RESPIROLOGY

Dr. C. Chan and Dr. J. Granton
Sonya Cook and Jolene Brady, chapter editors
Leora Horn, associate editor

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PULMONARY PHYSIOLOGY

Ventilation (Alveolar)
- the prime determinant of arterial pCO₂
- 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 O₂, CO₂, and H⁺)
    - central (medulla): increased H⁺ / increased pCO₂ stimulates ventilation
    - peripheral (carotid body, aortic arch): decreased pO₂ 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 pO₂ or increased pCO₂, the pulmonary vessels constrict to decrease Q in order to maintain a 1:1 V/Q ratio

Imbalances in V/O Ratio
- V > Q —> dead space ventilation that does not contribute to gas exchange
- V < Q —> hypoxemia that can be corrected with supplemental O₂
- Q but no V —> shunt (i.e. blood bypasses the alveoli, resulting in hypoxemia that cannot be corrected with supplemental O₂)

Oxygenation
- occurs by diffusion through alveolar-capillary membrane to form oxygenated Hb within the red blood cell
- normal PaO₂ = 80-100 mm Hg (O₂ sat = 98%)
- normal PaCO₂ = 35-45 mm Hg

Clinical Pearl
- Bohr Effect is a shift in the O₂-Hb curve to the right due to an increase in H⁺, pCO₂, temperature, or 2,3-diphosphoglycerate. This shift facilitates O₂ unloading in peripheral capillaries.
- Due to the sigmoid shape of the O₂-Hb curve, an O₂ saturation of <90% corresponds to a very low pO₂ of < 60 mm Hg.

Lung Compensation in Hypoxemia and Hypercapnia
(see Figure 2)
## Table 1. Differential Diagnosis of Dyspnea

<table>
<thead>
<tr>
<th>Category</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
</tr>
<tr>
<td>Airway disease</td>
<td>Asthma*</td>
</tr>
<tr>
<td></td>
<td>COPD exacerbation*</td>
</tr>
<tr>
<td></td>
<td>upper airway obstruction (anaphylaxis, foreign body, etc)*</td>
</tr>
<tr>
<td></td>
<td>mucus plugging*</td>
</tr>
<tr>
<td>Parenchymal lung disease</td>
<td>ARDS*</td>
</tr>
<tr>
<td></td>
<td>Pneumonia*</td>
</tr>
<tr>
<td></td>
<td>interstitial lung disease</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
<td>PE*</td>
</tr>
<tr>
<td></td>
<td>pulmonary HTN</td>
</tr>
<tr>
<td></td>
<td>pulmonary vasculitis</td>
</tr>
<tr>
<td>Pleural disease</td>
<td>pneumothorax*</td>
</tr>
<tr>
<td></td>
<td>pleural effusion</td>
</tr>
<tr>
<td>Neuromuscular and chest wall disorders</td>
<td>polymyositis, myasthenia gravis, Guillain-Barré syndrome</td>
</tr>
<tr>
<td></td>
<td>kyphoscoliosis</td>
</tr>
<tr>
<td></td>
<td>C-spine injury*</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Elevated pulmonary venous pressure</td>
</tr>
<tr>
<td></td>
<td>LVF with pulmonary edema*</td>
</tr>
<tr>
<td></td>
<td>mitral stenosis</td>
</tr>
<tr>
<td>Decreased cardiac output</td>
<td></td>
</tr>
<tr>
<td>Severe anemia</td>
<td></td>
</tr>
<tr>
<td>Anxiety/psychosomatic*</td>
<td></td>
</tr>
</tbody>
</table>

* denotes causes that should be considered for acute dyspnea

## Table 2. Differential Diagnosis of Cough

<table>
<thead>
<tr>
<th>Category</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Airway irritants</strong></td>
<td>inhaled smoke, dusts, fumes</td>
</tr>
<tr>
<td></td>
<td>aspiration</td>
</tr>
<tr>
<td></td>
<td>gastric contents</td>
</tr>
<tr>
<td></td>
<td>oral secretions</td>
</tr>
<tr>
<td></td>
<td>foreign body</td>
</tr>
<tr>
<td></td>
<td>postnasal drip</td>
</tr>
<tr>
<td><strong>Airway disease</strong></td>
<td>URTI including postnasal drip and sinusitis</td>
</tr>
<tr>
<td></td>
<td>acute or chronic bronchitis</td>
</tr>
<tr>
<td></td>
<td>bronchiectasis</td>
</tr>
<tr>
<td></td>
<td>neoplasm</td>
</tr>
<tr>
<td></td>
<td>external compression by node or mass lesion</td>
</tr>
<tr>
<td></td>
<td>asthma</td>
</tr>
<tr>
<td></td>
<td>COPD</td>
</tr>
<tr>
<td><strong>Parenchymal disease</strong></td>
<td>pneumonia</td>
</tr>
<tr>
<td></td>
<td>lung abscess</td>
</tr>
<tr>
<td></td>
<td>interstitial lung disease</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Drug-induced</strong></td>
<td></td>
</tr>
</tbody>
</table>

## Table 3. Differential Diagnosis of Hemoptysis

<table>
<thead>
<tr>
<th>Category</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Airway disease</strong></td>
<td>acute or chronic bronchitis</td>
</tr>
<tr>
<td></td>
<td>bronchiectasis</td>
</tr>
<tr>
<td></td>
<td>bronchogenic CA</td>
</tr>
<tr>
<td></td>
<td>bronchial carcinoid tumour</td>
</tr>
<tr>
<td><strong>Parenchymal disease</strong></td>
<td>TB</td>
</tr>
<tr>
<td></td>
<td>lung abscess</td>
</tr>
<tr>
<td></td>
<td>pneumonia</td>
</tr>
<tr>
<td></td>
<td>miscellaneous</td>
</tr>
<tr>
<td></td>
<td>Goodpasture’s syndrome</td>
</tr>
<tr>
<td></td>
<td>idiopathic pulmonary hemosiderosis</td>
</tr>
<tr>
<td><strong>Vascular disease</strong></td>
<td>PE</td>
</tr>
<tr>
<td></td>
<td>elevated pulmonary venous pressure</td>
</tr>
<tr>
<td></td>
<td>LVF</td>
</tr>
<tr>
<td></td>
<td>mitral stenosis</td>
</tr>
<tr>
<td></td>
<td>vascular malformation</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>impaired coagulation</td>
</tr>
<tr>
<td></td>
<td>pulmonary endometriosis</td>
</tr>
</tbody>
</table>

## Table 4. Differential Diagnosis of Chest Pain

<table>
<thead>
<tr>
<th>Nonpleuritic</th>
<th>Pleuritic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary</strong></td>
<td>pneumothorax</td>
</tr>
<tr>
<td>neoplastic</td>
<td>hemotorax</td>
</tr>
<tr>
<td>pneumonia</td>
<td>PE</td>
</tr>
<tr>
<td>MI</td>
<td>pneumonia</td>
</tr>
<tr>
<td>ischemia</td>
<td>bronchiectasis</td>
</tr>
<tr>
<td>myocarditis/pericarditis</td>
<td>neoplasm</td>
</tr>
<tr>
<td><strong>Esophageal</strong></td>
<td>TB</td>
</tr>
<tr>
<td>spasm</td>
<td>empyema</td>
</tr>
<tr>
<td>esophagitis</td>
<td>Cardiac</td>
</tr>
<tr>
<td>ulceration</td>
<td>pericarditis</td>
</tr>
<tr>
<td>achalasia</td>
<td>Dressler’s syndrome</td>
</tr>
<tr>
<td>neoplasm</td>
<td><strong>GI</strong></td>
</tr>
<tr>
<td><strong>Mediastinal</strong></td>
<td>pancreatitis</td>
</tr>
<tr>
<td>lymphoma</td>
<td>MSK</td>
</tr>
<tr>
<td>thymoma</td>
<td>costochondritis</td>
</tr>
<tr>
<td><strong>Subdiaphragmatic</strong></td>
<td>fractured rib</td>
</tr>
<tr>
<td>PUD</td>
<td>myositis</td>
</tr>
<tr>
<td>gastritis</td>
<td>herpes zoster</td>
</tr>
<tr>
<td>biliary colic</td>
<td></td>
</tr>
<tr>
<td>pancreatic</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular</strong></td>
<td></td>
</tr>
<tr>
<td>dissecting aortic aneurysm</td>
<td></td>
</tr>
<tr>
<td><strong>MSK</strong></td>
<td></td>
</tr>
<tr>
<td>costochondritis</td>
<td></td>
</tr>
<tr>
<td>skin</td>
<td></td>
</tr>
<tr>
<td>breast</td>
<td></td>
</tr>
<tr>
<td>ribs</td>
<td></td>
</tr>
</tbody>
</table>

HISTORY AND DIFFERENTIAL DIAGNOSIS
OF SYMPTOMS IN RESPIRATORY DISEASE

- **dyspnea/SOB** (Table 1)
  - PND/orthopnea: SOB when recumbent in CHF, asthma, COPD, or GERD
  - tachypnea: SOB when right or LLD position in CHF, cardiac mass
  - platypnea: SOB when upright in post-pneumonectomy, neurologic disease, hepatopulmonary syndrome (ie. liver failure), hypovolemia
  - episodic: in bronchospasm, transient pulmonary edema

- **cough** (Table 2)
  - 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) in children
  - positional: abscess, tumour

- **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** (Table 3)
  - hemoptysis vs. hematemeses
    - cough
    - sputum present
    - stable bubbles
    - alkaline pH
    - alveolar macrophages
  - no sputum
  - no stable bubbles
  - acid pH
  - no alveolar macrophages

- **chest pain** (Table 4)
  - due to parietal pleura, chest wall, diaphragm, or mediastinal involvement
  - pleuritic: sharp knife-like pain worse with deep inspiration or coughing

PHYSICAL EXAM AND DIFFERENTIAL DIAGNOSIS
OF SIGNS IN RESPIRATORY DISEASE

**Inspection**

- **face**
  - nasal flaring, pursed lip breathing
  - pallor: anemia
  - central cyanosis: inadequate SaO2

- **posture**
  - tripod sit

- **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) (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 (Hypertrophic Osteoarthropathy)

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF</td>
<td>Cyanotic congenital heart disease</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>Infective endocarditis</td>
</tr>
<tr>
<td>Chronic pus in the lung</td>
<td></td>
</tr>
<tr>
<td>(bronchiectasis, abscess,</td>
<td></td>
</tr>
<tr>
<td>infections, etc.)</td>
<td></td>
</tr>
<tr>
<td>Lung CA (primary or mets)</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td></td>
</tr>
<tr>
<td>A-V fistula</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td><strong>Mediastinal</strong></td>
</tr>
<tr>
<td>IBD</td>
<td>Esophageal CA</td>
</tr>
<tr>
<td>Chronic infections</td>
<td>Thymoma</td>
</tr>
<tr>
<td>Laxative abuse</td>
<td>Achalasia</td>
</tr>
<tr>
<td>Polyposis</td>
<td></td>
</tr>
<tr>
<td>Malignant tumours</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td></td>
</tr>
<tr>
<td>HCC</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Respiration Patterns in Normal and Disease States

<table>
<thead>
<tr>
<th>Respiration Pattern</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal inspiration and expiration</td>
<td></td>
</tr>
<tr>
<td>obstructive (prolonged expiration)</td>
<td>asthma, COPD</td>
</tr>
<tr>
<td>bradypnea (abnormal slowness of breathing)</td>
<td>drug-induced respiratory depression</td>
</tr>
<tr>
<td></td>
<td>diabetic coma</td>
</tr>
<tr>
<td></td>
<td>increased ICP</td>
</tr>
<tr>
<td>Kussmaul's (fast and deep)</td>
<td>metabolic acidosis</td>
</tr>
<tr>
<td></td>
<td>exercise</td>
</tr>
<tr>
<td></td>
<td>anxiety</td>
</tr>
<tr>
<td>Biot's/ataxic (irregular with long</td>
<td>drug-induced respiratory depression</td>
</tr>
<tr>
<td>apneic periods)</td>
<td>increased ICP</td>
</tr>
<tr>
<td></td>
<td>brain damage, especially medullary</td>
</tr>
<tr>
<td>Cheyne-Stokes (changing rates and depths</td>
<td>drug-induced respiratory depression</td>
</tr>
<tr>
<td>with apneic periods)</td>
<td>brain damage (especially cerebral)</td>
</tr>
<tr>
<td></td>
<td>CHF</td>
</tr>
<tr>
<td></td>
<td>uremia</td>
</tr>
<tr>
<td>apneustic (prolonged inspiritory pause)</td>
<td>pontine lesion</td>
</tr>
</tbody>
</table>
APPRAOCH TO THE RESPIRATORY PATIENT . . . CONT.

**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
    - pleural effusion
    - bronchial obstruction
    - pleural thickening
- trachea
  - deviated
    - contralateral: pneumothorax (especially tension), 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**

<table>
<thead>
<tr>
<th>Table 7. Breath Sounds</th>
<th>Bronchial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vesicular</strong></td>
<td></td>
</tr>
<tr>
<td>soft</td>
<td>loud</td>
</tr>
<tr>
<td>low-pitched</td>
<td>high-pitched</td>
</tr>
<tr>
<td>inspiratory &gt;&gt; expiratory phase</td>
<td>exspiratory &gt; inspiratory phase</td>
</tr>
<tr>
<td>normal over most of peripheral lung</td>
<td>normal over manubrium but represents consolidation elsewhere</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Decreased air entry</strong></th>
<th>Crackles (Rales/Crepitations)</th>
</tr>
</thead>
<tbody>
<tr>
<td>asthma</td>
<td>coarse crackles:</td>
</tr>
<tr>
<td>emphysema</td>
<td>bronchitis</td>
</tr>
<tr>
<td>pneumothorax</td>
<td>respiratory infections, pneumonia</td>
</tr>
<tr>
<td>pleural effusion</td>
<td>pulmonary edema</td>
</tr>
<tr>
<td>atelectasis</td>
<td>interstitial fibrosis</td>
</tr>
<tr>
<td>ARDS</td>
<td>CHF</td>
</tr>
<tr>
<td></td>
<td>excess airway secretions</td>
</tr>
<tr>
<td></td>
<td>fine crackles: interstitial fibrosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Wheeze (Rhonchi)</strong></th>
<th>Pleural rub</th>
</tr>
</thead>
<tbody>
<tr>
<td>asthma</td>
<td>pneumonia</td>
</tr>
<tr>
<td>bronchitis</td>
<td>pleural effusion</td>
</tr>
<tr>
<td>pulmonary edema</td>
<td>pulmonary infarction</td>
</tr>
<tr>
<td>CHF</td>
<td></td>
</tr>
<tr>
<td>foreign body</td>
<td></td>
</tr>
<tr>
<td>CF</td>
<td></td>
</tr>
<tr>
<td>aspiration</td>
<td></td>
</tr>
<tr>
<td>tumour, vascular ring</td>
<td></td>
</tr>
<tr>
<td>rapid airflow through obstructed airway</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Voice sounds</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>egophony (e to a)</td>
</tr>
<tr>
<td>whispered pectoriloquy</td>
</tr>
<tr>
<td>bronchophony</td>
</tr>
<tr>
<td>all are due to consolidation</td>
</tr>
</tbody>
</table>

**INVESTIGATIONS AND THEIR INTERPRETATIONS**

**PULMONARY FUNCTION TESTS (PFTs)**
- useful in differentiating the pattern of lung disease (obstructive vs. restrictive) (Table 8)
- assesses lung volumes, flow rates, and diffusion capacity (Figures 3 and 4)
APPROACH TO THE RESPIRATORY PATIENT . . . CONT.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Obstructive</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow Rates</td>
<td>FEV₁</td>
<td>↓ or N</td>
</tr>
<tr>
<td>(i.e. Lung</td>
<td>FVC</td>
<td>↓ or N</td>
</tr>
<tr>
<td>Mechanics)</td>
<td>FEV₁/FVC</td>
<td>↓ or N</td>
</tr>
<tr>
<td></td>
<td>FEF25-75%</td>
<td>↓ or N</td>
</tr>
<tr>
<td>Lung Volumes</td>
<td>TLC</td>
<td>↓ or N</td>
</tr>
<tr>
<td></td>
<td>FRC</td>
<td>↓ or N</td>
</tr>
<tr>
<td></td>
<td>VC</td>
<td>↓ or N</td>
</tr>
<tr>
<td></td>
<td>RV</td>
<td>↓</td>
</tr>
<tr>
<td></td>
<td>RV/TLC</td>
<td>↓</td>
</tr>
<tr>
<td>Diffusing</td>
<td>Dco</td>
<td>↓ or N</td>
</tr>
<tr>
<td>Capacity</td>
<td></td>
<td>↓ or N</td>
</tr>
</tbody>
</table>
Pulmonary Function Tests (PFTs)

Reduced FEV₁ < 80% predicted

Lung volumes normal

FEV₁/FVC > 80% predicted
Non Obstructive Defect

Lung volumes low, especially FRC, RV

FEV₁/FVC < 80% predicted
Airflow Obstruction

Give bronchodilator

Rise in FEV₁ > 12%

No change in FEV₁

Flow volume loop, lung volumes, Dco

High RV + normal TLC, FRC, and Dco

High FRC, TLC, and RV + low Dco

ASTHMA

CHRONIC BRONCHITIS

EMPHYSEMA

Figure 5. Interpreting PFTs

- 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? (Table 9)
   - metabolic compensation occurs over 2-3 days reflecting altered renal HCO₃⁻ production/excretion
   - respiratory compensation through ventilation control of PaCO₂ occurs immediately
   - inadequate compensation may indicate a second acid-base disorder
Table 9. Expected Compensation for Specific Acid-Base Disorders

<table>
<thead>
<tr>
<th>Disturbance</th>
<th>PaCO₂</th>
<th>HCO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Acidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Chronic</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Respiratory Alkalosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Chronic</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Metabolic Acidosis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Metabolic Alkalosis</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

4. If there is metabolic acidosis, what is the anion gap and osmolar gap? (see Nephrology Chapter)
   • anion gap = [Na⁺] – ([Cl⁻] + [HCO₃⁻]); normal = 10-15 mmol/L
   • osmolar gap = measured osmolarity – calculated osmolarity
     = measured – (2[Na⁺] + glucose + urea); normal = 10

Differential Diagnosis of Respiratory Acidosis

- characterized by increased PaCO₂ secondary to hypoventilation
- respiratory centre depression
  - drugs (anesthesia, sedatives)
  - trauma
  - increased ICP
  - post-encephalitis
  - stroke
  - sleep-disordered breathing (sleep apnea, obesity)
  - supplemental O₂ in chronic CO₂ retainers (i.e. COPD)

- 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)
   - On room air: FiO2 = 0.21, Patm = 760 mm Hg, PH2O = 47 mm Hg, RQ = 0.8 —> AaDO2 = [150 – 1.25(PaCO2)] – PaO2
   - the normal AaDO2 increases with age
3. What is the cause of the hypoxemia?

\[
\text{PaO}_2 < 95 \text{ mm Hg}
\]

- increased A-a gradient (> 15 mm Hg)
  - decreased diffusion capacity
  - interstitial lung disease
  - emphysema
- normal A-a gradient (< 10-15 mm Hg)
  - increased PaCO2
  - hypoventilation
  - low FiO2 (e.g. high altitude)

\[
\text{PaO}_2 \text{ improves}
\]

- V/Q mismatch
  - airway disease
    - asthma, COPD
  - interstitial lung disease
  - alveolar disease
  - pulmonary vascular disease

\[
\text{PaO}_2 \text{ does not improve}
\]

- shunt
  - atelectasis
  - intraalveolar filling
    - (e.g. pulmonary edema, pneumonia)
  - intracardiac shunt
  - vascular shunt within lungs

DISEASES OF AIRWAY OBSTRUCTION

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
- common (7-10% of adults), especially in children (10-15%)
- most children with asthma improve significantly in adolescence
- often family history of atopy (asthma, allergic rhinitis, eczema)

Clinical Pearl
- asthma triad: asthma, ASA/NSAID sensitivity, nasal polyps.

- 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, GERD)
  - often no identifiable trigger

Pathophysiology
- acute asthma: airway obstruction —> V/Q mismatch —> hypoxemia
  —> ventilation —> ↓ PaCO2/↑ pH AND fatigue —> ↓ ventilation ↑ PaCO2/↓ pH

Symptoms
- SOB, wheezing, cough (especially nocturnal), chest tightness
DISEASES OF AIRWAY OBSTRUCTION . . . CONT.

**Signs**
- tachypnea
- wheezing
- respiratory distress
  - nasal flare, accessory muscle use, tracheal tug, intercostal muscle indrawing, pulsus paradoxus, inability to speak (indicates severe asthma)
- Red flags
  - fatigue, cyanosis, silent chest, diminished respiratory effort, decreased LOC

**Profile of Patients at Risk for Severe Asthma**
- previous non-fatal episodes
  - loss of consciousness during asthma attack
  - frequent ER visits
  - prior intubation
  - ICU admission
- ominous symptoms and signs
  - night-time symptoms
  - limited activities of daily living
  - use of β2-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 β2-agonists.

**Investigations**
- O2 saturation
- 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)
- PFTs (may not be possible during severe attack)
  - spirometry: increase in FEV1 > 12% with β2-agonist, or > 20% with 10-14 days of steroids, or > 20% spontaneous variability
  - peak expiratory flows: > 20% PEF diurnal variability (not as reliable, but can be done at home)
  - provocation testing: decrease in FEV1 > 20% with methacholine challenge

**Treatment**
- 3 components of treatment
  - environmental control: address relevant triggers
  - patient education: features of the disease, goals of treatment, self-monitoring
  - pharmacological therapy:
    - "relievers" provide short-term relief (short-acting β2-agonist, anticholinergic)
    - "controllers" provide long-term prevention (inhaled/oral corticosteroids, anti-allergic agent, long-acting β2-agonist, methylxanthine, leukotriene antagonists (LRA))

**Table 10. Asthma Medications**

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchodilator</td>
<td>• short-acting β2-agonist (albuterol)</td>
</tr>
<tr>
<td></td>
<td>• long-acting β2-agonist (salmeterol)</td>
</tr>
<tr>
<td></td>
<td>• anticholinergic (ipratropium)</td>
</tr>
<tr>
<td></td>
<td>• methylxanthine (theophylline)</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>• inhaled corticosteroid (fluticasone)</td>
</tr>
<tr>
<td></td>
<td>• anti-allergic agent (cromolyn)</td>
</tr>
<tr>
<td></td>
<td>• LRA (monteleukast)</td>
</tr>
<tr>
<td></td>
<td>• oral corticosteroid (prednisone)</td>
</tr>
</tbody>
</table>
DISEASES OF AIRWAY OBSTRUCTION . . . CONT.

- medication plan
  - mild asthma (infrequent symptoms, normal PEFs)
    - inhaled short-acting β2-agonist PRN
    - low-dose inhaled steroid
  - moderate asthma (short-acting β2-agonist needed > 3x/wk, or abnormal lung function)
    - add high-dose inhaled steroid (and discontinue low-dose inhaled steroid)
    - +/- add additional therapy (LRA, anti-allergic agent, long-acting β2-agonist, theophylline, anticholinergic)
  - severe asthma (frequent symptoms, PEFs < 60% of predicted value, unable to perform daily activities)
    - add oral steroid (and discontinue high-dose inhaled steroid)
    - continue with bronchodilators

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 β2-agonist and anticholinergics given by wet nebulizer or meter dose inhaler (+/- epinephrine IM/IV if unresponsive)
  - 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 progressive development of airflow limitation that is irreversible/minimally reversible
- includes chronic bronchitis and emphysema; usually coexist to variable degrees in most patients
- five pathophysiological processes associated with COPD
  1. Inflammatory narrowing of respiratory and membranous bronchioles
  2. Proteolytic digestion of connective tissue framework of the lung resulting in decreased parenchymal tethering of airways
  3. Loss of alveolar surface area and capillary bed
  4. Lung hyperinflation caused by loss of lung elastic recoil
  5. Increased pulmonary vascular resistance caused by vasoconstriction and loss of capillary bed

Risk Factors

- smoking is the most important risk factor.
- minor risk factors include:
  - environmental factors: air pollution, occupational exposure, IV drug abuse or talcosis
  - treatable factors: low BMI, α₁-antitrypsin deficiency, bronchial hyperactivity
  - demographic factors: age, family history, male sex, history of childhood respiratory infections and socioeconomic status

Emphysema

- pathologic 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 α₁-antitrypsin deficiency (normal (MM), heterozygote (MZ), homozygote (ZZ))
    - ZZ can develop emphysema in their thirties, especially smokers

- clinical presentation (see table 11)
- investigations (see table 12)

Chronic Bronchitis

- clinical diagnosis
- definition: 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)
DISEASES OF AIRWAY OBSTRUCTION . . . CONT.

Table 11. Clinical Presentation of Chronic Bronchitis and Emphysema

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchitis Blue bloater</td>
<td>chronic productive cough</td>
<td>cyanotic (secondary to hypoxemia and hypercapnia)</td>
</tr>
<tr>
<td></td>
<td>purulent sputum, hemoptysis</td>
<td>peripheral edema from RVF (cor pulmonale)</td>
</tr>
<tr>
<td></td>
<td>mild dyspnea initially</td>
<td>crackles, wheezes</td>
</tr>
<tr>
<td>Emphysema Pink puffer</td>
<td>dyspnea (+/- exertion)</td>
<td>pink skin</td>
</tr>
<tr>
<td></td>
<td>minimal cough</td>
<td>pursed-lip breathing</td>
</tr>
<tr>
<td></td>
<td>increased minute ventilation</td>
<td>accessory muscle use</td>
</tr>
<tr>
<td></td>
<td>tachypnea</td>
<td>cachectic appearance due to anorexia + increased work of breathing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 12. Investigations and Findings in Chronic Bronchitis and Emphysema

<table>
<thead>
<tr>
<th>Investigation</th>
<th>PFT</th>
<th>CXR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchitis</td>
<td>↓flow rates (FVC, FEV₁, FEV₁/FVC, FEF₂₅-₇₅) normal TLC</td>
<td>AP normal or increased bronchovascular markings</td>
</tr>
<tr>
<td></td>
<td>↑RV/TLC prolonged FVC no change in FEV₁ with bronchodilator (rise in FEV₁ if asthma) increased or normal DCO</td>
<td>Enlarged heart with cor pulmonale</td>
</tr>
<tr>
<td>Emphysema</td>
<td>↓flow rates (FVC, FEV₁, FEV₁/FVC, FEF₂₅-₇₅) ↓lung volumes (RV, TLC, RV/TLC) prolonged FVC no change in FEV₁ with bronchodilator (rise in FEV₁ if asthma) decreased DCO</td>
<td>AP hyperinflated chest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>increased AP diameter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>flat hemidiaphragm (on lateral)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decreased heart shadow</td>
</tr>
<tr>
<td></td>
<td></td>
<td>increased retrosternal space</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decreased peripheral vascular markings</td>
</tr>
<tr>
<td></td>
<td></td>
<td>bullae</td>
</tr>
<tr>
<td></td>
<td></td>
<td>see Colour Atlas R11 and R12</td>
</tr>
</tbody>
</table>

Treatment of COPD

Non Pharmacological
- patient education: enables patients to take control of their disease and improves compliance
- smoking cessation: decreases rate of decline of FEV₁, reduce cough and sputum
- eliminate respiratory irritants/allergens (occupational/environmental)
- exercise rehabilitation to improve physical endurance
- nutrition: poor nutrition is associated with increased mortality
- intermittent mechanical ventilation to relieve dyspnea and rest respiratory muscles
- CPAP is used as an adjunct to weaning patients from mechanical ventilation and minimize dyspnea during exercise

Pharmacological Treatment
- vaccination with pneumovax and yearly H. influenza
- bronchodilators: mainstay of current drug therapy increase airflow and reduce dyspnea
  - anticholinergics eg. ipratropium bromide
    - inhaled, injected or taken orally
    - more effective than β2-agonists with fewer side effects.
    - slow onset of action take daily rather than on a PRN basis.
  - inhaled β2-agonist eg. salbutamol and albuterol, salmeterol
    - inhaled, injected or taken orally
    - rapid onset of action
    - significant side effects such as hypokalemia when used at high doses
DISEASES OF AIRWAY OBSTRUCTION . . . CONT.

- methylxanthines eg. theophylline
  - IV, orally or rectal
  - increases strength of respiratory muscles, collateral ventilation, ventilatory stimulation as well as increases mucociliary clearance and may even reduce airway inflammation
  - side effects include nervous tremor, N/V/D, tachycardia, arrhythmias, sleep changes, HA, gastric acid, toxicity

- corticosteroids eg. beclomethasone, dexamethasone, flunisolide
  - inhaled, oral or IV
  - COPD airways are usually inflamed, but NOT generally responsive to steroids
  - slightly reduce the severity and length of hospitalization in acute exacerbations

- nicotine replacement therapy (gum or patch) may aid in smoking cessation
  - buproprion (zyban) has been shown to be most effective in smoking cessation especially when used in conjunction with nicotine replacement

- antibiotics are commonly used during acute exacerbations
  - but not all are due to bacterial infections and therefore treatment is not always warranted

- diuretics in patients with right heart failure to avoid excess water retention

- α-1-antitrypsin replacement for documented deficiency (evidence is lacking that lung preservation is achieved with long term replacement and treatment is very expensive)

Surgical Treatment
- bullectomy of emphysematous parts of lung to improve ventilatory function
- lung transplant

Acute Exacerbations
- defined as increase in dyspnea, effort intolerance, change in cough/volume of sputum
- etiology most often viral but PE, MI, CHF must be considered
- 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 β2-agonist
- theophylline: 3rd line agent
- corticosteroids
- antibiotics often used to treat precipitating infection

Post-Exacerbation
- rehabilitation with chest physio, general conditioning to improve exercise tolerance
- always consider need for home O2 after exacerbation

Indications for Home O2
- O2 has been shown to decrease COPD complications such as cor pulmonale and to improve survival
- PaO2 < 55 mm Hg or PaO2 < 60 mm Hg with erythrocytosis (Hct > 55%)
- cor pulmonale, or O2 saturation < 88% on exertion/sleep
- 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 (FEV1)
  - development of complicating factors such as hypoxemia or cor pulmonale
- 5-year survival
  - FEV1 < 1 L = 50%
  - FEV1 < 0.75 L = 33%
- 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)

BRONCHIECTASIS
- an irreversible dilatation of airways due to inflammatory destruction of airway walls resulting in persistently infected mucus
- once bronchiectasis is established P. aeruginosa is the most common pathogen
- subtypes: cylindrical (bronchi = uniformly dilated tubules) vs. varicose (bronchi = irregular beaded pattern of dilatation) vs saccular/cystic (bronchi = ballooned appearance)
DISEASES OF AIRWAY OBSTRUCTION . . . CONT.

**Etiology**
- obstruction
  - tumours
  - foreign bodies
  - thick mucus
- 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: bronchiectasis, sinusitis, situs inversus)

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

**Diagnosis**
- PFTs
  - often demonstrate obstructive pattern but may be normal
- CXR (Colour Atlas R2)
  - nonspecific: increased markings, linear atelectasis
  - specific: "tram tracking" - parallel narrow lines radiating from hilum
- high-resolution thoracic CT (diagnostic)
  - "signet ring": dilated bronchi with thickened walls, diameter bronchus > diameter of accompanying vessel

**Treatment**
- vaccination: influenza and Pneumovax
- antibiotics (oral, IV, inhaled)
- bronchodilators
- steroids
- postural drainage/physiotherapy
- surgical excision: for localized disease refractory to medical treatment

**CYSTIC FIBROSIS (CF)** - see Pediatrics Chapter
- Cl− transport dysfunction: thick secretions from exocrine glands (lung, pancreas, skin, gonads) and blockage of secretory ducts
- results in severe lung disease, pancreatic insufficiency and azoospermia
- presents in childhood with recurrent lung infections that become persistent and chronic (see Pediatrics Chapter)
- chronic lung infections
  - S. Aureus: early
  - P. aeruginosa: most common
  - B. cepacia: worse prognosis but less common
  - aspergillosis

**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: only small airways will be affected
  - later: characteristics 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 males 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

Causes of interstitial lung disease
❏ 65% due to unknown agents

Table 13. Causes of Interstitial Lung Disease

<table>
<thead>
<tr>
<th>Upper Lung Disease</th>
<th>Lower Lung Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>F farmers lung</td>
<td>B bronchiectasis bronchiolitis organizing pneumonia (BOOP)</td>
</tr>
<tr>
<td>Aankylosing spondylitis</td>
<td>A asbestosis</td>
</tr>
<tr>
<td>S sarcoidosis</td>
<td>D drugs (nitrofurantoin, hydralazine, INH, amiodarone)</td>
</tr>
<tr>
<td>S silicosis</td>
<td>R rheumatologic disease</td>
</tr>
<tr>
<td>T TB</td>
<td>A aspiration</td>
</tr>
<tr>
<td>E eosinophilic granuloma</td>
<td>S Scleroderma</td>
</tr>
<tr>
<td>N neurofibromatosis</td>
<td>H Harmen Reich (Interstitial pulmonary fibrosis)</td>
</tr>
</tbody>
</table>

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

Investigations
❏ CXR (see Colour Atlas R1)
• decreased lung volumes, reticulonodular pattern (nodular (< 3 mm), Kerley B lines, hilar/mediastinal adenopathy, lytic bone lesions
• DDx: pulmonary fibrosis, pulmonary edema (CHF), PCP, TB (miliary), sarcoidosis, pneumoconiosis, lymphangitic carcinomatosis
• DDx of cystic lesions: end-stage emphysema, PCP, histiocytosis X, Lymphangiomatomyosis
❏ 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
❏ other categories
• nonspecific interstitial pneumonitis
• desquamative interstitial pneumonitis (DIP)
• respiratory bronchiolitis
• lymphatic interstitial pneumonitis (LIP)
❏ 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%
INTERSTITIAL LUNG DISEASE . . . CONT.

- **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 survival of 5 years after diagnosis

**SARCOIDOSIS**
- multi-system disease with lung involvement in 90%
- characterized by noncaseating granulomas throughout body
- typically affects young black women but other groups also affected
- 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 of interstitial disease also present, may have dyspnea, chest pain, nonproductive cough (crackles rare)

**Clinical Pearl**
- Sarcoid is silent on auscultation.
- as fibrosis occurs, CXR shows reticulonodular pattern especially in upper zones
- common extrapulmonary manifestations
  - cardiac
  - 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
- 2 sarcoid syndromes
  - Lofgren's syndrome = erythema nodosum, bilateral hilar lymphadenopathy, fever, and arthralgias
  - Heerfordt-Waldenstrom syndrome: fever, parotid enlargement, anterior uveitis, facial nerve palsy

**Laboratory Abnormalities**
- hypercalcemia, hypercalciuria in 10% (hypercalcemia more common)
- 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

**Langerhans-cell Histiocytosis**
- aka eosinophilic granuloma, histiocytosis X
- clonal proliferation of dendritic cells
- cells have X-bodies on EM
- typically affects young-middle aged smokers
- presentation: dyspnea, cough or both
  - spontaneous pneumothorax
INTERSTITIAL LUNG DISEASE . . . CONT.

- CXR: primarily in upper lung zones
  - cystic, nodular and/or reticulonodular changes that progress to honeycombing
- course: may stabilize in some patients or may be progressive
  - no treatment

PULMONARY INFILTRATES WITH EOSINOPHILIA (PIE SYNDROME)

- a broad group of disorders
  - known etiology
    - allergic bronchopulmonary aspergillosis (and other mycoses)
    - parasitic infestations (filariasis, ascariasis, tropical eosinophilia etc.)
    - drug reactions (ASA, MTX, imipramine, penicillins, sulfonamides, tetracyclines, INH)
    - eosinophilic myalgia syndrome
  - unknown etiology
    - idiopathic Löffler's syndrome
    - acute eosinophilic pneumonia
    - chronic eosinophilic pneumonia
    - Churg-Strauss Syndrome
    - hypereosinophilic pneumonia

Löffler's Syndrome

- transient and migrating peripheral lung infiltrates and eosinophilia
- 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 treatment of the underlying cause (e.g. parasite, drug) if known

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 x 10⁹) 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” (pattern is often migratory).

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 (> 1,000 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 may recur as corticosteroid treatment is tapered

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 section)

ASSOCIATED WITH COLLAGEN VASCULAR DISEASE
(see Pulmonary Vasculitis section)
**INTERSTITIAL LUNG DISEASE . . . CONT.**

**CRYPTOGENIC ORGANIZING PNEUMONIA**

- 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 peripheral infiltrates with alveolar pattern
- treatment: corticosteroids (responds faster and more frequently (except in RA) 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
- lymphocytic 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)
  - sauna taker’s lung (Aureobasidium spp)
- 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 mm 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
  - rounded melectasis
  - lower > upper lobe
  - early: fibrosis with linear streaking
  - later: cysts and honeycombing
  - 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 fibres coated in macrophages
- asbestos exposure also increases risk of bronchogenic CA and malignant mesothelioma
- risk dramatically increased for smokers
- clubbing is much more likely in asbestosis than silicosis or coal worker’s pneumoconiosis
- treatment: prevention of disease progression and development of complications
- reduce silica exposure
INTERSTITIAL LUNG DISEASE . . . CONT.

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 > lower lobe
  - early: nodular disease (simple pneumoconiosis)
  - late: nodules coalesce and enlarge (progressive massive fibrosis)
- 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)
  - egg shell calcification is classical
- no increase in mycobacterial or fungal infections
- treatment: prevention, removal from exposure

Coal Worker's Pneumoconiosis (CWP)
- coal is less fibrogenic than silica
- pathologic hallmark is coal macule:
  - coal dust surrounded by little tissue reaction and focal emphysema
  - found around respiratory bronchioles
- 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 (Colour Atlas R5)
  - 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 Angitis)
- 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 typically 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
  - risk increased in smokers
- renal biopsy shows linear immunofluorescence
PULMONARY VASCULAR DISEASE . . . CONT.

- 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 ("shrinking lung syndrome")
  - PE (due to lupus anticoagulant)

Rheumatoid Arthritis (RA)
- classical findings
  - pulmonary rheumatoid nodules (Caplan's syndrome CWP and RA)
  - 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
- may also cause an isolated PHTN (usually CREST)

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

PULMONARY HYPERTENSION
- pulmonary artery pressure is > 30 with exercise 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 (i.e. prostacyclin PGI2), 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 LVF, 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 Vasconstriction (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 DISEASE . . . CONT.

Pulmonary Vascular Occlusion (Obstructive)
- e.g. PE, schistosomiasis, veno-occlusive disease

Chronic thromboembolic disease (Obstructive)
- 2 types
  A. • large proximal thrombi
  - treatment: May be amenable to thromboendarterectomy
  B. • extensive thromboembolic occlusion of smaller vessels
  - may be due to embolic events or thrombosis at sites
  - treatment: anti-coagulation +/- vasodilators

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 AJR, peripheral edema, TR

Investigations
- CXR (see Colour Atlas R3, R4)
  • 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 hypoxic
- 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
- 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
  (see Colour Atlas DM8)
  - 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, S₁O₂T₃ 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) (see Colour Atlas DM6)
  - order scan if
    - CXR normal/mild abnormalites, 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 (see Colour Atlas DM8)
- ECHO: RVSP, RV hypokinesis
STEP 1.
Will the patient die in the next 48 hours of a PE?

- Poor cardiorespiratory reserve?
  - Yes: SVT, angina/MI, shock, syncope, \( \text{PaO}_2 < 50, \text{PCO}_2 > 45, \text{FEV}_1 < 1, \text{FVC} < 1.5 \text{ L} \)
  - Yes, +/- thrombolysis
  - No: IV Heparin +/- IVC filter

- Occlusive proximal leg DVT?
  - Yes: Positive leg examination and venous leg dopplers
  - No: Patient safe for at least 48 hours

STEP 2.
Did the patient have a PE?

- Clinical Assessment
  - > 2 respiratory symptoms/signs, HR > 90, leg symptoms, positive CXR, RF positive
  - Yes: IV Heparin
  - No: Non-invasive assessment

- Non-invasive assessment
  - Positive leg dopplers, D-dimer, V/Q Scan
  - Yes: IV Heparin
  - No: Is there adequate cardiorespiratory reserve?
    - Yes: serial leg dopplers for 14 days
    - No: invasive testing, treat for DVT/PE with anticoagulation

STEP 3.
Can the risk be reduced for future PE?
- Alleviate RF, TED stockings, antithrombotic treatment

**Figure 6. Management of Suspected PE**

**Prevention**
- early mobilization of peri-operative patients, in-patients
- prophylactic anticoagulation: limited mobility, chronically ill (e.g. heparin 5,000 units SC BID)
- peri-operative anticoagulation:
  - if low risk OR (GI surgery): heparin
  - if high risk OR (ortho): LMWH (enoxaparin)

**Treatment**
- have patient sit up as it aids respiration
- \( \text{O}_2 \)
- thrombolysis for large, hemodynamically significant emboli (ICU)
- anticoagulation to prevent further emboli
  - LMWH initial treatment (fragmin) (reliable dose-response curve at a given weight, so don't need to monitor PTTs with LMWH)
  - IV heparin
- 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
DISEASE OF THE MEDIASTINUM AND PLEURA

MEDIASTINAL DISEASES

Mediastinal Masses

• etiology
  • anterior compartment (sternum to anterior border of pericardium)
    • lymphoma, CA, lipoma, and the 4 T’s (thymoma, thyroid enlargement, teratoma, thoracic aortic aneurysm)
  • middle compartment (anterior to posterior pericardium)
    • pericardial cyst, bronchogenic cyst, lymphoma, CA, lymph node enlargement, aortic aneurysm
  • posterior compartment (posterior pericardium to vertebral column)
    • neurogenic tumours, meningocele, enteric cysts, lymphomas, diaphragmatic hernias, esophageal lesions, aortic aneurysm

• 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))

• investigations
  • CT most valuable imaging technique
  • biopsy (mediastinoscopy, percutaneous needle aspiration)

• treatment
  • if possible, surgical excision
  • +/- post-op radiotherapy/chemotherapy if malignant

Mediastinitis

• etiology
  • complication of endoscopy (e.g. esophageal perforation providing entry point for infection)
  • esophageal or cardiac surgery
  • tumour necrosis

• clinical features
  • fever
  • prostration
  • substernal pain
  • pneumomediastinum
  • mediastinal compression
  • Hamman's sign (auscultatory "crunch" during cardiac systole)

• treatment
  • antibiotics, drainage, +/- surgical closure of perforation

PLEURAL EFFUSIONS

• definition: A pleural effusion is present when there is an excess amount of fluid in the pleural space (normally up to 25 mL of pleural fluid is present in pleural space)
• etiology: pleural fluid formation exceeds pleural fluid absorption
  • excess pleural fluid formation from the parietal pleura, interstitial spaces of the lung or peritoneal cavity
  • decreased fluid removal by the lymphatics

Differential Diagnosis

Transudative Pleural Effusions

• pathophysiology: alteration of systemic factors that affect the formation and absorption of pleural fluid (i.e. increased capillary hydrostatic pressure, decreased plasma oncotic pressure)
  • CHF
  • cirrhosis
  • nephrotic syndrome
  • peritoneal dialysis
  • hypothyroidism
  • pulmonary embolism (may cause transudative or exudative effusion)
Exudative Pleural Effusions

- **Pathophysiology:** increased permeability of pleural capillaries or to lymphatic dysfunction
  - Infectious
    - Parapneumonic effusion (associated with bacterial pneumonia, lung abscess)
    - TB pleuritis
    - Viral infection
  - Neoplastic
    - Lung carcinoma (35%)
    - Lymphoma (10%)
    - Metastases: breast (25%), ovary, kidney
    - Mesothelioma
  - Collagen vascular diseases: RA, SLE
  - Pulmonary embolization
  - Uremia
  - Meig's syndrome
  - GI disease
    - Esophageal perforation (elevated pleural fluid amylase)
    - Pancreatic disease (elevated pleural fluid amylase)
    - Subphrenic abscess
  - Chylothorax: occurs when the thoracic duct is disrupted and chyle accumulates in the pleural space, cue to trauma, tumors
  - Hemothorax: due to rupture of a blood vessel, commonly by trauma or tumors

- **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
    - Dense opacification of lung fields with concave meniscus
    - Lateral: small effusion leads to blunting of posterior or costophrenic angle
    - P/A: blunting of lateral costophrenic angle
    - Decubitus: fluid will shift unless is loculated
    - Supine: fluid will appear as general haziness
  - Thoracentesis (essential):
    - Remove a maximum of 2 litres due to risk of re-expansion pulmonary edema if greater volumes are removed
    - 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
      - Lymphocytic TB, lymphoma
      - Cytopathy: Malignancy, infection
      - Low glucose: RA, TB, empyema, malignancy
      - Rheumatoid factor, ANA, complement
      - Amylase: Pancreatitis, esophageal perforation
      - pH: Empyema < 7.2; TB and mesothelioma < 7.3
      - Blood: Mostly traumatic, malignancy, PE with infarction, TB
      - TG: Chylothorax from thoracic duct leakage, mostly due to trauma, lung CA, lymphoma
  - Pleural biopsy: for suspected TB, mesothelioma, or other malignancy (if cytology negative)
  - +/- US: Detects small effusions and can guide thoracentesis

- **Treatment**
  - Treatment depends on cause, +/- drainage if symptomatic
  - Note: 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 14)

### Table 14. Laboratory Values in Transudative and Exudative Pleural Effusion

<table>
<thead>
<tr>
<th></th>
<th>Transudate</th>
<th>Exudate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural protein/serum protein</td>
<td>&lt; 0.5</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Pleural LDH/serum LDH</td>
<td>&lt; 0.6</td>
<td>&gt; 0.6</td>
</tr>
<tr>
<td>Pleural LDH (alternatively)</td>
<td>&lt; 2/3 upper limit of normal serum LDH</td>
<td>&gt; 2/3 upper limit of normal serum LDH</td>
</tr>
</tbody>
</table>
Clinical Pearl

- Transudates are usually bilateral and exudates are usually unilateral.

**EMPHYMA**
- **Definition:** grossly purulent pleural effusion
- **Etiology:** contiguous spread from lung infection (most commonly anaerobes), infection through chest wall (e.g. trauma, surgery)
- **Symptoms:** fever, pleuritic chest pain
- **Investigations:** pleurocentesis
  - PMNs (lymphocytes in TB), +/- visible organisms on Gram stain
- **Treatment**
  - Antibiotics, chest tube drainage (if pH < 7.2), surgical drainage (if loculated)

**EMPYEMA**
- **Definition:** grossly purulent pleural effusion
- **Etiology:** contiguous spread from lung infection (most commonly anaerobes), infection through chest wall (e.g. trauma, surgery)
- **Symptoms:** fever, pleuritic chest pain
- **Investigations:** pleurocentesis
  - PMNs (lymphocytes in TB), +/- visible organisms on Gram stain
- **Treatment**
  - Antibiotics, chest tube drainage (if pH < 7.2), surgical drainage (if loculated)

**PNEUMOTHORAX**
- **Definition:** the presence of gas in the pleural space
- **Pathophysiology:** intrapleural pressure positive instead of negative, preventing lung inflation
- **Etiology**
  - Traumatic
  - Iatrogenic (CVP line, thoracentesis, mechanical ventilation and alveolar pressure)
  - Spontaneous (no history of trauma)
    - Primary (no underlying lung disease)
      - Spontaneous rupture of apical subpleural bleb of lung at apex into pleural space
      - Predominantly healthy young tall males
    - Secondary (underlying lung disease)
      - Rupture of subpleural bleb (most common cause is COPD)
      - Necrosis of lung tissue adjacent to pleural surface e.g. pneumonia, abscess, PCP, lung CA
- **Symptoms**
  - Can be asymptomatic
  - Acute onset pleuritic chest pain
  - Acute onset dyspnea
- **Signs**
  - Shift of trachea to opposite side
  - Ipsilateral diminished expansion
  - Decreased tactile/vocal fremitus
  - Hyperresonant percussion note
  - Ipsilateral diminished breath sounds
- **CXR (see Colour Atlas R8)**
  - Small: separation of visceral and parietal pleura seen as fine crescentic line parallel to chest wall at apex
  - Large: increased density and decreased volume of lung on side of pneumothorax
  - See Diagnostic Medical Imaging Chapter
- **Treatment**
  - Small pneumothoraces resolve spontaneously
  - Large ones or those complicating underlying lung disease require placement of a chest tube connected to underwater seal +/- suction
  - For repeated episodes: pleurodesis with sclerosing agent or partial pneumectomy/bleb resection

**Tension Pneumothorax**
- Emergency! (see Emergency Medicine Chapter)

**ASBESTOS-RELATED PLEURAL DISEASE**
- Exudative pleural effusion
- Pleural thickening or calcification, pleural plaque (Hyalinosis Simplex)
- Mesothelioma
  - Primary malignancy of the pleura
  - Decades after even light asbestos exposure
  - Smoking is not a risk factor
- **Signs and Symptoms:** persistent chest pain, dyspnea, cough, bloody pleural effusion, weight loss, clubbing
- **Diagnosis:** biopsy (pleuroscopic or open)
- **Treatment:** resection (requires careful patient selection); however, rarely successful (average survival < 1 year)
PULMONARY INFECTIONS

PNEUMONIA
- definition: 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, toxic inhalation, aspiration, mechanical obstruction, ETT/NTT intubation, respiratory therapy, pulmonary edema, hypoxemia, acidosis, immunosuppression, splenectomy, uremia, DM, malnutrition, elderly age, decreased LOC
- 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 15) but in real life its often difficult to differentiate typical from atypical infections
  - elderly often present atypically; altered LOC is sometimes the only sign
  - epidemiology affects clinical presentation and treatment

Table 15. Clinical Features of Typical vs. Atypical Pneumonia

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Typical</th>
<th>Atypical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisms involved</td>
<td>S. pneumoniae,</td>
<td>Mycoplasma pneumoniae,</td>
</tr>
<tr>
<td></td>
<td>H. influenzae,</td>
<td>Chlamydia pneumoniae,</td>
</tr>
<tr>
<td></td>
<td>Endemic oral flora</td>
<td>Viral, Legionella</td>
</tr>
<tr>
<td>Onset</td>
<td>Sudden</td>
<td>Subacute</td>
</tr>
<tr>
<td>Cough</td>
<td>Productive</td>
<td>Dry</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>Pleuritic (some cases)</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Other Symptoms</td>
<td>Chills, rigors, SOB, nausea, diarrhea</td>
<td>Headache, myalgia</td>
</tr>
<tr>
<td>Temp &gt; 38°C</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>HR &gt; 110</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Consolidation Signs*</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>WBC count</td>
<td>Increased</td>
<td>Normal or slightly</td>
</tr>
<tr>
<td>CXR</td>
<td>Neutrophilia</td>
<td>Increased</td>
</tr>
<tr>
<td>(see Colour Atlas R10)</td>
<td>Unilateral,</td>
<td>Bilateral, diffuse,</td>
</tr>
<tr>
<td></td>
<td>Localized,</td>
<td>Interstitial +/-</td>
</tr>
<tr>
<td></td>
<td>Alveolar</td>
<td>Alveolar</td>
</tr>
</tbody>
</table>

* 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 and ventilatory insufficiency in more severe cases, oxygen saturation is sufficient in most
  - sputum culture and Gram stain, blood cultures, pleural fluid cultures, serology/viral cultures (epidemiology)
  - CXR (see Colour Atlas R10)
    - shows distribution, extent of infiltrate +/- cavitation
    - 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, hypersensitivity pneumonitis, BOOP, drug-induced pneumonitis, chronic eosinophilic pneumonia
- criteria for hospitalization
  - demographic factors: elderly, nursing home residents
  - co-existing illness: neoplasm, CHF, cerebrovascular disease, chronic liver/renal disease
  - physical examination: altered mental status, tachypnea, tachycardia, hypotension, extremes of temperature
  - laboratory findings: hyponatremia, acidemia, hyperglycemia, hypoxemia, azotemia, decreased hematocrit
  - radiographic findings: pleural effusion
PULMONARY INFECTIONS . . . CONT.

- treatment of CAP
  - based on epidemiology and 2000/2001 consensus guidelines from national societies
  - outpatient, otherwise healthy (no modifying factors): macrolides (e.g. erythromycin)
  - outpatient with COPD (recent systemic steroids) antibiotics/hospitalization: quinolones with enhanced activities against S. pneumoniae (e.g. levofloxacin) or macrolides (e.g. cefuroxime)
  - hospitalized patients: IV/PO quinolones (e.g. levofloxacin) or IV/PO macrolides plus IV/PO second/third generation cephalosporins (e.g. ceftriaxone)
  - severe hospitalized patients (ICU): IV quinolones (e.g. levofloxacin plus third generation cephalosporins) or IV macrolides plus third generation cephalosporin

Table 16. Common Organisms in Pneumonia

<table>
<thead>
<tr>
<th>Community Acquired</th>
<th>Nosocomial</th>
<th>HIV-associated</th>
<th>Alcoholics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>S. pneumoniae</td>
<td>enteric gram-negative rods</td>
<td>Pneumocystis carinii</td>
</tr>
<tr>
<td>Mycoplasma</td>
<td>H. influenzae</td>
<td>Pseudomonas</td>
<td>Klebsiella</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>gram-negative bacilli</td>
<td>S. aureus</td>
<td>Enteric</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>S. aureus</td>
<td>Oral anaerobes</td>
<td>gram-negative rods</td>
</tr>
<tr>
<td>Viral</td>
<td>Chlamydia</td>
<td>Legionella</td>
<td>S. aureus</td>
</tr>
<tr>
<td></td>
<td>Oral anaerobes</td>
<td></td>
<td>Anaerobes</td>
</tr>
<tr>
<td></td>
<td>Legionella</td>
<td></td>
<td>(aspiration)</td>
</tr>
</tbody>
</table>

* comorbidity includes COPD, CHF, diabetes, renal failure, recent hospitalization

Pathogens Causing Pneumonia (see Infectious Diseases Chapter)

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, meningoencephalitis)
- 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: macrolide, newer generation quinolones, doxycycline x 10-14 days
PULMONARY INFECTIONS . . . CONT.

**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
  - initial nonrespiratory symptoms: malaise, fever, GI symptoms, delirium, renal failure
  - subsequent respiratory symptoms: cough, chills, dyspnea, pleuritis, bronchopneumonia, blood-streaked mucoid sputum
- sputum: gram-negative coccobacillary organisms stain poorly
- labs: immunofluorescent serology, Legionella urine antigen, BAL
- treatment: macrolide, quinolone +/- rifampin

**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-clavulinate

**Moraxella catarrhalis**
- at risk: common in smokers, COPD patients, diabetics, patients with malignancies, alcoholics, patients on steroids; rare in normal adults
- clinical presentation: 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
PULMONARY INFECTIONS . . . CONT.

**Pneumocystis carinii**
- at risk: patients on immunosuppressants (e.g. transplant recipients) or chemotherapy, AIDS when CD4 count < 200
- clinical presentation: atypical, concurrent opportunistic infections
- CXR (see Colour Atlas R9)
  - 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
  - weight loss, anemia, clubbing --> chronic abscess
  - physical signs of consolidation
- investigations
  - imaging: CXR (thick-walled cavity with air-fluid level), CT, bronchoscopy
  - sputum: transtracheal/transthoracic aspiration, culture and Gram stain
- DDx
  - cavitating CA
  - bronchiectasis
  - TB, coccidioidomycosis
- treatment
  - antibiotics based on culture and sensitivity, postural drainage
  - surgical drainage and resection are rarely necessary

**FUNGAL INFECTIONS** (see Infectious Diseases Chapter)

**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 the immunocompetent
  - 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, fluconazole

MYCOBACTERIA

Mycobacterium tuberculosis
- pathogenesis
  - inhalation of aerosolized droplets from close contacts
  - primary TB: development of granulomatous reactions in the lungs, +/- local spread to lymph nodes and hematogenously to distant organs (extrapulmonary TB, e.g. kidneys, bone)
  - lesions usually heal and fibrose in the immunocompetent
  - secondary/post-primary TB: reactivation of dormant organisms and proliferation in aging/immunocompromised patients
- clinical presentation
  - usually asymptomatic but may have fever, lassitude, erythema nodosum, cough, sputum
  - post-primary TB: reactivation of dormant organisms in immunocompromised patients;
    - early systemic symptoms: malaise, fever, sweats, anorexia, weight loss
    - late localizing symptoms: dyspnea, pleuritic chest pain, cough, purulent sputum, hemoptysis
  - miliary TB (post-primary dissemination of multiple tiny granulomas in immunocompromised patients): fever, anemia, splenomegaly, meningitis
- CXR (see Colour Atlas R6)
  - 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): INH, rifampin, pyrazinamide, and ethambutol, then modified with sensitivities
  - if untreated, 50% will die within 5 years
  - 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 CXR, 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 immunocompetent patients after skin test conversion is 1% per year for the first 5 years and 0.1% per year subsequently (10% lifelong risk)
Atypical Mycobacteria
- etiology: *M. avium intracellulare*, *kansasii*, and *xenopi*
- at risk: immunocompromised, elderly, chronic lung disease, malnutrition
- 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 may be 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 Chapter)

<table>
<thead>
<tr>
<th>Induration</th>
<th>Groups in which infection is presumed to be present at the indicated induration</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 mm</td>
<td>Adolescents and children who are close contacts</td>
<td>Treat until 12 weeks after last exposure and then repeat the skin test</td>
</tr>
<tr>
<td>&gt; 5 mm</td>
<td>Close contacts&lt;br&gt; HIV-positive or unknown but at risk for HIV&lt;br&gt; Upper lobe fibrosis</td>
<td>Treat all ages for 6-12 months&lt;br&gt; Treat all ages for 12 months&lt;br&gt; Treat all ages for 12 months (if not previously treated for active TB) or 4 months of multidrug regimen</td>
</tr>
<tr>
<td>&gt; 10 mm</td>
<td>Silicosis&lt;br&gt; 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)&lt;br&gt; With risk factor: IV drug users, HIV positive, recent close contact, recent skin test conversion, CXR abnormality&lt;br&gt; Medical conditions at increased risk of disease if infected (gastrectomy, malnutrition, chronic renal failure, diabetes, high-dose steroids or other immunosuppressives, malignancies)</td>
<td>Treat all ages for 6-12 months&lt;br&gt; Treat all ages for 6-12 months&lt;br&gt; Treat all ages for 6-12 months</td>
</tr>
<tr>
<td>&gt; 15 mm</td>
<td>Low risk</td>
<td>Treat age &lt; 35 for 6-12 months</td>
</tr>
</tbody>
</table>

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 (Two-step testing)
- in persons infected with TB many years ago, skin reactivity to TB skin test may have waned, leading to false negative results
- however, in such previously infected persons, this first TB skin test boosts the reaction to a second test administered within 1-3 weeks of the first one
- i.e. if initial test negative, second TB skin test is given; if second test also negative, = no previous infection; if second test positive, = previous infection with TB
**NEOPLASMS**

**APPRAOCH TO THE SOLITARY PULMONARY NODULE**

(see Diagnostic Medical Imaging Chapter)

- **Definition:** A round or oval, sharply circumscribed radiographic lesion up to 3-5 cm which may or may not contain calcium

- **DDx**
  - Neoplasm (45%)
    - Primary bronchogenic cancer (70%)
    - Benign: eg. hamartoma, lipoma (15%)
    - Solitary metastasis (eg. breast, sarcoma) (10%)
  - Infection (53%)
    - TB, histoplasmosis, coccidiomycosis
  - Other (2%)
    - Healed granuloma
    - Vascular: A-V malformation, infarct
    - Congenital: cyst
    - Round pneumonia, round atelectasis, loculated effusion (=pseudotumour)

- **Investigations** (see Figure 8)
  - History and physical
  - CXR: always check old CXR first (see table 18)
  - CT thorax
  - Sputum cytology: usually poor yield
  - Biopsy (bronchoscopic or percutaneous): if sputum negative
  - Resection: if lesion is suspicious and there is no diagnosis with biopsy

<table>
<thead>
<tr>
<th>Table 18. Typical CXR Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign</strong></td>
</tr>
<tr>
<td><strong>Size</strong></td>
</tr>
<tr>
<td><strong>Margins</strong></td>
</tr>
<tr>
<td><strong>Features</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Doubling Time</strong></td>
</tr>
</tbody>
</table>

**Figure 7. Evaluation of a Solitary Pulmonary Nodule**
NEOPLASMS . . . CONT.

BENIGN
- less than 5% of all primary lung neoplasms
- bronchial adenomas and hamartomas comprise 90% of the benign neoplasms of the lung
- uncommon benign neoplasms of the lung include fibromas, lipomas, leiomyomas, hemangiomas, papillomas, chondromas, teratomas, and endometriosis
- clinical presentation: cough, hemoptysis, recurrent pneumonia, atelectasis
- may present without symptoms as a solitary pulmonary nodule
- slow-growing, benign endobronchial tumours that rarely metastasizes
- may be carcinoids (90%), adenocystic tumours, or mucoepidermoid
  - systemic symptoms usually absent
  - patients may complain of chronic cough, wheezing or give a history of recurrent pneumonia
  - hemoptysis may be present
- bronchial carcinoids
  - 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)
  - may secrete other hormones (such as ACTH) and cause paraneoplastic syndromes
  - treatment and prognosis: amenable to resection; 5-year survival is 95%
- hamartomas
  - peak incidence at age 60, more common in men vs. women
  - consist of normal pulmonary tissue components in a disorganized fashion
  - usually peripheral, clinically silent, and benign in behaviour
  - CXR: clustered “popcorn” pattern of calcification is pathognomonic for hamartoma

MALIGNANT

Epidemiology
- incidence
  - most common cancer in men and women
  - most common cause of cancer death in men and women
- risk factors
  - cigarette smoking: 85% of lung cancer related to smoking
  - asbestos (especially if smoker)
  - radiation: radon, uranium (especially if smoker)
  - 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 cancer (90%) (for characteristics, see Table 19)
  - incidence of adenocarcinoma is increasing
- bronchioloalveolar cancer (5%)
- bronchial adenoma (3%)
- lymphoma
- secondary metastases: breast, colon, prostate, kidney, thyroid, stomach, cervix, rectum, testes, bone, melanoma

<table>
<thead>
<tr>
<th>Table 19. Characteristics of Bronchogenic Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell Type</strong></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Squamous cell cancer (SCC) (may cavitate)</td>
</tr>
<tr>
<td>SCLC</td>
</tr>
</tbody>
</table>

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NEOPLASMS . . . CONT.

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
  - pericardium: 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
  - lung apex (Pancoast tumour): 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 20)
  - most often associated with SCLC

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 20. Paraneoplastic syndromes

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Associated Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skeletal</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertrophic pulmonary osteoarthropathy (clubbing)</td>
<td>Bronchogenic cancer (not SCLC)</td>
</tr>
<tr>
<td><strong>Dermatologic</strong></td>
<td></td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>Bronchogenic cancer</td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
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<tr>
<td>Hypercalcemia (osteolysis or PTH)</td>
<td>Squamous cell cancer</td>
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<tr>
<td>Hypophosphatemia</td>
<td>Squamous cell cancer</td>
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<tr>
<td>Hypoglycemia</td>
<td>Sarcoma</td>
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<tr>
<td>Cushing's syndrome (ACTH)</td>
<td>SCLC</td>
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<tr>
<td>Somatostatinoma syndrome</td>
<td>Bronchial carcinoid</td>
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<tr>
<td>SIADH</td>
<td>SCLC</td>
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<td><strong>Neuromyopathic</strong></td>
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<tr>
<td>Eaton-Lambert syndrome</td>
<td>SCLC</td>
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<tr>
<td>Polymyositis</td>
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<tr>
<td>Subacute cerebellar degeneration</td>
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<td>Spinocerebellar degeneration</td>
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<td>Peripheral neuropathy</td>
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<tr>
<td><strong>Vascular/Hematologic</strong></td>
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<tr>
<td>Nonbacterial endocarditis</td>
<td>Bronchogenic cancer</td>
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<tr>
<td>Trousseau's syndrome (migratory thrombophlebitis)</td>
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<td>DIC</td>
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<td><strong>Renal</strong></td>
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<tr>
<td>Nephrotic syndrome</td>
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Investigations
- initial diagnosis
  - imaging: CXR (see Colour Atlas R7), 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 Cancer**
- 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

**Figure 8. Staging and Treatment Algorithm for Bronchogenic Cancer**

**Therapy for Bronchogenic Cancer** (see Figure 8)
- 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 Cancer**
- 5 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
- NSCLC
  - Stage I 50%
  - Stage II 30%
  - Stage IIIA 15%
  - Stage IIIB 5%
  - Stage IV < 2%

**Bronchioloalveolar Cancer**
- A type of adenocarcinoma that grows along the alveolar wall in the periphery
- May arise at sites of previous lung scarring (a scar cancer)
- Clinical presentation: similar to bronchogenic cancer, late metastasis but 45% rate of treatment and prognosis; solitary lesions are resectable with a 60% 5-year survival rate; overall survival rate is 25%
RESPIRATORY FAILURE

- due to impairment of gas exchange between ambient air and circulating blood
  - hypoxemic (PaO₂ < 60 mm Hg), hypercapnic (PaCO₂ > 40 mm Hg)
  - 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
  - low inspired FiO₂
  - shunt
  - V/Q mismatch
  - diffusion impairment
  - low mixed-venous oxygenation
- treatment
  - reverse the underlying pathology
  - 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
  - hypoventilation
- treatment
  - reverse the underlying pathology
  - correct exacerbating factors
    - NTT/ETT suction: clearance of secretions
    - bronchodilators: reduction of airway resistance
    - antibiotics: treatment of co-morbid infections
    - maintain oxygenation (see above)
    - 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 acidemic 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
RESPIRATORY FAILURE . . . CONT.

Pathogenesis
- disruption of alveolar capillary membranes → 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
- hypoxic respiratory failure
- cardiac arrest

Treatment
- treat underlying disorder (e.g. antibiotics if infected)
- minimize ventricular induced lung trauma
- 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) if cardiac output inadequate
- pulmonary-arterial catheter is useful for monitoring hemodynamics
- mortality: 50% (infection is the most common cause)
- if patient survives, prognosis for recovery of lung function is good

MECHANICAL VENTILATION (see Anesthesia Chapter)
- artificial means of supporting ventilation and oxygenation
- two main indications
  - hypoxic respiratory failure: giving PEEP opens collapsed alveoli, decreasing the V/Q mismatch
  - hypercapnic respiratory failure: ventilator provides alveolar ventilation; may decrease 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 between ventilator breaths without triggering ventilator
  - 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 (bi-level positive airway pressure) (a boost of pressure during inspiration and constant pressure during expiration)
      - CPAP (continuous positive airway pressure)

SLEEP-RELATED BREATHING DISORDERS
- a group of disorders characterized by decreased airflow occurring only in sleep or worsening in sleep
- affects 9% of men, 4% of women
- 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
  - obesity-hypoventilation syndrome (Pickwickian syndrome)
  - respiratory neuromuscular disorders
SLEEP-RELATED BREATHING DISORDERS . . . CONT.

Sleep Apnea
- Apnea/Hypopnea Index (AHI) = # of apneic (no breathing) and hypopneic (> 50% reduction in ventilation) events > 10 seconds during sleep episode
- diagnosis: AHI > 15
- risk factors: obesity, upper airway abnormality, neuromuscular disease, hypothyroidism, alcohol/sedative use, nasal congestion, sleep deprivation
- clinical presentation
  - secondary to arousal from sleep: daytime somnolence, personality and intellectual change, insomnia, snoring
  - secondary to hypoxemia and hypercapnia: morning headache, polycythemia, pulmonary/systemic HTN, cor pulmonale/CHF, nocturnal angina, arrhythmias
  - OSA typically presents in a middle-aged obese male snorer
  - CSA can be due to neurological disease
- complications
  - depression, weight gain, cardiac complications (see above)
- sleep study investigations
  - evaluates sleep staging, airflow, ribcage movement, ECG, O2 saturation, limb movements
  - indications
    - excessive daytime sleepiness
    - unexplained pulmonary HTN or polycythemia
    - daytime hypercapnia
    - titration of optimal nasal CPAP
    - assessment of objective response to interventions
- treatment
  - modifiable factors: decreased alcohol/sedatives, weight loss, nasal decongestion, treatment of underlying medical conditions
  - OSA or MSA: nasal CPAP, uvulopharyngoplasty, nasal septoplasty, tonsillectomy
  - CSA or hypoventilation syndromes: nasal BiPAP/CPAP, respiratory stimulants (e.g. progesterone) in select cases
  - tracheostomy rarely required and should be used as last resort

REFERENCES


