
 - farmer's lung (thermophilic actinomycetes)
 - bird fancier's lung (bird droppings)
 - humidifier lung (*Aureobasidium pullulans*)
- ❑ acute presentation (4-6 hours after exposure)
 - dyspnea, cough, fever, chills, malaise
 - PFTs: modestly and transiently restrictive
 - CXR: diffuse infiltrates
 - Type 3 (immune complex) reaction
- ❑ chronic presentation
 - insidious onset
 - dyspnea, cough, malaise, anorexia, weight loss
 - PFTs: progressively restrictive
 - CXR: predominantly upper lobe, nodular/reticulonodular pattern
 - Type 4 (cell mediated, delayed hypersensitivity) reaction
- ❑ in both acute and chronic reaction, serum precipitins detectable; however, neither sensitive nor specific
- ❑ treatment
 - avoidance of further antigen exposure as chronic changes are irreversible
 - steroids for persistent disease

PNEUMOCONIOSES

- ❑ reaction to inhaled inorganic dusts 0.5-5 µm in size
- ❑ no effective treatment, therefore key is exposure prevention through the use of protective equipment

Asbestosis

- ❑ workers at risk: insulation, shipyard, construction, brake linings
- ❑ usually need > 10-20 years of exposure; may develop with shorter but heavier exposure
- ❑ CXR
 - fibrosis: linear streaking, especially at the bases
 - asbestos exposure can also cause pleural thickening (+/- calcification) or pleural effusion
- ❑ microscopic examination characteristically reveals ferruginous bodies: yellow-brown rod-shaped structures which represent asbestos fibers coated in macrophages
- ❑ asbestos exposure also increases risk of bronchogenic CA and malignant mesothelioma
- ❑ clubbing is much more likely in asbestosis than silicosis or coalworker's pneumoconiosis

Silicosis

- ❑ workers at risk: sandblasters, rock miners, quarry workers, stone cutters
- ❑ generally need > 20 years of exposure; may develop with much shorter but heavier exposure
- ❑ CXR: upper lobe reticulonodular disease
- ❑ when nodules become larger and coalescent, disease has changed from simple silicosis to complicated silicosis (progressive massive fibrosis)
- ❑ possible hilar lymph node enlargement (frequent calcification)
- ❑ risk factor for mycobacterial infection (i.e. TB)

Coal Worker's Pneumoconiosis (CWP)

- simple CWP
 - no signs or symptoms
 - CXR: multiple nodular opacities, mostly upper lobe
 - respiratory function well preserved
- complicated CWP (also known as progressive massive fibrosis)
 - dyspnea
 - CXR: opacities larger and coalesce
- only small minority progress to complicated

Drug-Induced

- chemotherapeutics: bleomycin, mitomycin, busulfan, cyclophosphamide, MTX
- amiodarone
- gold
- nitrofurantoin

Radiation-Induced

- early pneumonitis: 1-3 months post-exposure
- late fibrosis: 6-12 months post-exposure
- infiltration conforms to the shape and field of the irradiation

PULMONARY VASCULAR DISEASE

PULMONARY VASCULITIS

Wegener's Granulomatosis

- triad: necrotizing granulomatous lesions of the upper and lower respiratory tract, focal necrotizing lesions of arteries and veins and focal glomerulonephritis
- generalized symptoms of fever, anorexia, weight loss
- CXR (see Colour Atlas K5)
 - solitary or multiple lesions, 1-10 cm in diameter, with a marked tendency to cavitate
- definitive diagnoses by positive C-ANCA, renal or lung biopsy
- treatment: corticosteroids and cyclophosphamide
- prognosis: excellent with treatment (complete and long term remission in > 90% of patients)

Churg-Strauss Syndrome (Allergic Granulomatosis and Angiitis)

- blood eosinophilia
- presents as late-onset asthma (prodromal phase that can last for years)
- followed by constitutional symptoms of malaise, fever, weight loss, and a life-threatening systemic vasculitis involving the lungs, pericardium and heart, kidneys, skin, and peripheral nervous system
- treatment: corticosteroids and cyclophosphamide sometimes effective

Goodpasture's Syndrome

- rapidly progressive glomerulonephritis and hemoptysis
- mediated by an anti-GBM which cross-reacts with BM of pulmonary endothelium
- onset of disease may follow an influenza infection
- renal biopsy shows linear immunofluorescence
- CXR: may be normal but alveolar infiltrates may be seen if hemorrhage is profuse
- treatment
 - acutely: corticosteroids; plasmapheresis to remove anti-GBM antibodies
 - immunosuppressive therapy (corticosteroids, cyclophosphamide) to decrease anti-GBM antibody production
 - severe/unresponsive cases: bilateral nephrectomy

Systemic Lupus Erythematosus (SLE)

- lungs and/or pleura are involved in > 50% of patients
- classical findings
 - pleural effusion (common)
 - pulmonary vasculitis

- diffuse interstitial lung disease (relatively uncommon)
- acute lupus pneumonitis and pulmonary hemorrhage
- diaphragmatic weakness
- PE (due to lupus anticoagulant)

Rheumatoid Arthritis (RA)

- classical findings
 - pulmonary rheumatoid nodules
 - pleural effusions
 - diffuse interstitial lung disease (rare)
 - pulmonary vasculitis
 - cryptogenic organizing pneumonia
 - bronchiolitis obliterans

Scleroderma

- technically not a vasculitis since vessel wall changes are due to fibrosis without actual inflammation
- scleroderma most often affects the lungs and can cause severe interstitial fibrosis and/or pulmonary HTN
- may also have lung disease secondary to recurrent aspiration if esophageal dysfunction is present
- pleural disease uncommon
- may have increased incidence of lung cancer

Clinical Pearl

- Scleroderma is the most common collagen vascular disease to affect the lung

PULMONARY HYPERTENSION

- resting pulmonary artery pressure is > 30/10 mm Hg with a mean > 25 mm Hg

Primary Pulmonary Hypertension

- idiopathic change in arterial walls
- commonly complain of dyspnea, fatigue, syncope, chest pain
 - disease of young women (20-40 years)
 - positive serology (ANA) > 30%
 - patients frequently have Raynaud's syndrome
 - treatment: vasodilators, long term anticoagulation, transplantation
 - prognosis: poor, with 2-3 year mean survival from time of diagnosis
 - may be associated with the use of anorexic drugs (e.g. aminorex, fenfluramine)

Secondary Causes of Pulmonary Hypertension

Cardiac Disease (Passive)

- increased LAP (e.g. chronic LVE, mitral stenosis)
- increased pulmonary vascular flow
 - as with a L → R shunt (ASD, VSD, PDA)
 - as right sided pressure increases due to increased flow, pressure eventually becomes greater than left sided pressure resulting in a R → L shunt and cyanosis (irreversible Eisenmenger's complex)

Pulmonary Vasoconstriction (Reactive)

- primary response to hypoxia but also to acidosis from hypercapnia (i.e. with chronic lung disease)
- note: chronic hypoxia also causes polycythemia which will increase viscosity and increase pulmonary arterial pressure

Loss of Pulmonary Vessels (Destructive)

- loss of vascular bed surface area as with interstitial lung disease/pulmonary fibrosis, emphysema, scleroderma, pneumonectomy, multiple lobectomies, bronchiectasis, CF
- pulmonary arterial pressure may be normal at rest but increased with exercise due to insufficient recruitment/distention of vessels

Pulmonary Vascular Occlusion (Obstructive)

- e.g. PE, schistosomiasis, veno-occlusive disease

Clinical Presentation

- symptoms
 - dyspnea
 - fatigue
 - substernal chest pain
 - syncope
 - symptoms of underlying disease
- signs
 - loud, palpable P2
 - RV heave
 - right sided S4 (due to RVH)
 - if RV failure: right sided S3, increased JVP, positive HJR, peripheral edema, TR

Investigations

- CXR (see Colour Atlas K3, K4)
 - enlarged central pulmonary arteries
 - cardiac changes due to RVH/failure (filling of retrosternal air space)
- ECG
 - RVH/strain and RA enlargement, rightward axis deviation
- 2-D echo doppler assessment of RVSP
- cardiac catheterization: direct measurement of pulmonary artery pressures
- spiral CT and PFTs to rule out lung disease
- V/Q scan +/- pulmonary angiogram to rule out thromboembolic disease

Management

- O₂ if hypoxia
- treat underlying condition
- phlebotomy for polycythemia (rarely required)
- treatment of exacerbating factors
 - smoking
 - sedatives
 - obesity
 - infection
- CCB/vasodilators (prostacyclin, NO)
- lung transplant

Clinical Pearl

- Survival is best predicted by hemodynamic profile

PULMONARY EMBOLI (PE)

- thrombi usually start in calf, but must propagate into proximal veins (i.e. thigh) to create a sufficiently large thrombus for a clinically significant PE
- only 50% of patients have previous clinical evidence of DVT (i.e. tenderness, swelling of lower extremity)
- always suspect PE if patient suddenly collapses 1-2 weeks after surgery

Risk Factors (Virchow's Triad)

- stasis
 - immobilization: bed rest, prolonged sitting during travel, immobilization of an extremity after fracture
 - obesity, CHF
 - chronic venous insufficiency
- endothelial cell damage
 - post-operative complications, trauma
- hypercoagulable states
 - underlying CA (particularly adenocarcinoma)
 - high dose exogenous estrogen administration
 - pregnancy, post-partum
 - coagulopathies: inherited deficiencies of antithrombin III, protein C, protein S, activated protein C resistance, antiphospholipid antibody, hyperhomocysteinemia, factor V Leiden mutation
 - prior history of DVT/PE, family history

Other Causes (all rare)

- tumour cells/fragments
- fat
- amniotic fluid
- foreign bodies
- air

Clinical Presentation

- respiratory symptoms/signs (neither sensitive nor specific)
 - tachypnea
 - SOB +/- wheeze
 - pleuritic chest pain or non-pleuritic non-central chest pain
 - hemoptysis
 - SaO₂ < 92%
 - pleural rub
- other (neither sensitive nor specific)
 - tachycardia +/- hypotension
 - syncope
 - +/- fever, elevated white count
 - leg symptoms

Chronic Thromboemboli

- progressive SOB due to pulmonary HTN
- in severe hemodynamic compromise
 - increased pulmonary arterial pressure, RVH (RV heave, loud/palpable P2, right-sided S4)
 - if RV failure (right sided S3, distention of jugular veins), TR
 - decreased LV filling (decreased cardiac output, syncope, shock)

Investigations

- CXR
 - frequently normal
 - Hampton's hump- cone-shaped area of opacification representing atelectasis/infarction
 - Westermark's sign- area of oligemia/decreased vascular markings (difficult to assess without prior films)
 - rarely - dilatation of proximal PA
 - often nonspecific (e.g. areas of atelectasis, elevation of a hemidiaphragm, pleural effusion)
- ECG
 - sinus tachycardia most common
 - RAD, S1Q3T3 with large embolus
- ABG
 - PaO₂ usually decreased, PaCO₂ decreased (due to increase in overall minute ventilation)
 - increased A-a gradient
- D-dimers (products of thrombotic/fibrinolytic process)
 - ELISA better than latex agglutination
 - D-dimer results alone do not rule in or out DVT/PE
 - need to use in conjunction with leg dopplers, other investigations
- venous duplex ultrasound or doppler (high specificity)
 - with leg symptoms
 - positive test can rule in a proximal or distal DVT
 - negative test can only rule out a proximal DVT
 - without leg symptoms
 - positive test rules in proximal DVT
 - negative test does not rule out a DVT (a possible non-occlusive DVT?)
- V/Q scan (very sensitive but low specificity)
 - order scan if
 - CXR normal/mild abnormalities, no COPD
 - normal leg dopplers but abnormal D-dimers
 - avoid scan if
 - CXR very abnormal or COPD
 - leg dopplers and D-dimers are normal
- pulmonary angiogram is gold standard but more invasive
- spiral CT scan with contrast may show larger, more proximal emboli
- ECHO: RVSP, RV hypokinesis

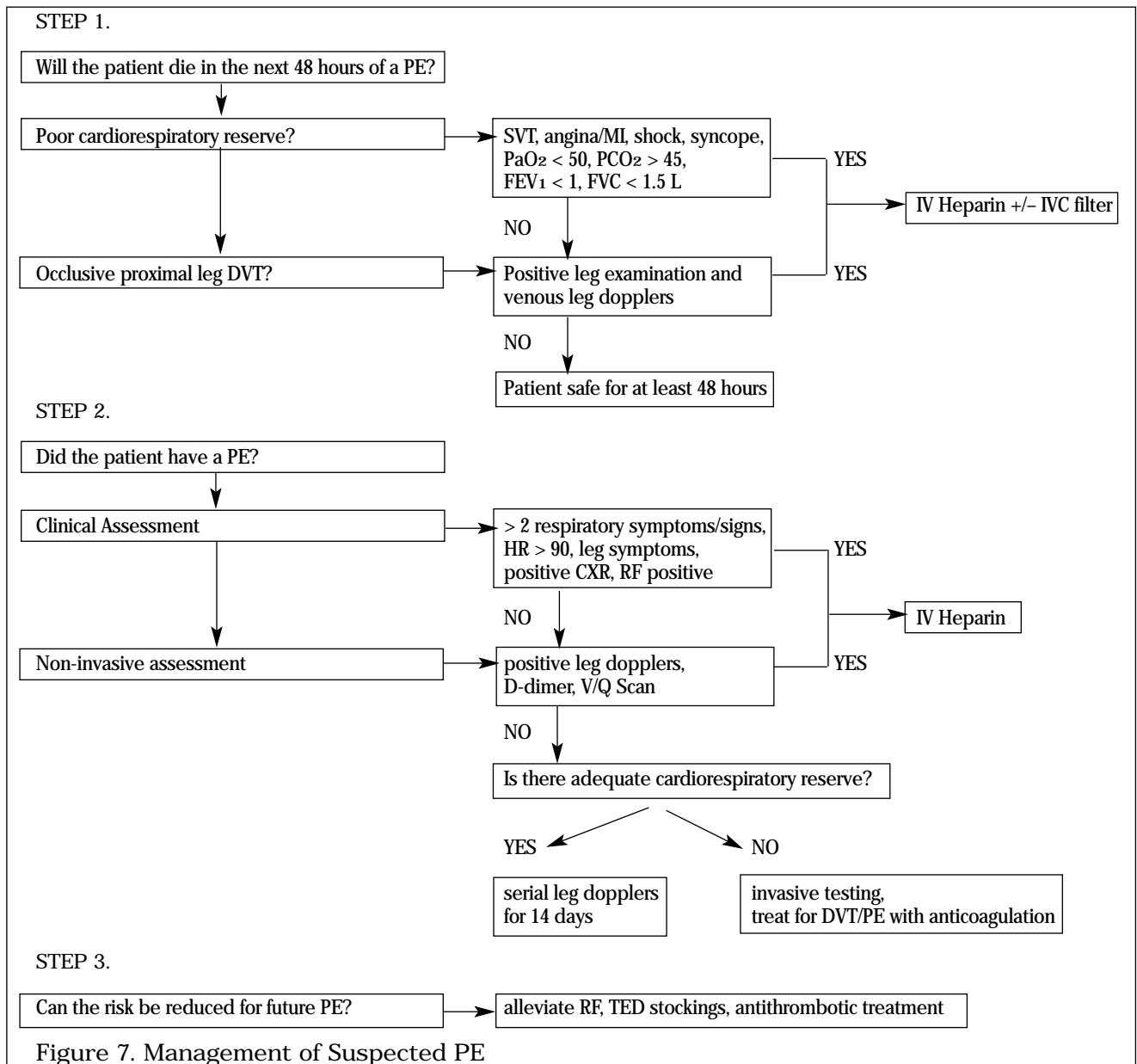


Figure 7. Management of Suspected PE

Treatment

- have patient sit up as it aids respiration
- O₂
- thrombolysis for large, hemodynamically significant emboli
- anticoagulation to prevent further emboli
 - IV heparin, LMWH initial treatment
- 6-24+ weeks oral warfarin (started one day after heparin started)
- IVC filter if
 - anticoagulant therapy contraindicated or fails
 - pulmonary vascular reserve is such that another PE would be fatal
- prevention: early postsurgical mobilization, prophylactic anticoagulation peri-operatively (e.g. heparin 5000 units SC BID)

MEDIASTINAL DISEASE

Masses

- ❑ > 50% asymptomatic (most of these are benign)
- ❑ symptomatic (50% are malignant)
 - chest pain, cough, dyspnea, recurrent respiratory infections
 - hoarseness, dysphagia, Horner's syndrome, facial/upper extremity edema (SVC compression)
 - paraneoplastic syndromes (e.g. myasthenia gravis (thymomas))
- ❑ anterior compartment (from sternum to anterior border of pericardium)
 - 4 T's (thymoma, thyroid enlargement, teratoma, thoracic aortic aneurysm)
 - lymphoma, CA, lipoma
- ❑ middle compartment (between anterior and posterior pericardium)
 - pericardial cyst, bronchogenic cyst, lymphoma, CA, lymph node enlargement, aortic aneurysm
- ❑ posterior compartment (between posterior pericardium and vertebral column)
 - neurogenic tumours (meningocele), enteric cysts, lymphomas, diaphragmatic hernias, esophageal lesions, aortic aneurysm
- ❑ investigations
 - CXR, CT, biopsy (mediastinoscopy, percutaneous needle aspiration or biopsy)
- ❑ treatment
 - if possible, surgical excision
 - if malignant, possibly radiotherapy and chemotherapy post-op

Mediastinitis

- ❑ acute
 - most common as complication of endoscopy (e.g. esophageal perforation providing entry point for infection)
 - can also occur after esophageal surgery
 - also due to tumour necrosis
 - clinical features: fever, prostration, substernal pain, Hamman's sign (auscultatory "crunch" during cardiac systole with pneumomediastinum and mediastinal compression)
 - treatment
 - antibiotics, drainage, +/- surgical closure of perforation
- ❑ chronic
 - usually granulomatous process (e.g. histoplasmosis, TB, syphilis)

PLEURAL EFFUSIONS

- ❑ normally up to 25 mL of pleural fluid present in pleural space
- ❑ symptoms
 - dyspnea (varies with size of effusion)
 - pleuritic chest pain
 - rarely asymptomatic
- ❑ signs
 - trachea deviates away from effusion
 - ipsilateral decreased expansion
 - decreased tactile fremitus
 - dullness to percussion
 - decreased breath sounds
 - bronchial breathing and egophony at upper level
 - pleural friction rub
- ❑ investigations
 - CXR
 - must have > 250 mL of pleural fluid for visualization
 - upper border of density appears concave (if horizontal, then probably a hydro-pneumothorax)
 - small effusion: blunting of posterior costophrenic angle in lateral film
 - fluid will shift in decubitus film unless fluid is loculated
 - in supine film, fluid will appear as general haziness

- thoracentesis (essential!): analyze fluid for
 - protein, LDH (transudate vs. exudate, see Table 10)
 - Gram stain, Ziehl-Neilsen stain (TB), culture
 - cell count and differential (neutrophils vs. lymphocytes)
 - cytology (malignancy, infection)
 - low glucose (RA, TB, empyema, malignancy)
 - rheumatoid factor, ANA, complement
 - amylase (pancreatitis, esophageal perforation)
 - pH (in empyema < 7.2; in TB and mesothelioma < 7.3)
 - blood (mostly traumatic, malignancy, PE with infarction)
 - TG (chylothorax from thoracic duct leakage, mostly due to trauma, lung CA, lymphoma)
- pleural biopsy: for TB or malignancy
- U/S: detects small effusions and can guide thoracentesis
- ❑ treatment depends on cause, +/- drainage if symptomatic
- ❑ to determine if transudate or exudate, use fluid from thoracentesis and blood sample (taken at same time); all criteria for transudate must be fulfilled (see Table 10)

Table 10. Laboratory Values in Transudative and Exudative Pleural Effusion

	Transudate	Exudate
pleural protein/serum protein	< 0.5	> 0.5
pleural LDH/serum LDH	< 0.6	> 0.6
pleural LDH (alternatively)	< 2/3 upper limit of normal serum LDH	> 2/3 upper limit of normal serum LDH

Causes of Transudates

- ❑ increased capillary hydrostatic pressure
 - CHF (both RHF and LHF)
 - fluid overload
 - constrictive pericarditis
- ❑ decreased plasma oncotic pressure
 - nephrotic syndrome
 - cirrhosis, hepatic failure
 - other causes of hypoalbuminemia (e.g. protein losing enteropathy)

Causes of Exudates

- ❑ may be due to increased leakiness of pleural capillaries
- ❑ neoplastic
 - lung CA (35%)
 - lymphoma (10%)
 - metastases: breast (25%), ovary, kidney
 - mesothelioma
- ❑ inflammatory
 - noninfectious
 - collagen vascular diseases (RA, SLE)
 - subdiaphragmatic irritation (pancreatitis)
 - PE and infarction
 - chylothorax - caused by obstruction of thoracic duct
 - chronic CHF
 - infectious
 - pneumonia (parapneumonic effusion)
 - empyema, lung abscess
 - subphrenic abscess

Clinical Pearl

- ❑ Transudates are usually bilateral and exudates are usually unilateral

EMPHYEMA

- ❑ pus in the pleural space
- ❑ symptoms: fever, pleuritic chest pain
- ❑ usually due to contiguous spread from lung infection
 - most common with anaerobic infections
- ❑ may also result from infection through the chest wall from trauma, surgery
- ❑ effusion characterized by PMNs, organisms may be visible on Gram stain
 - lymphocytic in TB
- ❑ treatment
 - antibiotics, chest tube drainage, surgical drainage if loculated

PNEUMOTHORAX

- ❑ air in pleural space makes intrapleural pressure positive instead of negative, preventing lung inflation
- ❑ etiology
 - primary (simple)
 - spontaneous rupture of subpleural bleb of lung at apex into pleural space
 - predominantly healthy young tall males
 - secondary (complicated)
 - trauma, especially iatrogenic (e.g. CVP lines, post thoracentesis, mechanical ventilation)
 - alveolar rupture due to increased alveolar pressure
 - rupture of subpleural bleb (e.g. COPD)
 - necrosis of lung tissue adjacent to pleura surface (e.g. pneumonia, abscess, PCP, lung CA)
- ❑ symptoms
 - can be asymptomatic
 - acute onset pleuritic chest pain
 - acute onset dyspnea
- ❑ signs
 - ipsilateral diminished expansion and breath sounds
 - trachea deviates away
 - decreased tactile/vocal fremitus
 - hyperresonant percussion note
 - ipsilateral diminished breath sounds
- ❑ CXR (see Colour Atlas K8)
 - if small: separation of visceral and parietal pleura seen as fine crescentic line parallel to chest wall at apex
 - if large: increased density and decreased volume of lung on side of pneumothorax
 - see Diagnostic Medical Imaging Notes
- ❑ treatment
 - small pneumothoraces resolve spontaneously
 - large ones or those complicating underlying lung disease require placement of a chest tube connected to underwater seal +/- suction
 - pleurodesis with sclerosing agent for repeated episodes
 - bleb resection

Tension Pneumothorax

- ❑ emergency! (see Emergency Medicine Notes)

ASBESTOS-RELATED PLEURAL DISEASE

- ❑ exudative pleural effusion
- ❑ pleural thickening or calcification, pleural plaque (Hyalinosis Simplex)
- ❑ mesothelioma
 - smoking is not a risk factor
 - primary malignancy
 - 20+ years after even light asbestos exposure
 - persistent chest pain, dyspnea, cough, pleural thickening, bloody pleural effusion, weight loss, clubbing
 - diagnosis: by biopsy (pleuroscopic or open)
 - treatment: rarely successful (average survival < 1 year)

PNEUMONIA

- infection of the pulmonary parenchyma
- normal lung defences
 - cough reflex, reflex closure of the glottis
 - tracheobronchial mucociliary transport
 - alveolar macrophages
 - inflammatory immune system response
- risk factors impairing lung defences
 - smoking, alcohol use, ETT/nasotracheal intubation, respiratory therapy, hypoxemia, acidosis, toxic inhalation, pulmonary edema, uremia, malnutrition, immunosuppression, mechanical obstruction, DM, splenectomy, elderly age, decreased LOC, risk of aspiration
- pathogenesis
 - aspiration of upper airway organisms (*S. pneumoniae*, *S. pyogenes*, *Mycoplasma*, *H. influenzae*, *M. catarrhalis*)
 - inhalation of infectious aerosols (*Mycoplasma*, *TB*, *influenza*, *Legionella*, *Histoplasma*, *C. psittaci*, Q fever)
 - other: hematogenous (*S. aureus*, *Fusobacterium*), direct (trauma)
- clinical presentation
 - typical and atypical pneumonia syndromes (see Table 11)
 - elderly often present atypically; altered LOC is sometimes the only sign
 - epidemiology affects clinical presentation and treatment

Table 11. Clinical Features of Typical vs. Atypical Pneumonia

Clinical Feature	Typical	Atypical
organisms involved	<i>S. pneumoniae</i> , <i>H. influenzae</i> , endemic oral flora	<i>Mycoplasma</i> , <i>Chlamydia</i> , viral, <i>Legionella</i>
onset	sudden	subacute
cough	productive	dry
chest pain	pleuritic (some cases)	uncommon
other symptoms	chills, rigors, SOB, nausea, diarrhea	headache, myalgia,
temp > 38°C	common	uncommon
HR > 110	common	uncommon
consolidation signs*	common	uncommon
WBC count	increased	normal or slightly
CXR	neutrophilia	increased
(see Colour Atlas K10)	unilateral, localized, alveolar	bilateral, diffuse, interstitial +/- alveolar
* dullness to percussion, increased tactile and vocal fremitus, bronchial breath sounds, crackles, bronchophony, egophony, whispered pectoriloquy		

- general investigations
 - routine labs: determine prognosis and need for hospitalization
 - ABGs: assess adequacy of gas exchange in more severe cases
 - sputum culture and Gram stain, blood cultures, pleural fluid cultures, serology/viral cultures (epidemiology)
 - CXR (see Colour Atlas K10)
 - shows distribution, extent of infiltrate +/- cavitations
 - bronchoscopy +/- washings for severely ill patients unresponsive to treatment and the immunocompromised
- DDx
 - acute bronchitis, effusion (can be due to pneumonia), PE, CA, pulmonary edema, bronchiectasis, HSP, BOOP, drug-induced pneumonitis, chronic eosinophilic pneumonia
- criteria for hospitalization
 - age > 65
 - significant comorbidity (e.g. DM, immunosuppression, neoplasm)
 - leukopenia NYD
 - *S. aureus*, gram-negative rods, anaerobes as etiological agents

- infectious complications (empyema, arthritis, endocarditis, meningitis)
- failure of outpatient management, inability to take oral medications
- severe tachypnea, tachycardia, hypotension, hypoxemia, altered LOC
- ☐ treatment
 - empiric based on epidemiology
 - age < 60 or outpatient: macrolide (e.g. erythromycin)
 - age > 60 or underlying comorbidity: second generation cephalosporin, β lactam or β lactamase inhibitor, or TMP-SMX +/- macrolide
 - hospitalized patients: third generation cephalosporin, or β lactam or β lactamase inhibitor +/- macrolide
 - severe disease: macrolide + third-generation cephalosporin +/- rifampin

Table 12. Common Organisms in Pneumonia

Community Acquired		Nosocomial	HIV-associated	Alcoholics
Healthy Adults	Elderly/Comorbidity*/Nursing Home			
<i>S. pneumoniae</i> <i>Mycoplasma</i> <i>Chlamydia</i> <i>H. influenzae</i> viral	<i>S. pneumoniae</i> <i>H. influenzae</i> gram-negative bacilli <i>S. aureus</i> oral anaerobes <i>Legionella</i>	enteric gram-negative rods <i>Pseudomonas</i> <i>S. aureus</i> oral anaerobes	<i>Pneumocystis carinii</i> TB	<i>Klebsiella</i> enteric gram-negative rods <i>S. aureus</i> anaerobes (aspiration)
* comorbidity includes COPD, CHF, diabetes, renal failure, recent hospitalization				

Pathogens Causing Pneumonia (see Infectious Diseases Notes)

Streptococcus pneumoniae

- ☐ most common bacterial pneumonia
- ☐ at risk: secondary complication to a viral RTI
- ☐ clinical presentation: abrupt onset with fever, rigor, pleurisy, and "rusty" sputum; watch for meningeal involvement
- ☐ CXR: classically causes a lobar consolidation
- ☐ sputum: PMNs and gram-positive oval-shaped diplococci
- ☐ labs: leukocytosis (10,000-30,000 is common, but may be leukopenic on admission)
- ☐ treatment: penicillin G (erythromycin if penicillin allergic; vancomycin, ceftriaxone or cefotaxime if resistant) x 7-10 days
- ☐ prevention: Pneumovax (give once only)

Staphylococcus aureus

- ☐ sudden onset bronchopneumonia
- ☐ at risk: secondary complication of influenza infection or in hospitalized patient with underlying disease, severe diabetes, drug abusers, immunocompromised
- ☐ clinical presentation: high fever, chills, progressive dyspnea, cyanosis, cough, pleuritic pain, quite toxic-appearing
- ☐ complications: cavitation (necrotizing pneumonia), pneumothorax, empyema, pneumatoceles in children
- ☐ sputum: PMNs and gram-positive cocci in clusters, chains, and pairs
- ☐ treatment: cloxacillin or vancomycin (if penicillin allergic) x 7-10 days and drain any empyema

Mycoplasma pneumoniae

- ☐ most common atypical pneumonia; "walking pneumonia"
- ☐ at risk: young adults (especially 5-15 years old)
- ☐ incubation: 12-14 days (insidious onset)
- ☐ clinical presentation: constitutional illness with fever, persistent hacking cough +/- scant sputum, chills uncommon

- ❑ extrapulmonary features: headache, diarrhea, non-exudative pharyngitis, skin (e.g. erythema multiforme), arthralgia, myalgia, hemolytic crises, bullous myringitis, CNS (e.g. myelitis, Guillain-Barré syndrome, meningoenzephalitis)
- ❑ CXR: classically worse than clinical presentation; usually bilateral, patchy air-space disease
- ❑ sputum: more mononuclear cells and fewer PMNs than bacterial pneumonia, but mycoplasma not visualized
- ❑ labs: complement fixation shows significant titre rise in up to 80%, anti-I (IgM) increased in 50%, cold agglutinins, WBC not significantly increased (PMNs slightly elevated)
- ❑ treatment: erythromycin, doxycycline x 10-14 days

Legionella pneumophila

- ❑ Legionnaire's disease; found in contaminated water, air conditioners
- ❑ at risk: smokers, age > 65, male, immunocompromised, chronic lung disease, cancer, chronic heart and kidney disease
- ❑ incubation: 2-10 days
- ❑ clinical presentation: prominent nonrespiratory symptoms which may precede pulmonary problems; malaise, fever, GI symptoms, delirium, renal failure
- ❑ abrupt onset of cough, chills, dyspnea, pleuritis, bronchopneumonia, blood-streaked mucoid sputum
- ❑ sputum: gram-negative coccobacillary organisms stain poorly
- ❑ labs: immunofluorescent serology, *Legionella* urine antigen, BAL
- ❑ treatment: erythromycin x 2-3 weeks

Viral pneumonia

- ❑ most common cause of pneumonia in children (mostly RSV)
- ❑ < 10% of adult pneumonia (mostly influenza virus)
- ❑ at risk: influenza pneumonia in elderly; chronic heart, lung, or renal disease
- ❑ influenza predisposes to superimposed bacterial pneumonia, especially pneumococcal or *S. aureus*
- ❑ CXR: worse than clinical presentation
- ❑ sputum: more monocytes, fewer PMNs than bacterial pneumonia
- ❑ treatment: usually none, but if immunocompromised then amantadine (for influenza A) or ribavirin (for RSV)
- ❑ prevention: annual influenza vaccination

Hemophilus influenzae

- ❑ at risk: children, smokers, associated with COPD exacerbations
- ❑ encapsulated and unencapsulated strains cause lung infections
- ❑ clinical presentation: similar to pneumococcal pneumonia, lobar pneumonia
- ❑ sputum: gram-negative coccobacilli
- ❑ treatment: (lots of penicillin resistance) cephalosporin (second generation), TMP/SMX, quinolones, amoxicillin-clavulanate

Moraxella catarrhalis

- ❑ at risk: common in smokers, COPD patients, diabetics, patients with malignancies, alcoholics, patients on steroids; rare in normal adults
- ❑ clinical presentation: as typical pneumonia
- ❑ CXR: lobar consolidation
- ❑ sputum: gram-negative cocci, singly or in pairs
- ❑ treatment: tetracycline or doxycycline, TMP-SMX, cephalosporins, macrolides, fluoroquinolones

Enteric gram-negative rods (including *Pseudomonas aeruginosa*) pneumonia

- ❑ at risk: hospital/nursing home (50-70% of nosocomial pneumonias)
- ❑ bilateral bronchopneumonia
- ❑ complications: septic shock with bacteremia, abscess
- ❑ treatment: cephalosporin (third generation) +/- aminoglycoside or ciprofloxacin; *Pseudomonas aeruginosa* usually requires penicillin/cephalosporin + aminoglycoside sensitive to organism

Klebsiella pneumoniae

- ❑ at risk: alcoholics
- ❑ clinical presentation: explosive onset of fever, prostration; similar to pneumococcus; bloody sputum ("red currant jelly")
- ❑ complications: rapid cavitation, abscess, high mortality
- ❑ CXR: classically lobar consolidation with bulging fissure
- ❑ sputum: large gram-negative encapsulated rods
- ❑ treatment: cephalosporin and aminoglycoside; adequate drainage of empyema (can cause extensive scarring)

Anaerobic pneumonia

- ❑ at risk: those who cannot protect airway with risk of aspiration (i.e. patients with LOC, inhibited airway reflexes, seizures, alcoholics)
- ❑ clinical presentation: gradual onset, foul-smelling sputum
- ❑ complications: necrotizing pneumonia with abscess formation; empyema
- ❑ CXR: dependent areas of lung involved; usually infiltrates inferior segment of right upper lobe or apical segment of lower lobe
- ❑ sputum: tends to be a polymicrobial infection
- ❑ treatment: high dose penicillin G or clindamycin

Pneumocystis carinii

- ❑ at risk: patients on immunosuppressants or chemotherapy, AIDS when CD4 count < 200
- ❑ clinical presentation: atypical, concurrent opportunistic infections
- ❑ CXR (see Colour Atlas K9)
 - diffuse interstitial infiltration, often isolated to upper lobes
- ❑ sputum: Giemsa stain; lower yield in patients on prophylaxis; diagnosis may require BAL or transbronchial biopsy
- ❑ treatment: TMP-SMX, pentamidine, TMP-dapsone, clindamycin-primaquin, atovaquone; add corticosteroids if PaO₂ < 70 mm Hg or AaDO₂ > 35 mm Hg
- ❑ prevention: in AIDS, after an episode of PCP or when CD4 count < 200 use TMP-SMX, TMP-dapsone, or pentamidine

LUNG ABSCESS

- ❑ a localized cavity with pus resulting from tissue necrosis, with surrounding pneumonitis
- ❑ pathogenesis
 - aspiration of upper airway anaerobic organisms
 - inadequately treated pneumonia (especially *S. aureus*, *Klebsiella pneumoniae*)
 - bronchial obstruction (tumour, foreign body)
 - pulmonary infarction
 - septic emboli
- ❑ clinical presentation
 - acute or insidious with early symptoms like pneumonia
 - purulent sputum, may be blood streaked; putrid odor --> anaerobes
 - chronic abscess: weight loss, anemia, clubbing
 - physical signs of consolidation
- ❑ investigations
 - CXR (thick-walled cavity with fluid level), CT
 - sputum culture and Gram stain
 - transtracheal/thoracic aspiration, bronchoscopy with culture for anaerobes
- ❑ DDx
 - cavitating CA
 - bronchiectasis
 - TB, coccidioidomycosis
- ❑ treatment
 - Abx depending on culture and sensitivity, postural drainage
 - surgical drainage and resection are rarely necessary

FUNGAL INFECTIONS (see Infectious Diseases Notes)

Primary Pathogenic Fungi

- ❑ etiology: *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*
- ❑ pathogenesis
 - primary granulomatous lung infection
 - systemic hematogenous dissemination
 - fungus is usually destroyed if patient immunocompetent
 - persists as chronic systemic granulomatous infection in immunocompromised
- ❑ clinical presentation
 - usually asymptomatic or mild respiratory illness
 - acute pneumonia that resolves with granuloma formation and calcification
 - chronic cavitary pneumonia clinically and radiologically like TB or CA
 - disseminated disease: meninges, brain, bone, liver, spleen, kidney, joints, skin
- ❑ diagnosis: tissue biopsy for staining and culture
- ❑ treatment: amphotericin B, itraconazole

Opportunistic Fungi

Aspergillosis

- ❑ etiology: mostly *Aspergillus fumigatus*
- ❑ clinical presentation
 - allergic bronchopulmonary aspergillosis (see Pulmonary Infiltrates with Eosinophilia)
 - aspergilloma (fungus ball)
 - noninvasive ball of hyphae colonizes a preexisting lung cavity
 - ranges from asymptomatic to massive hemoptysis
 - CXR: round opacity surrounded by a thin lucent rim of air, often in upper lobes ("air crescent" sign)
 - invasive aspergillosis
 - at risk: immunosuppressed, especially neutropenics
 - severe symptoms with fever, cough, dyspnea, pleuritic pain, tends to cavitate
 - CXR: local or diffuse infiltrates +/- pulmonary infarction
 - endobronchial pulmonary aspergillosis
 - at risk: chronic lung disease
 - chronic cough and hemoptysis
- ❑ treatment: amphotericin B, itraconazole; resection of aspergilloma

Cryptococcosis

- ❑ etiology: *Cryptococcus neoformans*
- ❑ clinical presentation
 - acute: usually resolves spontaneously in immunocompetent people
 - chronic: intense pulmonary granulomatous reaction with hematogenous spread to brain causing fatal meningoencephalitis if not treated; immunocompromised patients at risk
- ❑ treatment: amphotericin B +/- flucytosine

Candidiasis

- ❑ etiology: *Candida albicans*
- ❑ clinical presentation
 - fever, septicemia
 - usually hematogenous spread to lungs
 - CXR: diffuse, vaguely nodular infiltrate visible only when numerous abscesses are present
- ❑ treatment: amphotericin B

MYCOBACTERIA

Mycobacterium tuberculosis

- ❑ pathogenesis
 - inhalation of aerosolized droplets from close contacts
 - development of granulomatous reactions in the lungs
 - local spread to lymph nodes and hematogenously to distant organs
 - lesions heal and fibrose in the immunocompetent
 - lesions proliferate in the immunocompromised
- ❑ clinical presentation
 - usually asymptomatic but may have fever, lassitude, erythema nodosum, cough, sputum
 - post-primary TB: reactivation of dormant organisms in immunocompromised patients; cough, purulent sputum, hemoptysis, weight loss, fever, sweats, malaise, anorexia, dyspnea, pleuritic chest pain
 - miliary TB (post-primary dissemination of multiple tiny granulomas in immunocompromised patients): fever, anemia, splenomegaly
- ❑ CXR (see Colour Atlas K6)
 - primary TB: nonspecific lower lobe calcified infiltrates, hilar and paratracheal node enlargement, pleural effusion
 - post-primary TB: cavitation in apical regions and posterior segments of upper lobe and/or superior segment of the lower lobes +/- calcification
 - miliary TB: uniformly distributed, very fine nodules (like seeds) throughout
- ❑ investigations
 - culture of involved sites and identification of acid-fast bacilli (Ziehl-Nielsen stain)
 - Mantoux Skin Test (see below)
 - CXR

Clinical Pearl

- ❑ Ghon Complex: CXR finding of a calcified nodule plus calcified hilar/mediastinal lymphadenopathy, pathognomonic of previous primary infection by TB

- ❑ treatment
 - INH and rifampin x 6 months with pyrazinamide x the first 2 months
 - multiple drug resistant strains (MDR-TB) should be treated with INH, rifampin, pyrazinamide, and ethambutol, then modified with sensitivities
- ❑ prophylaxis
 - INH +/- vitamin B₆ for 6-12 months for patients
 - with skin test conversion within the last two years
 - with positive skin test: < 35 years old, abnormal chest x-ray, immunocompromised or predisposed to TB
 - who are close contacts of someone with active TB
 - HIV contact of infected person
 - rifampin for contacts of INH-resistant TB carriers
 - the risk of developing TB in non-immunocompromised patients after skin test conversion is 1% per year for the first 5 years and 0.1% per year subsequently

Atypical Mycobacteria

- ❑ etiology: *M. avium intracellulare*, *kansasii*, and *xenopi*
- ❑ at risk: immunocompromised, elderly, chronic lung disease, malnourishment
- ❑ clinical presentation: similar to TB
- ❑ treatment: none without evidence of progression; usually multiple resistance to conventional antituberculous drugs, but new agents like macrolides, quinolones, and rifabutin in combination are effective

The Tuberculosis Skin Test (Mantoux Test)

- performed by intradermal injection of 0.1 ml of PPD (purified protein derivative) tuberculin containing 5 TU (tuberculin units)
- check 48-72 hours later for amount of induration
- guidelines for screening and contact management (see Community Health Notes)

Induration	Groups in which infection is presumed to be present at the indicated induration	Treatment
< 5 mm	Adolescents and children who are close contacts	Treat until 12 weeks after last exposure and then repeat the skin test
> 5 mm	Close contacts HIV-positive or unknown but at risk for HIV Upper lobe fibrosis	Treat all ages for 6-12 months Treat all ages for 12 months
> 10 mm	Silicosis High incidence of disease or high risk to others (from endemic areas, low SES, residents of long-term care facilities) or employees of health care facilities, schools, or child care facilities) With risk factor: IV drug users, HIV positive, recent close contact, recent skin test conversion, CXR abnormality	Treat all ages for 12 months (if not previously treated for active TB) or 4 months of multidrug regimen Treat all ages for 12 months (if not previously treated for active TB) or 4 months of multidrug regimen Treat if ages < 35 for 6-12 months Treat all ages for 6-12 months
> 15 mm	Medical conditions at increased risk of disease if infected (gastrectomy, malnutrition, chronic renal failure, diabetes, high-dose steroids or other immunosuppressives, malignancies) Low risk	Treat all ages for 6-12 months Treat age < 35 for 6-12 months

Conversion of TB Skin Test

- change in TB skin test within 2 years from < 10 mm to > 10 mm or an increase of 6 mm from previous skin test

Booster Phenomenon

- persons infected with TB many years ago may have waned skin reactivity
- persons tested many years later may not respond at all or may respond only weakly
- a second TB skin test within 3 weeks boosts the reaction size in such infected persons but does not sensitize uninfected persons
- if the initial TB skin test is negative, a second TB skin test is given; if the second TB skin is also negative, the individual has not been previously infected with TB; if the second TB skin test is positive, the individual has been previously infected with TB

APPROACH TO THE SOLITARY PULMONARY NODULE

(see Diagnostic Medical Imaging Notes)

- a round or oval, sharply circumscribed radiographic lesion up to 3-5 cm
- DDx
 - neoplasm (45%)
 - primary bronchogenic CA (70%)
 - benign (e.g. hamartoma, lipoma) (15%)
 - solitary metastasis (e.g. breast, sarcoma) (10%)
 - infection (53%)
 - TB, histoplasmosis, coccidiomycosis
 - other (2%)
 - vascular: A-V malformation, infarct
 - congenital: cyst
 - round pneumonia, round atelectasis, loculated effusion
- investigations (see Figure 8)
 - history and physical
 - CXR: always check old CXR first
 - CT thorax
 - sputum cytology: usually poor yield
 - bronchoscopy with biopsy or percutaneous biopsy: if sputum negative
 - resection: if lesion is suspicious and there is no diagnosis with biopsy
- typical CXR findings

benign <ul style="list-style-type: none"> • < 3 cm, round, regular • smooth margin • calcified pattern: central, "popcorn," diffuse, or concentric • usually no cavitation; if cavitated, wall is smooth and thin • satellite lesions • no other lung pathology • doubles in < 1 month or > 2 years 	vs.	malignant <ul style="list-style-type: none"> • > 3 cm, irregular, spiculated • ill-defined or notched margin • usually not calcified; if calcified, pattern is eccentric or speckled • cavitation with thick wall • no satellite lesions • may have pleural effusions, lymphadenopathy • doubles in > 1 month, < 2 years
---	-----	--

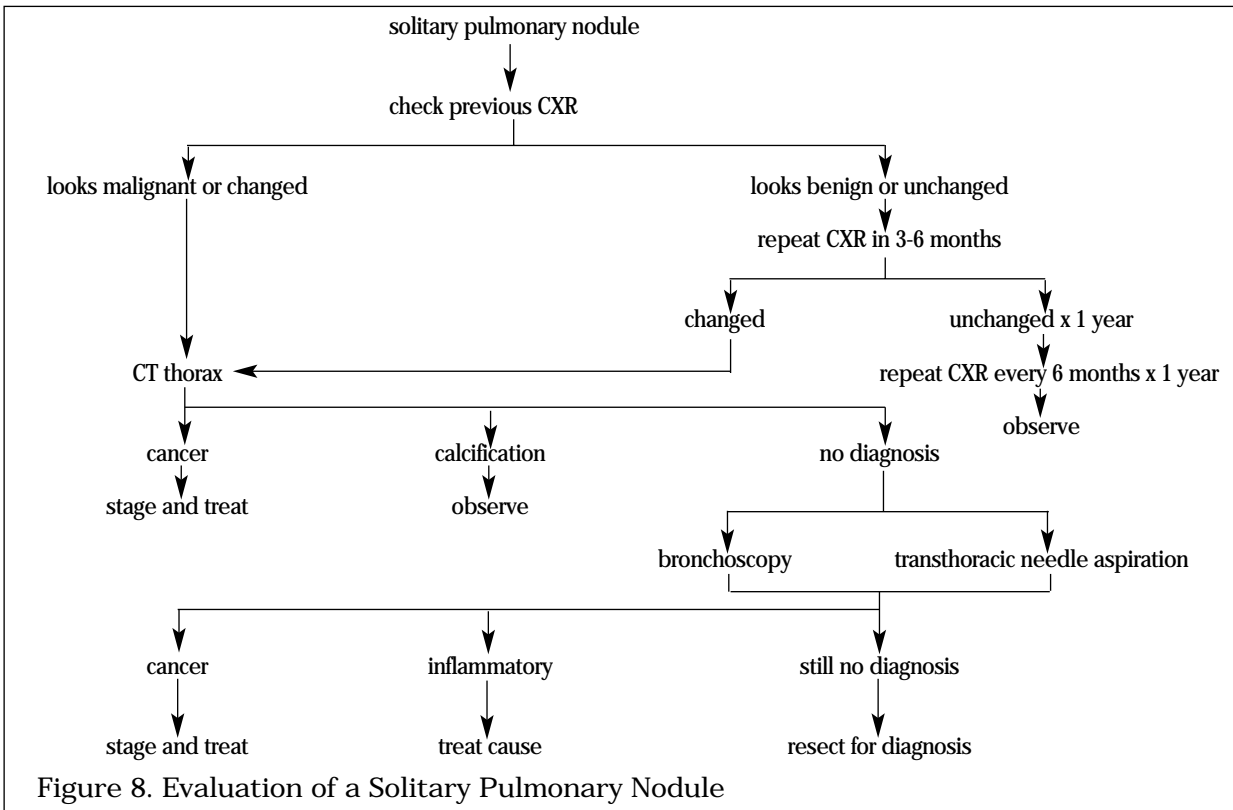


Figure 8. Evaluation of a Solitary Pulmonary Nodule

BENIGN

- ❑ less than 5% of all primary lung neoplasms
- ❑ hamartoma (most common), fibroma, lipoma, leiomyoma, hemangioma, papilloma
- ❑ clinical presentation: cough, hemoptysis, recurrent pneumonia, hamartoma (most common), fibroma, atelectasis
- ❑ CXR: clustered “popcorn” pattern of calcification is pathognomonic for hamartoma

MALIGNANT

Epidemiology

- ❑ incidence
 - most common CA in men and women
 - most common cause of CA death in men and women
- ❑ risk factors
 - cigarette smoking: 85% of lung CA related to smoking
 - asbestos
 - radiation: radon, uranium
 - arsenic, chromium, nickel
 - genetic damage
 - parenchymal scarring: granulomatous disease, fibrosis, scleroderma
 - passive exposure to cigarette smoke
 - air pollution: exact role is uncertain

Pathological Classification

- ❑ bronchogenic CA (90%) (for characteristics, see Table 14)
- ❑ bronchioloalveolar CA (5%)
- ❑ bronchial adenoma (3%)
- ❑ lymphoma
- ❑ secondary metastases: breast, colon, prostate, kidney, thyroid, stomach, cervix, rectum, testes, bone, melanoma

Cell Type	Frequency	Correlation with Smoking	Location	Histology	Metastasis
adenocarcinoma	35%	weak	peripheral	glandular; mucin producing	early, distant
squamous cell CA	30%	strong	central	keratin; intercellular bridges	slow, local invasion (may cavitate)
SCLC	25%	strong	central	oat cell, neuroendocrine origin in endobronchial (Kulchitsky) cells	disseminated at presentation
large cell CA	10%	yes	peripheral	anaplastic, undifferentiated	early, distant (may cavitate)

Clinical Presentation

- ❑ initial symptoms and signs
 - cough (75%); beware of chronic cough that changes in character
 - dyspnea (60%)
 - chest pain (45%)
 - hemoptysis (35%)
 - other pain (25%)
 - clubbing (21%)
 - constitutional signs (anorexia, weight loss, fever, anemia)
- ❑ local extension
 - lung, hilum, mediastinum, pleura: pleural effusion, atelectasis, wheezing
 - pericarditis, pericardial tamponade
 - esophageal compression: dysphagia
 - phrenic nerve: paralyzed diaphragm
 - recurrent laryngeal nerve: hoarseness

- superior vena cava syndrome: collateral circulation in chest and neck, facial/upper extremity edema and plethora, dyspnea, orthopnea, headache, nausea, syncope, visual changes, dizziness
- Pancoast's tumour (lung apex): Horner's syndrome, brachial plexus palsy
- rib and vertebral erosion
- ❑ distant metastasis: from lung to brain, bone, liver, adrenals
- ❑ paraneoplastic syndromes (a group of disorders associated with malignant disease, not related to the physical effects of the tumour itself) (see Table 15)
 - most often associated with SCLC
 - squamous cell CA is associated with hypercalcemia

Clinical Pearl

- ❑ 2/3 of primary lung CA is found in the upper lung; 2/3 of metastases in the lower lung (hematogenous spread secondary to increased blood flow to the base of the lung)

Table 15. Paraneoplastic syndromes

	Clinical Presentation	Associated Malignancy
Skeletal	hypertrophic pulmonary osteoarthropathy	bronchogenic CA (not SCLC)
Dermatologic	acanthosis nigricans dermatomyositis	lung CA bronchogenic CA
Endocrine	hypercalcemia (osteolysis or PTH) hypophosphatemia hypoglycemia Cushing's syndrome (ACTH) somatostatinoma syndrome SIADH	squamous cell CA squamous cell CA sarcoma SCLC bronchial carcinoid SCLC
Neuromyopathic	Eaton-Lambert syndrome polymyositis subacute cerebellar degeneration spinocerebellar degeneration peripheral neuropathy	SCLC
Vascular/Hematologic	nonbacterial endocarditis Trousseau's syndrome (migratory thrombophlebitis) DIC	bronchogenic CA
Renal	nephrotic syndrome	

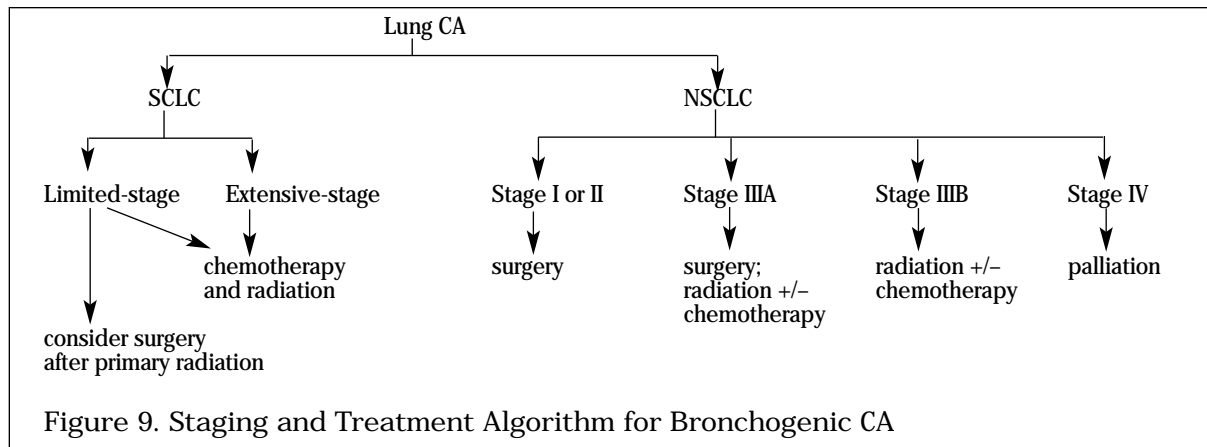
Investigations

- ❑ initial diagnosis
 - imaging: CXR (see Colour Atlas K7), CT
 - cytology: sputum
 - biopsy: bronchoscopy, percutaneous
- ❑ staging work-up
 - blood work: LETs/LFTs, calcium, ALP
 - imaging: CXR, CT thorax and abdomen, skeletal survey, bone scan, neuroimaging
 - invasive: bronchoscopy, mediastinoscopy, mediastinotomy, thoracotomy

Management of Bronchogenic CA

- ❑ clinical classification as SCLC or NSCLC
- ❑ staging SCLC
 - presents as early metastasis (i.e. poor prognosis, surgical cure impossible)
 - limited-stage: all disease within a single radiation port in chest and supraclavicular fossa

- extensive-stage: extends outside a single radiation port within the chest
- staging NSCLC (TNM staging)
 - stage I: negative nodal involvement, easily resectable tumour
 - stage II: easily resectable tumour, ipsilateral peribronchial or hilar nodes
 - stage IIIA: easily resectable tumour, ipsilateral mediastinal and subcarinal nodes; marginally resectable tumour +/- ipsilateral nodes
 - stage IIIB: any tumour with contralateral node involvement or local extension
 - stage IV: distant metastases



Therapy for Bronchogenic CA (see Figure 9)

- chemotherapy
 - cisplatin and etoposide
 - paclitaxel, vinorelbine, and gemcitabine are new NSCLC therapies
 - complications
 - acute: tumour lysis syndrome, infection, bleeding, myelosuppression, hemorrhagic cystitis (cyclophosphamide), cardiotoxicity (doxorubicin), renal toxicity (cisplatin), peripheral neuropathy (vincristine)
 - chronic: neurologic damage, leukemia, second primary neoplasms
- radiotherapy
- surgery
 - only chance for cure is resection when tumour is still localized
 - contraindications
 - any evidence of local extension or metastases
 - poor pulmonary status (i.e. unable to tolerate resection of lung)
 - patients with surgically resectable disease must undergo mediastinal node sampling since CT thorax is not accurate in 20-40% of cases
- palliative care for end-stage disease

Prognosis of Bronchogenic CA

- Five-year survival rates for different subtypes
 - squamous 25%
 - adenocarcinoma 12%
 - large cell carcinoma 13%
 - SCLC 1%
- SCLC has the poorest prognosis
 - greatest tendency to metastasize
 - 70% present with extensive disseminated disease at initial diagnosis
 - limited-stage: 15-20% cure rate
 - extensive-stage treated: median survival of 6 months, but can live up to two years with a rare cure (1%); untreated median survival is 2-3 months
- Five-year survival rate for NSCLC
 - Stage I 50%
 - Stage II 30%
 - Stage IIIA 15%
 - Stage IIIB 5%
 - Stage IV < 2%

Bronchioloalveolar CA

- ❑ a type of adenoCA that grows along the alveolar wall in the periphery
- ❑ may arise at sites of previous lung scarring (a scar CA)
- ❑ clinical presentation: similar to bronchogenic CA; late metastasis but 45% rate
- ❑ treatment and prognosis: solitary lesions are resectable with a 60% 5-year survival rate; overall survival rate is 25%

Bronchial Adenoma

- ❑ a group of benign tumours that rarely metastasizes
- ❑ bronchial carcinoid
 - atypical subtype of adenoma with a high metastasis rate (70% vs. 5%)
 - often in young adults; smoking not a risk factor
 - clinical presentation: follows a slow course, metastasizes late, can cause symptoms of carcinoid syndrome (flush, diarrhea, cardiac valvular lesions, wheezing)
 - treatment and prognosis: amenable to resection; 5-year survival is 95%

RESPIRATORY FAILURE

- ❑ due to impairment of gas exchange between ambient air and circulating blood
 - hypoxemic, hypercapnic
 - acute (life threatening), chronic (compensatory mechanisms activated)
- ❑ etiology
 - airway obstruction: COPD, bronchiectasis, CF, asthma, bronchiolitis
 - abnormal parenchyma: sarcoidosis, pneumoconiosis, fibrosing alveolitis, idiopathic pulmonary fibrosis, systemic sclerosis, lymphoma, drug-induced, pneumonia, pulmonary edema, pulmonary hemorrhage, ARDS
 - hypoventilation without bronchopulmonary disease: CNS disorder (drugs, increased ICP, spinal cord lesion, sepsis), neuromuscular (myasthenia gravis, Guillain-Barré, muscular dystrophies), chest wall (kyphoscoliosis, obesity)
- ❑ clinical presentation
 - signs of underlying disease
 - hypoxia: restlessness, confusion, cyanosis, coma, cor pulmonale
 - hypercapnia: headache, dyspnea, drowsiness, asterixis, warm periphery, plethora, increased ICP (secondary to vasodilation)
 - best assessed by serial ABGs

HYPOXEMIC RESPIRATORY FAILURE

- ❑ PaO₂ decreased, PaCO₂ normal or decreased
- ❑ pathophysiology
 - shunt
 - V/Q mismatch
 - low inspired FiO₂
 - hypoventilation
 - diffusion impairment
 - low mixed-venous oxygenation
- ❑ treatment
 - reverse the underlying pathology if possible
 - maintain oxygenation
 - enrichment of FiO₂: remember that if shunting and V/Q mismatch are the problems, supplemental O₂ is not nearly as effective (may need to use 60-100% O₂)
 - positive pressure: use of PEEP and CPAP will recruit alveoli and redistribute lung fluid
 - hemodynamic support: fluids, pressors, inotropes, reduction of O₂ requirements
 - if PaO₂ is less than 60 mm Hg and FiO₂ > 60% consider intubation and mechanical ventilation

HYPERCAPNIC RESPIRATORY FAILURE

- PaCO₂ increased, PaO₂ decreased
- pathophysiology
 - increased CO₂ production
 - increased dead space
 - decreased minute ventilation
- treatment
 - reverse the underlying pathology
 - correct exacerbating factors
 - clearance of secretions: suction with NTT or ETT
 - bronchodilators: decreases airway resistance
 - antibiotics
 - maintain oxygenation (see above)
 - in chronic hypercapnia, supplemental O₂ may decrease the hypoxic drive to breathe, BUT DO NOT deny oxygen if the patient is hypoxic
 - increased carbohydrate feeding can increase PaCO₂ in those with mechanical or limited alveolar ventilation; high lipids decreases PaCO₂
 - if PaCO₂ > 50 mm Hg and pH is severely acidic consider intubation and mechanical ventilation

ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

- respiratory failure associated with various acute pulmonary injury
- characterized by non-cardiogenic pulmonary edema, respiratory distress, hypoxemia
- usually part of Multiple Organ Dysfunction Syndrome

Etiology

- airway: aspiration (gastric contents, drowning), gas inhalation (oxygen toxicity, nitrogen dioxide, smoke), pneumonia
- circulation: sepsis (most common), shock, trauma, pancreatitis, DIC, multiple blood transfusions, embolism (fat, amniotic fluid), drugs (narcotics, sedatives)
- neurogenic: head trauma, intracranial hemorrhage, seizures

Pathogenesis

- disruption of alveolar capillary membranes (especially with sepsis)
 - > leaky capillaries --> interstitial and alveolar pulmonary edema
 - > reduced compliance, V/Q shunt, hypoxemia, and pulmonary HTN

Four Phases of Clinical Presentation

- beginning several hours after injury and lasting a few hours to days: hyperventilation, cyanosis on air, respiratory alkalosis, normal CXR
- tachypnea > 20/min, respiratory distress, marked hypoxemia, alkalosis, interstitial pulmonary edema on CXR
- hypoxemic respiratory failure
- cardiac arrest

Treatment

- treat underlying disorder (e.g. antibiotics if septic)
- support gas exchange: usually mechanical ventilation with PEEP
- minimize lung extravascular volume: lowest intravascular volume possible while maintaining adequate organ perfusion
- inotropic therapy (e.g. dopamine and dobutamine) if cardiac output inadequate
- Swan-Ganz catheter is useful for monitoring hemodynamics
- mortality: 50% die (infection is the most common cause)
- if patient survives, prognosis for recovery of lung function is good

MECHANICAL VENTILATION (see Anesthesia Notes)

- artificial means of supporting ventilation and oxygenation
- two main indications
 - hypoxemic respiratory failure: giving PEEP opens collapsed alveoli, decreasing the V/Q mismatch
 - hypercapnic respiratory failure: ventilator provides alveolar ventilation thereby decreasing the work of breathing, allowing respiratory muscles to rest
- ventilatory modes
 - assist-control ventilation (initial mode of ventilation)
 - ventilator delivers a minimum respiratory rate at a set tidal volume

- ventilator will also deliver a breath with each patient-initiated one
- intermittent mandatory ventilation
 - ventilator provides breaths at fixed rate and tidal volume
 - patient can breathe spontaneously without triggering ventilator
 - useful for weaning-off mechanical ventilation
- pressure-support ventilation
 - patient given a boost of pressure with each breath
 - patient determines the rate and duration of each breath
 - useful for weaning
 - noninvasive ventilation
 - achieved without intubation by using a nasal mask with BiPAP (a boost of pressure during inspiration and constant pressure during expiration)
- other modes and settings
 - inverse ratio ventilation, pressure-targeted ventilation, independent lung ventilation, high-frequency ventilation, partial liquid ventilation, mechanical ventilation with inhaled nitric oxide

SLEEP-RELATED BREATHING DISORDERS

- ❑ a group of disorders characterized by decreased airflow occurring only in sleep or worsening in sleep
 - ❑ sleep apnea
 - obstructive (no airflow with persistent respiratory effort): secondary to airway obstruction (e.g. uvula, pharyngeal wall)
 - central (no airflow with no associated respiratory effort): secondary to transient abolition of CNS drive to breathe
 - mixed (loss of hypoxic drive to breathe secondary to overcompensatory hyperventilation upon awakening from OSA-induced hypoxia)
 - ❑ hypoventilation syndromes
 - primary alveolar hypoventilation: idiopathic
 - respiratory neuromuscular disorders
 - obesity-hypoventilation syndrome (Pickwickian syndrome)
- Sleep Apnea
- ❑ diagnosed as 30 apneic episodes during a 7-hour nocturnal polysomnogram (sleep study) → 4 episodes/hour
 - ❑ risk factors: obesity, upper airway abnormality, neuromuscular disease, hypothyroidism, alcohol use, sedative use, nasal congestion, sleep deprivation
 - ❑ clinical presentation
 - secondary to arousal from sleep: morning headache, daytime somnolence, personality and intellectual change, insomnia, snoring
 - secondary to hypoxemia and hypercapnia: polycythemia, pulmonary HTN, cor pulmonale, CHF, systemic HTN, nocturnal angina
 - OSA typically presents in a middle-aged obese male snorer
 - CSA can be due to neurological disease
 - ❑ sleep study investigations
 - evaluates sleep staging, airflow, respiratory effort, ECG, FiO₂, periodic limb movements
 - indications
 - excessive daytime sleepiness
 - unexplained pulmonary HTN or polycythemia
 - disturbance of respiratory control in patients with daytime hypercapnia
 - titration of optimal nasal CPAP
 - assessment of objective response to interventions
 - ❑ treatment
 - modifiable factors: decrease alcohol and sedatives, weight loss, nasal decongestion, treat underlying medical conditions
 - OSA or MSA: nasal CPAP maintains airflow during inspiration; uvulopharyngoplasty, nasal septoplasty, tonsillectomy
 - CSA or hypoventilation syndromes: nasal BiPAP can assist ventilation; respiratory stimulants (e.g. progesterone) in select cases
 - tracheostomy rarely required and should be used as last resort