**Etiology**

- @ irreversible dilation of the airways caused by an inflammatory destruction of the airways
- Most commonly due to INFECTION ➞ bacterial pneumonia, TB, measles, pertussis
- Seen in rheumatic dz [Sjorgen’s]

Infection and obstruction are the two underlying causes of the dilation

- **Allergic bronchopulmonary aspergillosis**: due fungal infection ➞ seen exclusively in pts w/ underlying asthma
- Obstruction: tumor, mucous plug, COPD
  - superimposed infection sec. to obst can contribute to dmg

Predisposition Syndromes:

- **dyskinetic cilia syndrome** ➞ think Kartagener’s Syndrome: noted with sinusitis, situs inversus bronchiectasis
- Impaired humoral immune response
- **Cystic Fibrosis**

**DDx:**

Dx is made in light of a Hx of copious sputum production with periodic hemoptysis

**NOTES:**

Pursuit of Etiology:

- CF: sweat chloride, CFTR genotyping
- PCD: nasal scrape, exhaled NO level, look at cilia in EM
- ABPA: skin tests, IgE levels

**Labs/Workup**

- Localized Dz: ABGs nl
  - CXR: shows abnormal Si ➞ ring shadows in saccular variant
  - HRCT: Dx tool of choice, shows extent & location
  - PFTs: for funct assessment

- Extensive Dz:
  - ABG show Si of hypoxemia, hypercapnia
  - cor pulmonale

**Sputum Culture**: for H. influ, Staph. Aureus, Pseudomonas, MAC

**Si/Sx**

- cough, copious sputum
- sputum often purulent
- 10-20% are “dry” w/out sputum Si/Sx
- hemoptysis
- may hear local rales, rhonci
- clubbing

**Pathophysiology**

- Specific patterns: cylindrical, varicose, saccular
  - filled w/ copious secretions, often grossly purulent ➞ micro shows ulceration and squamous metaplasia
  - Blood supply will be increased to the area due to inflammation
  - Inflammatory erosion results in hemoptysis often seen
  - Once dilated the defense mechs are compromised; bacteria colonize; often a stable infection, w/ acute periodic Sx ➞ PFTs may actually be w/in nl range, abnormalities, if seen, are due to extensive bronchiectasis compromising a large area and coexistent with another generalized airway disease ➞ i.e think chronic bronchitis
  - Often see concomitant infection w/ Pseudomonas aeruginosa

**Therapy [Tx]**

**Antibiotics**: amox, TMP-SMX for Strep, Haemoph; oral ciprofloxacin for Pseudomonas

**Chest PT**: chest PT and postural drainage for copious sputum
  - Inflatable vest, or mechanical vibrators for ↑ mucous and secretion clearance

**Bronchodilators**: for pts w/ concomitant airway obstruction which is reversible

**Surgery**: reserved for uncontrolled Sx pt w/ a single localized area of Dz
### Cystic Fibrosis

**Etiology**
- Most common lethal genetic disease affecting Caucasian population
- Autosomal recessive trait; 1 in 2.5k LBs
- Two Major Abnormalities:
  - Production of thick tenacious secretions from exocrine glands
  - Elevated Na, Cl, K, in sweat

**Genetics**:
- Long arm of c.7 is the most common defect; defect in CFTR (imp for chloride transport across apical face of epith cells)
- ΔF508 deletion, thought responsible for the high electrolyte concentrations in sweat

**DDx:**
- Dx made with one 1+ phenotypic features AND evidence of CFTR malfunction
- Immunodeficiency states
- Celiac Dz
- Asthma
- Recurrent pneumonia

### Labs/Workup

- + pilocarpine ionophoresis, ie sweat test
- Sweat chloride greater than 60mEq/L
- Incr Na, Cl, K, in sweat
- Specific for homozygotes

CT/CXR:
- Si of bronchiectasis

**Si/Sx**
- Neonatal period: Si are meconium ileus obstruction [seen 15% of time]
- Pancreatic insufficiency
- Males are sterile, females reduced fertility
- Hemoptysis
- Hear coarse rales, wheezing
- Clubbing
- Pneumothorax
- Resp insuff
- Nasal polyps, sinusitis
- Persistent P. aeruginosa

### Pathophysiology

Pathology thought to be due to obstruction of ducts or tubes by the secretions
- Pancreas: causes fibrosis, atrophy of acini, cystic Δ [hence the name]
- Airways: mucous plugs block bronchi and block airflow and drainage
- Can lead to pneumonitis, bronchiectasis, and abscess
- Cardiac: cor pulmonale, and/or RVH

**Pathophysiology/genesis:**
- Pancreas: pancreatic insufficiency leads to malabsorption especially of fats
- Lung: recurrent tracheobronchial infection, bronchiectasis
- Infection often due to Staph aureus and/or Pseudomonas aeruginosa
- Infection due to local airway host defense compromise
- Cascade of dz: ΔCFTR⇒altered ion transport⇒vol-depleted airway surface liquid⇒reduced mucociliary clearance⇒chronic infection/inflammation⇒progressive bronchiectasis

**Consequences of obstruction:**
- V/Q mismatch
- Hypoxemia
- Pulmonary HTN
- If severe, cor pulmonale

### Therapy [Tx]

- Aimed at diminishing the clinical consequences
- Bronchopulmonary drainage
  - PT, postural drainage
- Antibiotics: azithromycin
- Bronchodilators, where indicated
- Decrease sputum viscosity [due to DNA dumping from inflam cells]
- INH recombinant DNase to decrease mucous viscosity, since DNA is a large portion of it [the viscous nature]
- BL lung transplant in severe conditions
- Reduction of inflammation has been shown to slow the dz progression

- Infection w/ B. capacia or S. maltophilia are very negative prognostic factors; given bug resistance to Tx

- Prospect for gene therapy, plagued by lack of effective means to deliver and sustain the replacement gene
Cystic Fibrosis: continued

Phenotypic Features of CF:
- GI: meconium ileus, rectal prolapse, pancreatic insufficiency, malnutrition, fat soluble vitamin deficiency
- Lung:
  - Chronic Sinopulmonary Dz: persistent infxn with *P. aeruginosa, Staph aureus*; chronic cough/sputum;
  - PFTs show **obstructive pattern**; bronchiectasis; nasal polyps, sinusitis, digital clubbing
- Other: **salt loss syndromes; chronic metabolic alkalosis;** obstructive azoospermia [CBAVD]

**Extra Pulmonary Complications:**
- CF-related diabetes [CFRD]: incidence is age related
- gall bladder dz: w/ sludge or gall stones in 10-30%
- osteopenia/osteoporsis
- nephrolithiasis:

**Pulmonary Complications:**
- acute exacerbations: cause for hospitalization; due to ↑ bacterial burden and inflammation
- hemoptysis
- pneumothorax: send in 20% of CF patients over time
- resp failure

**Tx for acute exacerbations of CF:**
- Dx by the drop in lung function and ↑ Sx
- intensify airway clearance promoting Tx
- antibiotics: IV & INH; 2 agents against all Gm"-" pathogens; Tx for 2+ weeks
- PFT assessment

---

### Defect

- Abnormal Gene
- Abnormal CFTR
- Abnormal Sodium Chloride & Water Movement Through Cell
- Abnormally Thick and Dry Mucous
- Bronchial Airway Obstruction

---

### Therapy

- Gene Replacement
- Protein Replacement
- Correction of Electrolytes
- Mucoytics
- Mucous Clearance Techniques
- Anti Inflammatory Agents
- Anti Microbials
- Lung Transplants

---

**Vicious Cycle**

- Infection
- Inflammation
- Progressive Lung Tissue Destruction
- Relases of Proteases & DNA
- Thickened Mucous
- Respiratory Failure
@ the episodic and reversible airway narrowing due to s.m. contraction of the airway wall secondary to hyperresponsiveness of the airways.
- 3-5% of population suffers from asthma

**Etiology**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrinsic asthma</td>
<td>Type I hypersensitivity response; childhood, FamHx, IgE mast cell and eosinophil regulated</td>
</tr>
<tr>
<td>Intrinsic asthma</td>
<td>Adult; lack of atopy; may be triggered by URTI or psych stress; eosinophil is again a key player</td>
</tr>
<tr>
<td>Drug-induced asthma</td>
<td>See w/ NSAIDs, β-blockers, sulfites, certain foods</td>
</tr>
</tbody>
</table>

**Pathophysiology**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest tightness</td>
<td>Dyspnea, more prominent on expiration than inspiration</td>
</tr>
<tr>
<td>Cough</td>
<td>Bronchodilation, Requires high-dose corticosteroids (IV) + bronchodilation</td>
</tr>
<tr>
<td>Wheezing</td>
<td>Bronchodilation, Requires high-dose corticosteroids (IV) + bronchodilation</td>
</tr>
</tbody>
</table>

**Diagnosis (Dx)**

- Intrinsic asthma: Robbins p.456
- Extrinsic asthma: Th2 response is fundamental to the pathogenesis

**DDx:**

- CHF, COPD, PE, FB aspiration, Wegener’s granulomatosis, anxiety DO, hypersensitivity pneumonitis, TB

**Therapy (Tx):** Table pg 86, Weinberger

- Avoidance of trigger factors.
- PharmTx dependent on stage

**Bronchodilators:** β2-AR specific

- Albuterol, salmeterol (long-acting)
- Inhalational form for [often albuterol] Tx of acute episode or prophylaxis

**Methylxanthines:** cAMP levels, Promoting bronchodilation

- Also decr mast cell degranulation
- Theophylline [po], aminophylline [IV, po]
- Approved for COPD not asthma
- Ipratropium: Muscarinic antagonist

**Anti-inflammatory agents:**

- Corticosteroids: eosinophil#, lymphocytes, inflammatory cytokines
- Imp for acute Tx and management
- Prednisone, methylprednisone
- Maintenance dosing often given inhalational, SEs
- Cromolyn and nedocromil: Inhaled
- Not bronchodilators, Inhibit inflammatory processes; used for prophylaxis, not acute Tx

**Newer therapy:**

- Zafirlukast, Motelukast: Leukotriene mediators
- Alternate Tx when standard Tx failing to regulate
- Monoclonal Ab to IgE

**Tx model:**

1. Try β2-AR agonist
2. Try Anti-inflammatory maintenance
3. Add Cromolyn, Nedocromil as indicated
4. If unregulated, regular use of β2-AR agonist inhalational + methylxanthines

**Labs/Workup**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum</td>
<td>Many eosinophils on sputum smear</td>
</tr>
<tr>
<td>Methacholine or histamine challenge</td>
<td>Isocapneic hyperpnea challenge</td>
</tr>
<tr>
<td>ABG</td>
<td>Low PO2; V/Q mismatch</td>
</tr>
</tbody>
</table>

**Si/Sx**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
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<tbody>
<tr>
<td>Episodic dyspnea</td>
<td>Wheezing, more prominent on expiration than inspiration</td>
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<td>Cough</td>
<td>Bronchodilation, Requires high-dose corticosteroids (IV) + bronchodilation</td>
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<tr>
<td>Chest tightness</td>
<td>Bronchodilation, Requires high-dose corticosteroids (IV) + bronchodilation</td>
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</table>

**Severe asthma:**

- Pulsus paradoxus
- RR > 30
- Tachycardia > 120

**CXR:**

- Normal, or hyperinflation

**PFTs:**

- During attack
- FEV1 < 1L
- FEV1/FVC ratio
- TLC

**Gases:**

- CO2, Oxygen

**Path:**

- See overdistention of lungs w/ airways occluded with thick mucous plugs
- Edema & cellular infiltrates [eosinophils, lymphocytes] of lamina propria
- “Fragile” epithelium
- Hypertrophy and hyperplasia of SM layer
- Thickening of the basement membrane
- Hypertrophy of mucous glands and goblet cells

**Pathophysiology:**

- Narrowed airways restricts insp and exp; but affects expiration most [due to positive intrapleural pressure]
- The RV is thought to be due to airtrapping as the airways close prematurely during expiration
- The FRC is due to persistent activity of the inspiratory muscles keeping the lung open @ higher than normal volumes during expiration & also due to dynamic hyperinflation, where the lung cannot expel fully the vol from the previous breath
Asthma cont’d:
Other Si/Sx:
- allergic shiner: this is discoloration and edema around the eye
- atopic dermatitis

Occupational asthma:
- think about the population that would be exposed to the specific allergens; and be suspect when that working groups shows signs of asthma
- ie. Painters and plastic workers, common allergens are Anhydrides
- vegetable gums, seen in print-workers

More on Intrinsic Asthma:
- once exposed and sensitized, can have perennial reactions even w/ allergen avoidance
- can sometimes be due to aspirin
- non-specific bronchial hypersensitivity

more on PFTs:
- see increased DLCO [diffusing capacity] sometimes, paradoxical, but helpful in Dx
- auto-PEEP with respiratory rate ??

More Findings:
- mucous casts of small airway in sputum
- Charcot-Leyden crystals: formed from eosinophils, “asthma crystals”
- Creola Body: agglomerated bronchial epithelial cells

Point on Beta agonist Tx:
- Tx with a β-agonist may actually worsens the V/Q mismatch

Signs of Respiratory Failure:
- mental status changes
- failing PEFRs
- hypercapnea, CO2 retention
- asymmetric movement of abdomen and thorax
- cyanosis
CHRONIC BRONCHITIS [COPD]

L=nl; R=chronic inflammation

**Etiology**
- @ common DO of COPD
  - smoking is #1
  - environmental factors and RTI’s non-etiologic, just exacerbating
  ⇒ occupational pollutants are particularly exacerbating for chronic bronchitis

**DDx:**
- • clinical Dx made for pts w/ chronic cough and sputum production
- • Dx requires prod cough @ least 3mo of the year for 2yrs

**NOTES:**
Think “Blue Bloater” not Blu-Blocker

**Pathophysiology :: TYPE B pathophysiology**
Path: characterized by the enlargement of the mucous-secreting glands and ↑goblet cells
- • causes ↑ Reid Index

Gross: erythematous, edematous mucosae with copious mucous airway secretions and possibly pus
- in bronchioles: see peribronchiolar fibrosis, airway obstruction, ie chronic bronchiolitis

Airway Narrowing Due To:
- • hypersecretion of mucous
- • hypertrophy of mucous glands
- • ↑ goblet cells in bronchioles an bronchi
- • squamous metaplasia and dysplasia of bronchial epithelium
  ⇒ Loss of ciliated epithelium also decreases mucous mobilization

**Therapy [Tx]**

Modalities of Tx for COPD:
1) bronchodilators
2) antibiotics
3) corticosteroids
4) supplemental O2
5) exercise rehab
6) chest PT
7) surgery, last resort

• give pts pneumovax and flu vaccine

- the surgery can be Lung transplant or lung volume reduction surgery, allowing the diaphragm to return to a more normal shape; it also removes the less-elastic Dz’d portions of the lung, improving lung compliance
EMPHYSEMA [COPD] •

arterial deficiency, increased markings, overinflation

Etiology
• smoking is #1
• defic. In serum α1-antitrypsin is a predisposing factor in a few cases
genetic: 75 alleles of α1-antitrypsin; labeled Pi for protease inhibitor; Pi M = nl; PiZ=abnormal
⇒ PiZZ homozygotes have 15% of nl serum levels; strong predisposition for emphysema, esp if a smoker
• α1-antitrypsin: thought to help maintain the proper balance of elastin in the lung parenchyma; it keeps the elastin-destructive properties of elastase in check

DDx:
This Dx is made pathologically, morphologically.
DDx: CHF, asthma, RTIs, CF, PE, sleep apnea [obstructive], hypothyroidism

NOTES:
Think “Pink Puffer”
• in severe COPD, emphysema is the major contributor to airway obstruction
• Dz limited to the terminal acinus, whereas chronic bronchitis can affect large and small airways
• LESS hypoxemic than a Type B pathology
• secondary pulmonary HTN develops gradually in all COPD pts

Pathophysiology :: TYPE A pathophysiology
The destruction of alveolar walls and enlargement of the terminal air spaces.
• Centriacinar type caused by smoking and coal dust.
• Centrilobular is specific for smokers.
⇒ these are mainly in the resp bronchioles
⇒ gross appearance is more irregular than panacinar
⇒ more common in upper lobes
• Panacinar is pathognomonic for α1-antitrypsin defect.
⇒ more uniform distribution of Dz through lung parenchyma
⇒ seen more often in the lower lobe
• Distal acinar: less imp, underlies spontaneous pneumothorax; occurs adjacent to fibrosis, scarring, atelectasis
⇒ more severe in upper half of lung

Mech of Decr expiratory flow rate:
• due to loss of elastic recoil of lung, leading to:
⇒ lower driving pressure for exp flow
⇒ loss of radial traction on airways, [loss of interdependency] allowing for premature collapse
⇒ ↓resistance to expansion [less stiff], thus CPL curve shifted up and left; and holds more volume @ any point in the resp cycle
⇒ ↑TLC due to loss of resistant elastic force during inspiration
⇒ ↑FRC as the outward recoil of chest wall dominates the lungs now
⇒ ↑RV due to premature collapse of airways during expiration, air-trapping

Therapy [Tx]
Modalities of Tx for COPD:
1) bronchodilators
2) antibiotics
3) corticosteroids
4) supplemental O2
5) exercise rehab
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7) surgery, last resort
• give pts pneumovax and flu vaccine

Labs/Workup
PFTs [for COPD]
• ↓FVC, ↓FEV1, ↓ratio, ↓MMFR
• ↑RV, ↑FRC, ↑TLC for emphysema:
• diffusing capacity limited ↓
CXR: AD pattern =
• large lung vol
• flat diaphragm
• ↑AP diameter
• ↓ vascular markings
ABGs: ↓PO2, nl/↑PCO2

Si/Sx
• dyspnea,
• ↑minute ventilation
• non-cyanotic
• elastic recoil ↓
• thin, wasted appearance
• purse-lip breathing
• decr breath sounds

Therapy [Tx]
Modalities of Tx for COPD:
1) bronchodilators
2) antibiotics
3) corticosteroids
4) supplemental O2
5) exercise rehab
6) chest PT
7) surgery, last resort
• give pts pneumovax and flu vaccine

• the surgery can be Lung transplant or lung volume reduction surgery, allowing the diaphragm to return to a more normal shape; it also removes the less-elastic Dz’d portions of the lung, improving lung compliance
Smoking and COPD relation:

- Smoking is the number one preventable cause of COPD
- Smoking affects the lungs @ the bronchi, bronchioles, and lung parenchyma
- Promotes an ↑ # and size of mucous glands
  - Leads to ↑ mucous release into lumen
- ↑ the influx of inflammatory cells
  - ↑ PMN s, macrophages
    - ↑ cytokines
    - ↑ oxidative stress, more reactive species released locally
- impaired mucociliary clearance secondary to bronchial epithelial damage
- Small airways: bronchiolar narrowing, fibrosis, inflammation
  - Airflow obstruction
- ↑ cough and sputum production ⇒ chronic bronchitis
- pulmonary parenchyma effects secondary to inflammation, and effects of smoke ⇒ emphysema
- protease-antiprotease hypothesis:
  - alveolar integrity is balancing act
  - smoke incr the # of PMNs
  - PMNs produce elastase
    - Elastase degrades elastin ⇒ pathological changes seen in emphysema
  - Smoke oxidants and oxidants from inflammatory cells modify α1-antitrypsin impairing it’s anti-elastase activity
  - Neutrophil elastase also stimulates mucus release
  - PMNs and macrophages make matrix metalloproteinases
    - Shifting the balance of that system towards degradation also

Pulmonary HTN:

- Potential complication of COPD
- High pressures w/in the pulmonary arterial system
- Leads to RVH, due to added workload on right heart
  - Can lead to cor pulmonale
    - A R-sided failure secondary to pulmonary HTN
- Hypoxia leads to both in COPD
  - A decr in PO2 is a strong stimulus for the constriction of the pulmonary arteries
- Other factors leading to pulmonary HTN in COPD are:
  - Hypercapnia, polycythemia [↑HCT, secondary to chronic hypoxia], reduction of pulmonary vascular bed area [↑ resistance to flow]
### Etiology

Pulmonary interstitium and alveolar spaces infiltrated by eosinophils and to a lesser extent, macrophages.

### DDx:

### Labs/Workup

<table>
<thead>
<tr>
<th>CXR: pulmonary infiltrates, peripheral distribution</th>
<th>• eosinophils in peripheral smear</th>
</tr>
</thead>
</table>

### Si/Sx

- dyspnea
- NON-productive cough
- fever
- weight loss

### Pathophysiology

### Therapy [Tx]

- responds quite well to corticosteroids
- Tx improves Sx in days-weeks, but Tx is continued for mo's to prevent recurrence

### NOTES:

Not For Exam Material
**Bronchiolitis Obliterans w/ Organizing Pneumonia (BOOP)**

<table>
<thead>
<tr>
<th>Etiology &amp; Epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dz of connective tissue plugs in small airways accompanied by mononuclear infiltration of the surrounding parenchyma [org pneumonia part]</td>
</tr>
<tr>
<td>AGE: 40-75</td>
</tr>
<tr>
<td>Known etiologic agents:</td>
</tr>
<tr>
<td>radTx</td>
</tr>
<tr>
<td>infxn: <em>Coxiella burnetii, Pseudomonas aeruginosa, or Mycoplasma</em></td>
</tr>
<tr>
<td>drugs &amp; toxins: gold, cephalosporins, amiodarone, free-base cocaine</td>
</tr>
<tr>
<td>When no cause can be determined for the BOOP it is referred to as cryptogenic organizing pneumonia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Labs/Workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR: patchy pulmonary infiltrates</td>
</tr>
<tr>
<td>=&gt; w/ alveolar pattern</td>
</tr>
<tr>
<td>=&gt; but no Rad findings are diagnostic</td>
</tr>
<tr>
<td>DLCO</td>
</tr>
<tr>
<td>widened A-a gradient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Si/Sx</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-productive cough</td>
</tr>
<tr>
<td>low-gd fever</td>
</tr>
<tr>
<td>malaise</td>
</tr>
<tr>
<td>SOB</td>
</tr>
<tr>
<td>PFTs: show restrictive pattern</td>
</tr>
<tr>
<td>influenza-like Sx</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subacute presentation</td>
</tr>
<tr>
<td>building over weeks to months</td>
</tr>
<tr>
<td>show systemic and respiratory Si/Sx</td>
</tr>
<tr>
<td>BOOP, disease characterized pathologically by the presence of granulation tissue polyps in the lumen of bronchioles and alveolar ducts and patchy areas of organizing pneumonia, consisting largely of mononuclear cells and foamy macrophages.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Therapy [Tx]</th>
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<tbody>
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<td>Responds quite well to corticosteroids, but not antibiotics</td>
</tr>
<tr>
<td>Tx improves Sx in days-weeks, but Tx is continued for mo’s to prevent recurrence</td>
</tr>
<tr>
<td>Overall BOOP mortality is 10%</td>
</tr>
</tbody>
</table>

**NOTES:**

- on CXR it looks very similar to community-acquired pneumonia
<table>
<thead>
<tr>
<th>Etiology</th>
<th>Labs/Workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDx:</td>
<td>Si/Sx</td>
</tr>
<tr>
<td>NOTES:</td>
<td>Pathophysiology</td>
</tr>
<tr>
<td></td>
<td>Therapy [Tx]</td>
</tr>
</tbody>
</table>
SARCOIDOSIS

Etiology
@ A chronic systemic granulomatous idiopathic disease, characterized by nonspecific non-caseating granulomas.
• still idiopathic
• theory: an immune response to an exogenous agent in a genetically predisposed person
• cells critical to the process are:
  ⇒ macrophages & T lymphocytes

Workup & DDx:
• presents most commonly in winter or early spring
• somewhat common in 20-40 y/o
• Dx is one of exclusion, since infxn from fungi, mycobacteria, and beryliosis can also form non-caseating granulomas
workup: CXR, Bx of involved tissue [bronchosopy + transbronchial Bx used for lung involvement]
DDx:
• TB, lymphoma, HD, Mono, parasitic infxn, alveolar cell carcinoma

NOTES:
EPI: high incidence in Danish, Swedish, and US AA
⇒ higher prevalence in NON-smokers!
• see familial and racial clustering
• certain HLA types suspected

Labs/Workup
• hypergammaglobulinemia
• hypercalcemia, hypercalciuria
• sometimes see low lymphocytes; periph counts that is
• ACE elevated in 60% of pts, nonspecific

HR-CT: shows common small nodular bronchovascular bindle distribution
•Anergy to skin test Ags like Candida or PPD

CXR: adenopathy of the hilar and w/w/out paratracheal nodes
⇒ parenchymal changes
⇒ w/ adv Dz see honey-combing, bullae, cysts, emphysema

Gallium-67 scan: reveals location of the granulomas
⇒ “panda sign”, lacrimal, salivary gland localization is suggestive of Dz

Si/Sx
• can be aSx, disc incidentally on routine CXR
• dyspnea
• nonproductive cough
⇒ common to see night sweats, retrosternal pain
• many other organ systems can be involved

Eye: anterior uveitis
Skin: skin papules, plaques
Lofgren’s Syndrome: acute onset; BL hilar lymphadenopathy; erythema nodosum; fever; arthralgias

Pathophysiology
Path: non-caseating granulomas; multi-nucleated giant cells; alveolitis [macrophages, lymphocytes]
• interalveolar CD4:CD8 ratio will be higher than 3.5
• ↑ IL-2, IFN-gamma

Pathophysiology:
• macrophages and T lymphs [CD4+, Th1] process antigen
• pro-inflammatory cyto/chemokines recruit, activate, prolong inflammation, and promote granuloma formation
• profibrotic cytokines [TGF-β, PDGF, IGF-1] might promote fibrosis
• the localization of CD4+ cells @ the granulomatous sites, results in a rel ↓ in periph blood CD4+ counts
• the T lymph non-specifically activate B cells leading to the ↑ production of various Ig’s
• the altered Ca metabolism is secondary to the ↑ vitD active formation, leading to ↑ Ca absorption, GI

• the ↑ ACE is caused by the vasc. Epithelial cells of the granulomas producing it, but it is nonspecific

Therapy [Tx]
• aSx pts or Pts w/ little organ involvement may nnot need to be treated
• the Dz sometimes spontaneously regresses also
⇒ Tx is indicated w/ Sx pt and w/ significant organ involvement
Tx: systemic corticosteroids
• w/ refractory Dz add immunosuppressive drugs
• the Dz course is unpredictable, remissions are often permanent
### Etiology

- Immunologically induced inflammation of the lung parenchyma caused by repeat or intense inhalation of an organic agent.
- Occurs at level of the alveoli.
- Also called extrinsic allergic alveolitis.
- Bird fancier's lung; farmer's lung; humidifier lung; chemical worker's lung.
- Can be due to numerous environmental agents; often occupationally related.
- But, since not all workers develop, there must be some genetic component.

### Common sources:
- Moldy hay, grain, vegetables, silage, bird feces/feathers, LMW chemicals.

### Workup & DDx:
- Should be suspect with bronchitis and dyspnea w/out obvious cause.
- Workup: Hx [exposures], CXR, PFTs, skin tests NOT helpful.
- DDx: Sarcoidosis, collagen-vascular Dz, eosinophilic pneumonia, idiopathic pulmonary fibrosis, drug-induced parenchymal Dz.

### Pathophysiology

- **Path:** Allveolitis composed mostly of CD8 T cells and macrophages, and often see granulomas.
- **Granulomas** will be poorly formed and often in the peribronchiolar region.
- **Pathogenesis:** Type IV rxn believed key to pathogenesis.
  - LRT T cells become sensitized to Ag, they release cytokines, attract m.phages, granulomas form.
  - Type III response probable role also [immune-complex].

### Therapy [Tx]

- **#1 is Ag avoidance.**
  - Acute: usu require no Tx, but if severe give glucocorticoids [prednisone].
  - Chronic: prednisone, then tapered to maintenance dose for adequate functional status.

- The chronic form, in advanced stages, can lead to diffuse interstitial fibrosis.

### Labs/Workup

<table>
<thead>
<tr>
<th>CXR: Patchy infiltrates</th>
<th>CXR: Nodular pattern; upper lobe predominance</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFTs: Acutely ↓ LV, DLCO, &amp; CPL</td>
<td>HR-CT: Mosaic ground-glass appearance,</td>
</tr>
<tr>
<td>Exercise-induced asthma</td>
<td>BAL [bronchoalveolar lavage]</td>
</tr>
<tr>
<td>Chronic Dz shows restrictive pattern and sometimes obstructive</td>
<td>Shows ↑ T cell #s</td>
</tr>
<tr>
<td>During acute rxn see ↑ pro-inflammatory cytokines [IL-8]</td>
<td></td>
</tr>
</tbody>
</table>

### Si/Sx

<table>
<thead>
<tr>
<th>Acute: 4-6hrs post exposure</th>
<th>Chronic: Diffuse parenchyma Dz; insidious onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea, cough, fever</td>
<td>Slow, progressive SOB, cough,</td>
</tr>
<tr>
<td>CXR: Patchy infiltrates</td>
<td>Fatigue, LOA, weight loss</td>
</tr>
<tr>
<td>CXR: Nodular appearance to reticulonodular; upper-lobe predominance</td>
<td></td>
</tr>
<tr>
<td>HR-CT: Often see mosaic ground-glass pattern</td>
<td></td>
</tr>
</tbody>
</table>

### NOTES:

- Medscape®  www.medscape.com
# Pneumoconiosis: Silicosis

## Etiology

Pneumoconiosis represents several types of interstitial lung disease caused by the inhalation of inorganic dusts.

**Common Agents:**
- silica, coal, talc, mica, aluminium, beryllium
- particles with a diameter of 0.5-5 micrometers likely to reach the respiratory bronchioles and alveoli

**Siliconosis:**
- persons at risk for Silicosis are sandblasters, rock miners, quarry workers, stonecutters

**DDx:**
- occupational and exposure Hx is key

**DDx:** other pneumoconiosis, Sarcoidosis, TB, hypersens pneumonitis, histiocytosis X, lung CA

## Notes:

**Simple pneumoconiosis:** when just small rounded opacities on CXR

**Complicated:** larger or coalesced opacities

- **Progressive massive fibrosis:** term for complicated Dz
- pts w/ upper lobe Dz are more affected

## Labs/Workup

- CXR: small rounded opacities, when simple
  - enlargement of the hilar nodes, w/ or w/o calcification

## Si/Sx

- dyspnea, cough, wheezing
- abnormal CXR in aSx person

Susceptible to secondary infxns from **mycobacteria**

## Pathophysiology

**Silicosis:** most often of the quartz form
- proposed toxicity modality of silica with macrophages
  - cycle of ingestion, death of m.phages, release, re-ingestion
  - this leads to release of oxidants from the m.phages causing cell injury and inflammation; leads to fibrosis also
  - usu a localized inflammation, but can lead to diffuse parenchymal involvement
  - characteristic acellular nodule, silicotic nodule, made of CT; as the Dz progresses the nodules may enlarge and coalesce

**Path:** see hyperplasia of the alveolar epithelial cells
- collagen accumulation in the interstitium
- PMN accumulation and tissue destruction

## Therapy [Tx]

- Prevention and education is key, since no Tx exists for several forms of this Dz
- chronic silicosis is amenable w/ exposure avoidance, whereas acute can be fatal w/ or w/o re-exposure
- Tx: limited; supportive Tx, O2, bronchodilators
- lung transplant
Etiology
@ pneumoconiosis due to inhalation of coal dust
• much less fibrogenic than silica

DDx:
DDx: other pneumoconiosis

NOTES:
Simple: CXR shows small discrete densities more nodular than linear; often aSx
Complicated: coalescent and more extensive densities, Sx, and called:
⇒ progressive massive fibrosis

Labs/Workup
• Coal macules on Bx
  Complicated:
  • lowered PFTs

Si/Sx
Simple:
• aSx
Complicated:
• lowered PFTs
• extensive opacities on CXR
  • dyspnea, cough

Pathophysiology :: TYPE B pathophysiology
Path: the coal macule, a focal collection of coal dust
• small regions of focal emphysema

pathophysiology: there is relatively little tissue reaction around the coal macules; initial focal emphysema lesion are often aSx

Therapy [Tx]
• exposure avoidance
### Etiology

@ pneumoconiosis due to inhalation of fibrous silicate, known as asbestos.
- a slowly progressive diffuse interstitial fibrosis
- prolonged period 20-30y btw exposure and clinical Sx

Persons @ risk:
- insulation workers, shipyard workers, remodelers, reinsulators, tile workers

### DDx:

**DDx:** siderosis, silicosis, lung CA, atelectasis

### Labs/Workup

- Not generally all that helpful
  - mild elevation of ESR
- ABGs: hypoxemia, hypercarbia in adv stage Dz
- PFTs: ↓VC, ↓TLC, ↓CO gas transfer on testing

### CXR:
- small irregular shadows in lower zones; thickened pleural, calcified plaques
- pattern is linear streaking
- honeycombing w/ adv Dz

### Si/Sx

- insidious onset of SOB
- worsening dyspnea
- cough: paroxysmal, dry, nonproductive
- fine end-respiratory cracles [rales, crepitus]
- digital clubbing, edema, JVD

### Pathophysiology

**Path:** 1<sup>st</sup> see respi bronchioles involved⇒alveolitis⇒peribronchiolar fibrosis

⇒**ferruginous body:** typical, w/ rod-shape and clubbed ends; yellow-brown in stained tissue

**Pathophys:**
- the asbestos fibers activate m.phages, induction of release of attractants of inflammatory cells; PMN, lymphocytes, m.phages
- thought them.phages play a major role in the resulting fibrosis

⇒by release of factors [fibronectin, IGF-1, PDGF] that recruit fibroblasts and promote their replication

- regions of lung most involved are the lower zones and subpleural region

### Therapy [Tx]

**Non-pharm:**
- cessation of smoking if an issue
- home O2, prn
- exposure avoidance

There is no specific Tx for asbestosis. Death is usually secondary to resp failure or cor pulmonale
**Etiology**

@ pneumoconiosis due to the inhalation of metal dusts from beryllium  
• seen in fluor light manufacturers, aerospace, nuclear weapons builders, and electronic manufacturers  
• EPA estimates that 2-6% of these workers will develop Berylliosis  

**Genetics:**  
• proposed susceptibility in a variant form of the HLA DPB1 molecule

**DDx:**  
DDx: Sarcoidosis, other pneumoconiosis

---

**Labs/Workup**

| CXR: mimics sarcoidosis | + “beryllium transformation test”  
⇒ BeLPT test, performed on a BAL sample |

| Si/Sx |  
Sx mimic sarcoidosis  
ACUTE:  
⇒ coughing, SOB, acute weight loss  
• dyspnea  
• nonproductive cough |

**Pathophysiology**

**Path:** the granulomas formed are much more defined, similar to those seen in Sarcoidosis

**Pathogenesis:** a cellular immune response against beryllium  
• Th1 class of CD4+ cells implicated in response  
• see granulomatous inflammation in multiple organ systems

**Therapy [Tx]:**  
• avoidance of exposure  
• Acute Attacks: ventilation support and corticosteroids  
• Chronic: corticosteroids

**Future Therapies:**

**Chelation therapy**  
A treatment using chelating agents, compounds that surround and bind to target substances allowing them to be excreted from the body
### Usual Interstitial Pneumonia

- **Etiology**
  - @ one of the idiopathic interstitial pneumonias.
  - often referred to as idiopathic pulmonary fibrosis, and/or cryptogenic fibrosing alveolitis
  - although UIP presentation can result from inhalation of dust particulates, or from systemic rheumatic CT Dz
  - 5-6th decade; M:F = 1:1
  - increased occurrence of bronchogenic CA
  - genetics: can be AD inherited w/ variable penetrance

- **DDx:**
  - Surgical Bx: is the gold standard for Dx
  - DDx: other idiopathic interstitial pneumonias

- **NOTES:**
  - average survival of 4-6 years; 87% mortality
  - smoking has a linked correlation of incidence
  - honeycombing in lates stages; is collagen sheets w/ cystic spaces; these regions

### Labs/Workup

- fine bibasilar inspiratory crackles are common
  - Velcro-like sounds
- hypoxemia, cyanosis, can see digital clubbing;
- peripheral edema, cor pulmonale in adv stage Dz

### Si/Sx

- insidious exertional dyspnea
- nonproductive cough
- dyspnea will become prominent
- tachypnea to make up for noncompliant lung
- possible clubbing

### Pathophysiology

- characterized by patchy areas of interstitial inflammation and fibrosis interspersed among areas of preserved lung
- also characterized by a temporal heterogeneity as presented by the above path: fibrosis is king
- NEVER see granulomas
- notable fibroblastic foci, collection of proliferating fibroblasts
- hallmark is heterogeneous appearance
- also see honeycombing; the resulting cystic spaces formed as the fibrotic tissue retracts

- pathogen.phys: In its early stages, UIP is characterized histologically by alveolitis and increased cellularity of the alveolar wall. As this process progresses, pulmonary fibrosis and honeycombing develop.
  - inflammatory process of the alveolar walls is nonspecific
  - hyperplasia of the type II pneumocytes, in response to destruction of type I cells
  - inflammation thought to precede fibrosis, but uncertain
  - thought now that fibrosis is the dysregulated response to the damage of alveolar epithelial cells
- fibrosis linked with TGF-β and PDGF made by m.phages

Weinberger p.137 shows algorithm common to IIP’s

### Therapy [Tx]

- Tx aimed at suppressing the inflammatory response with corticosteroids, or immunosuppressives like cyclophosphamide
- but mean survival is still low
- in some cases lung transplant may be the only option

- according to lecture the only life-prolonging therapy is oxygen therapy for the hypoxemic pt; but some studies refute this as being only a Tx for treating Sx, with no impact on long-term survival
### Pathophysiology

**Path:** Fibroblast proliferation and Type II pneumocyte proliferation, due to damage to type I cells

**Pathogenesis/phys:** Damage to type I cells and the pulmonary capillary endothelial cells seems to be the major pathogenesis.
- Thought that the lung injury is due to an imbalance of proinflammatory and anti-inflammatory cytokines.
- PMNs seem to play a major role in pathogenesis also, secreting oxidants, proteases, and platelet activators.

### Exudative phase:
- Fluid seen in the interstitial space of the alveolar septum and lumen.
- Scattered region of bleeding due to dmg to type II cells and loss of surfactant production, surfactant preventing collapse.
- Inflammatory cells infiltrating the lung parenchyma and alveolar lumen also.
- **Hyaline membranes:** Seen, thought a combination of fibrin and cellular debris on alveolar surface.

### Proliferative [organizing] phase:
- Seen 1-2 weeks after the exudative phase.
- Hyperplasia of type II cells in an attempt to replace the damaged type I cells.
- Accumulation of fibroblasts in the pulmonary parenchyma.
- Sometimes repair is ineffective and leads to scarring, this is accompanied by changes in the pulmonary vasculature.

### Therapy [Tx]
- Ventilatory support w/ or without mechanical ventilation.
- Identify and treat precipitating conditions.
- DVT prophylaxis.
- Lateral decubitus positioning.
- Fluid management for hemodynamic concerns.

---

#### Labs/Workup

<table>
<thead>
<tr>
<th>Labs/Workup</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ABGs: hypoxemia, resp alkalosis; widened A-a gradient</td>
<td></td>
</tr>
<tr>
<td>BAL: ↑ # of PMNs</td>
<td></td>
</tr>
<tr>
<td>CXR: bl pulmonary infiltrates</td>
<td></td>
</tr>
<tr>
<td>• bl, coarse crepitations on auscultation</td>
<td></td>
</tr>
</tbody>
</table>

#### Si/Sx

- Acute onset dyspnea
- Chest discomfort
- Anxiety

- Pulmonary edema, noncardiogenic
- Tachypnea, tachycardia

---

#### Etiology

- Also thought to be represented by **acute interstitial pneumonia [AIP]**

- Organizing phase of Diffuse Alveolar Damage [DAD]

- DDx: cardiogenic pulmonary edema, viral pneumonitis, lymphangitic carcinomatosis

### NOTES:

- Mortality of 30-40% now w/ proper management. [ARDS]

- Note the edematous alveolar walls; hyaline exudates lining the alveolar walls and ducts [arrow]; see type II pneumocyte hyperplasia, indicating an attempt @ repair.

---

#### Exudative phase:
- Early in ARDS.
- Fluid seen in the interstitial space of the alveolar septum and lumen.
- Scattered region of bleeding due to dmg to type II cells and loss of surfactant production, surfactant preventing collapse.
- Inflammatory cells infiltrating the lung parenchyma and alveolar lumen also.
- **Hyaline membranes:** Seen, thought a combination of fibrin and cellular debris on alveolar surface.

- Suggest alveolar injury and permeability problem.

---

#### Proliferative [organizing] phase:
- Seen 1-2 weeks after the exudative phase.
- Hyperplasia of type II cells in an attempt to replace the damaged type I cells.
- Accumulation of fibroblasts in the pulmonary parenchyma.
- Sometimes repair is ineffective and leads to scarring, this is accompanied by changes in the pulmonary vasculature.

- Intimal and medial proliferations causing vessel compromise and occurrence of microthrombi.

- Once the proliferative phase is passed one may enter a chronic phase of interstitial fibrosis.

---

#### Therapy [Tx]
- Ventilatory support w/ or without mechanical ventilation.
- Identify and treat precipitating conditions.
- DVT prophylaxis.
- Lateral decubitus positioning.
- Fluid management for hemodynamic concerns.
Etiology
Hamartomas of the lung are benign lesions composed of an abnormal mixture of epithelial and mesenchymal elements. Traditionally, they were considered to be developmental abnormalities, but now they are considered to be benign mesenchymal neoplasms: the epithelial component is reactive
- more frequent in men than women
- more common in 6th-7th decades

DDx:
DDx: Endobronchial:
- bronchogenic CA, papilloma, lipoma, Metastatic tumor, leiomyoma
DDx: peripheral:
- mets tumor
- infectious granuloma
- amyloidoma
- Carney’s Triad

Pathophysiology
Path: The tumor consists of lobules of cartilage, fat, fibromyxoid tissue, and sometimes smooth muscle and bone (the benign neoplasm) that are separated by clefts lined by non-neoplastic respiratory epithelium.
⇒ think excess & disarray of collagen fibers in the lung
Gross: lobulated, pearly white cartilage appearance; translucent areas of loose myxoid tissue;
Slow growing nodules.

Therapy [Tx]
- wedge resection
- radTx for patients refusing surgery; or patients whose CA has spread to nearby structures

Dx focal fat collection on CT

Labs/Workup
Rad: solid round nodules
- punctate, popcorn calcification
HRCT: lesions are considered to be diagnostic of hamartoma if they are less than 2.5 cm in diameter, have a sharp, smooth wall, and contain fat, or calcification and fat
FNA: Dx if peripheral lesions are diagnostic if cartilage or fibromyxoid fragments are recognized
- immunoperoxidase staining for S-100, supportive

Si/Sx
- periph nodules are most often aSx
- endobronchial lesion show obstructive pattern

NOTES:
Not the benign cartilage on the right
Squamous Cell Carcinoma

**Etiology**
- There is a strong association of incidence in smokers
  ⇒ Tobacco exposure is the main risk factor
- They originate in the epithelial layer of the bronchial wall
  • 2/3 are found centrally in the lung
  ⇒ Often found in the large or proximal airways; @ the level of the bifurcation of the segmental or subsegmental bronchi

**DDx:**
Other non-small cell carcinomas of the lung
- Per Rivera: hypercalcemia is only seen in Squamous cell, among the lung CA

**NOTES:**
- Better prognosis than other cell type carcinomas of the lung

**Labs/Workup**
- Sputum cytology: sometimes shows abnormal cells
- CT-guided FNA, Bx: sometimes informative
- Hypercalcemia:
  - ↑PTH-like subst

**Si/Sx**
- Initially aSx
- Persistent cough
- Hemoptysis
- SOB, wheezing
- Fatigue, weight loss
- Dysphagia
- Recurrent pneumonia
- Hoarseness
- Digital clubbing
- Horner’s in late stages, and if superior sulcus locale
- Superior vena cava syndrome

**Pathophysiology**
**Histopath:** initial metaplasia of normal columnar epithelium
  ⇒ Look for keratinized squamous pearls, and interconnecting bridges
  ⇒ Bronchial epithelium adjacent to tumor may show squamous metaplasia
  Funk, says ⇒ look for desmosomes [interconnecting bridges] and keratin
**Pathophys/gen:** slow growth
- Often see growth into the airway causing obstructive problems and/or collapse
  ⇒ This can lead to post-obstructive pneumonia
  ⇒ Sometimes see cavitation of the tumor; this can lead to erosion of adjacent structures
  ⇒ The mass often elaborates a PTH-like substance promoting hypercalcemia
  ⇒ Bronchogenic carcinoma tends to form an intraluminal mass which may partially or completely obstruct the bronchus. The neoplasm also may compress or invade local structures such as aorta, esophagus, superior vena cava or cervical sympathetic chain.

**Mets:** spreads through local lymphatics, or to direct-local parenchyma; often contained to the thorax
  ⇒ When it does mets outside the thorax, common sites are brain, bone, adrenals

**Therapy [Tx]**
**Surgery is the primary Tx:** survival is dependent on staging of the malignancy
- If spread is extensive; chemoTx is recommended for control of the Sx; not curative
## Small Cell Carcinoma

### Etiology & Epi
- 20% of all lung CA
  - Important subtype is oat cell carcinoma
  - Often originate at the proximal level and within the bronchial wall
  - **Strong correlation** w/ smoking
  - Older theory of etiology proposed K cell [neuroendocrine cell] as originating cell; versus newer model of pluripotent cell origin

### DDx:
- Other bronchogenic carcinomas, TB, other mets to lung, sarcoidosis, granulomatous dz, lung abscess

### Notes:
- Worst prognosis of the bronchogenic carcinomas

### Oat-cell type
- Consists of lymphocyte-like cells growing in sheets or nest, in sparse connective tissue stroma
  - See very high cavitation rate w/ oat cell carcinoma
  - Higher mag small cells

### Labs/Workup
<table>
<thead>
<tr>
<th>Clinical</th>
<th>Pathological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum cytology</td>
<td>Cell looks small, darkly stained w/ sparse cytoplasm; size of small cells often referred to as 3X size of a lymphocyte; see geographic staining in tumor mass</td>
</tr>
<tr>
<td>Bx key: FNA or bronchoscopy</td>
<td>Cell molding</td>
</tr>
<tr>
<td>Endocrine: ↑ACTH</td>
<td>Lack nucleoli</td>
</tr>
<tr>
<td>Sometimes see water, sodium imbalance</td>
<td>↑# of mitotic figures</td>
</tr>
</tbody>
</table>

### Si/Sx
- A persistent cough
- Coughing up blood (hemoptysis)
- Shortness of breath or wheezing
- Unexplained weight loss or loss of appetite
- Fatigue
- Difficulty swallowing
- Horner's in late stages, and if superior sulcus locale
- Superior vena cava syndrome
- Pain in the chest, shoulder or arm
- Bone pain
- Hoarseness
- Headaches, confusion or seizures
- Swelling of the face, neck or upper extremities

### Endocrine Sx:
- Cushingoid Sx due to ↑ACTH
  - Also can see ↑ADH secretion; leads to SIADH
  - Can see Eaton-Lambert Sx
  - Can see carcinoid Sx; cutaneous flushing and reph diarrhea

### Pathophysiology
- Histopath: cell looks small, darkly stained w/ sparse cytoplasm; size of small cells often referred to as 3X size of a lymphocyte; see geographic staining in tumor mass
- Pathopys/gen: local growth follows a submucosal pattern; then invades lymphatics and submucosal vessels; hilar and mediastinal node involvement is prominent early in dz process
- Often centrally located
- Tumor grows in sheets w/out pattern
- Bronchogenic carcinoma tends to form an intraluminal mass which may partially or completely obstruct the bronchus. The neoplasm also may compress or invade local structures such as aorta, esophagus, superior vena cava or cervical sympathetic chain.

### Mets:
- See early, distant, mets
- Fav sites are brain, bone, liver, adrenals

### Therapy [Tx]
- Dependent on mets, staging, response to chemoTx
  - Worst prognosis of the bronchogenic carcinomas
- ChemoTx is the cornerstone of Tx; often combined with radiotherapy
  - Sometimes preventative radTx to prevent brain mets
  - Patients often present @ high stage, but also respond to therapy often; but mortality is still high; no one surviving more than 5yrs

### Prognosis:
- Dep on staging and performance status
## Adenocarcinoma

### Etiology & Epi
- thought derived from bronchial glands
- thought to arise @ the level of the bronchioles or alveolar walls
- characterized by a mutated K-ras gene
- associated risk factors:
  - smoking, radon, asbestos

- most common lung cancer of women and nonsmokers
- most frequent cell-type CA

### DDx:
Mets adenocarcinoma

### NOTES:
- bronchioalveolar carcinoma

- arise and spreads along the alveolar walls, using them as scaffolding for growth
  - arises in the Clara cells or type II pneumocytes
  - can present as nodule or mass lesion or a more widespread parenchymal dz

- RAD can present as multifocal or bilateral
- Path: lepidic growth pattern, non destructive, rule out primary from mets
- markedly abnormal gas exchange; since replacement of nl epithelium w/ mucin containing cells

**Sx:** bronchorrhea; a frothy sputum

### Labs/Workup

<table>
<thead>
<tr>
<th>May see endocrine effects:</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑GH, ↑corticotropin,</td>
</tr>
<tr>
<td>↑calcitonin, ↑FSH</td>
</tr>
</tbody>
</table>

Standard workup for other bronchogenic CA:
- FNA, Bx, thoracentesis, CT, bone scans; sputum cytology, bronchoscopy

### Si/Sx

- A persistent cough
- Coughing up blood (hemoptysis)
- Shortness of breath or wheezing
- Unexplained weight loss or loss of appetite
- Fatigue
- Difficulty swallowing

- Pain in the chest, shoulder or arm
- Bone pain
- Hoarseness
- Headaches, confusion or seizures

- evidence of endocrine dysfunction

### Pathophysiology

**Histopath:** see glandular or papillary formations containing mucin; rem. to look for lumens
- FUNK.says: look for glands or mucin

**Pathophys/gen:** usual presenting pattern is a solitary peripheral lung mass or nodule
- in the subpleura and lung periphery
- often presents @ sites of preexisting scars
- will spread to local hilar mediastinal nodes

**mets:** often mets to liver, adrenals, bone, CNS

### Therapy [Tx]

**Surgery** of the the Tx of choice
  - lobectomy, wedge resection, pneumonectomy

  ➞ dep on dissemination, may also include chemoTx and radTx

<table>
<thead>
<tr>
<th>CEA: carcinogenic embryonic Ag used to follow Tx progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT: will show size and location of mass lesion</td>
</tr>
<tr>
<td>PAS stain to light up mucin on Bx</td>
</tr>
</tbody>
</table>
**Large Cell Carcinoma**

### Etiology & Epi
- 15-20% of lung CA
- Also associated w/ smoking
- Hard to define, since defined by the lack of specific architecture

### DDx:
- Other bronchogenic carcinomas, TB, other mets to lung, sarcoidosis, granulomatous dz, lung abscess

### NOTES:
- Large cell tumors are usually large at the time of diagnosis. They tend to be accompanied by extensive bleeding and tissue damage. They often are called undifferentiated tumors because the cells lack the specific architecture found in other types of cancer cells.

### Labs/Workup
- Std workup for Lung CA: CXR, CT, FNA, sputum cytology, MRI, Bx, bronchoscopy
- Rad: variable, often large peripheral mass

### Si/Sx
- A persistent cough
- Coughing up blood (hemoptysis)
- Shortness of breath or wheezing
- Unexplained weight loss or loss of appetite
- Fatigue
- Difficulty swallowing

### Pathophysiology
- **Histopath:** Notable for the presence of **Emperipolesis**, pleomorphic giant cells w/ leukocyte fragments in the cytoplasm
  - A highly anaplastic undifferentiated CA
  - Lower N:C ratio
  - Coarse chromatin
  - No molding as seen in SCLC

- **Pathophys/gen:** Behave similarly to adenocarcinomas
  - **Periphery lung mass lesions:** But tend to be larger than adenocarcinomas
  - Variable location
  - Mets: Similar pattern to adenocarcinoma

### Therapy [Tx]
- Surgery, and combined modality Tx as w/ adenocarcinoma
### Etiology & Epi

- a rare neoplastic lesion associated w/ asbestos exposure
- contains 3 histological subtypes: epithelial, spindle cell, biphasic
- main general types are epithelial and sarcomatous
- R-sided involvement is more common
- more common in older men >60yr
- smoking is NOT an associated risk factor

⇒ involves the pleura rather than airways or parenchyma

**DDx:**

Metastatic adenocarcinomas

### Labs/Workup

| pleural mass workup and staging evaluation: |
|⇒CT, Hx, PE, Bx, thoracentesis |
|⇒PFTs [for surg eval] |
| EM: [board?] longer microvilli, v/s short in adenocarcinoma |

| generally CEA NEG, v/s + adenocarcinomas |
| may find anemia and thrombocytosis |
| CXR: pleural plaques or calcifications in the diaphragm |
| CT: effusions, and lung encasing |

### Si/Sx

- dyspnea
- nonpleuritic chest pain
- may find dullness to percussion
- may find bl loss of breath sounds

| Horner’s in late stages, and if superior sulcus locale |
| superior vena cava syndrome |
| fever, weight loss, LOA |
| dysphagia |

### Pathophysiology

**Histopath:** neoplastic cells may resemble mesenchymal stroma [sarcoma-like] or appear more epithelial

⇒ Keratin+ staining

**Pathophys/gen: deeply invasive, Keratin+ process**

Dx requires a Bx of the pleura and histologic demonstrations of malignancy.

⇒ see pleural effusion; irregular or lobulated pleural thickening

⇒ the tumor will eventually envelop and trap the lung leading to respiratory collapse; if untreated

⇒ Secondary to asbestos exposure Hx.

• also potential causal factors are: prior radTx, zeolite, or erionite fibers

### Therapy [Tx]

*if a surgical candidate: decortication [pluerectomy], or extrapleural pneumonectomy

⇒ w/ post-op chemoTx often and f/u beam radiation

*if NON-operable: combination Tx [chemo+rad+/-surgery], or instillation chemoTx, + supportive care

⇒ alternate Tx is sclerosing of the pleural space; pleurodesis

### Prognosis

is poor; less than 10% of patients survive 3 yrs
### Etiology

@ pneumonia is an infxn of the pulmonary parenchyma

- 3 routes of transmission: inhalation, aspiration, blood stream
  - common causative bug is *strep pneumoniae*, 2nd is *H. influenza*
  - also think Legionella, Klebsiella

- contributing factors for pneumonia development in immunocompetent:
  - viral upper resp tract infxn, EtOH abuse, smoking, COPD

Epi: CAP, bacterial incidence is 1 in 100, HAP [bacterial] is 8 in 1000 per yr
- most often occurs in the winter and in elderly pts

### DDx:

- sarcoidosis, exacerbation of chronic bronchitis, PE, lung neoplasm, bronchiolitis, pulmonary edema, viral/fungal/parasitic pneumonias, atypical pneumonia, TB

### NOTES:

- the elderly and immunocompromised may actually show minimal Sx early on

- *strep pneumoniae*: Gm+ cocci
- *H. influenza*: pleomorphic, Gm-
- *K. pneumoniae*: encapsulated, Gm-, bacilli

### Labs/Workup

- **Sputum stain:** ↑↑ PMNs
  - look @ Gm stain and cultures; but can give flas results w/ oral flora contaminants
  - Bronchoscopy in the seriously ill
  - DFA stain on sputum for Legionella

- **WBC:** elevated, L-shifted
  - blood culture positive 20% of the time
  - **ABGs:** hypoxemia, pO2<60mmHg on room air
  - **CXR:**
    - pneumococcus: segmental lobe infiltrate
    - L. pneumophila, M. pneumoniae, viral, aspergillus: diffuse infiltrate

- **Presentation can be variable**
  - Fever
  - tachypnea, tachycardia
  - cough
  - crackles and diminished breath sounds

- **Strep. pneum infxn Si/Sx:**
  - high fever, shaking chills, pleuritic chest pain, cough, copious purulent sputum

### Pathophysiology

- **Histopathology:** Neutrophils filling the alveolar space as in acute pneumonia
  - pneumococcal: see
  - **early red haptization** of pulm edema, bacterial proliferation, intra-alveolar PMNs and RBCs
  - **late grey hepatization** of serum and fibrinous exudates, intra-alveolar organization, and m.phages

- **Pathophy/genesis:** most bacteria are normal flora of nasopharynx and oropharynx; can be aspirated into lung
  - other moeds of infxn are INH, hematogenous seeding, rarely a direct spread

- **Patterns:**
  - pneumococcus and K. pneumoniae often present as lobar pneumonias
  - Staphylococci and Gm"-" bugs present as diffuse bronchopneumonias
  - Viral agents begin as interstitial pneumonias

### Therapy [Tx]

- avoid smoking
- O2 to maintain PO2>60mm
- IV hydration
- appropriate antibiotic
  - azithromycin, clarithromycin, levofloxacin all good for CAP
  - if hospitalized, use heavy hitters, ceftriaxone, cefotaxime

- most pts respond well to antibiotics

- **Indications for hospitalization:** hypoxemia, hemodynamic instability, non-tolerable to meds, complicating coexisting condition
BACTERIAL PNEUMONIAS: continued

**Pneumonia of anaerobic bacteria:**
- Anaerobic bacteria are normal oropharyngeal flora
- **Aspiration is a predisposing factor:**
  - Alcoholism is a predisposing factor for abscesses
  - Impaired cough reflex
  - Abundant aerobic bugs
  - Seizure DO
- Cause necrosis → foul smelling sputum, can lead to abscess
- Si/Sx: fever, cough, foul-smelling sputum

**Complications of bacterial pneumonias:**

**Abscesses:**
- From walled off area of infxn, with resulting destruction of the pulmonary parenchyma, ie loss of architecture
- Alcoholism is a predisposing factor for abscesses
  - Impaired cough reflex
  - Abundant aerobic bugs
- More common on RIGHT lung
- Si/Sx: fever, cough, foul-smelling sputum

**Pyothorax/empyema:**
- Purulent infxn of pleural fluid
- Can loculate [wall itself off with fibrous material]; necessitating drainage and antibiotics

**Bacteremia:** seeding, endocarditis, meningitis

---

**CAP & HAP KEY POINTS:**

**CAP:** 10% of hospital admissions; 6th leading cause of death

**HAP:** 2nd leading cause of nosocomial infxn; most common lethal nosocomial infxn

**How?**

**Lung defense failure:**
- Common causes: viral infxn, cigarette smoking, COPD
- Severe causes: AIDS, medications, malignancies, endotracheal tubes [in HAP]

**Route to infxn town:**
- Aspiration: microaspiration of oropharyngeal flora; or larger volume with vomit or impaired swallowing in stroke or seizure
  - Both in HAP & CAP
- Inhalation: INH of ambient particles
- Hematogenous: IVDA; think Staph. Aureus

**Common CAP pathogens:** most important is Strep. pneumoniae, and most common
- Other of note:
  - H. influenza: seen in smokers and COPD
  - K. pneumoniae: seen in alcoholics
  - P. aeruginosa: often nosocomial also
  - Mycoplasma pneumoniae: younger host

**Clinical Spectrum of Si/Sx: these are not pathogen specific**
- **Typical pneumonia: think S.pneumo, S. aureus, Gm”-“ bacilli**
  - Rapid onset, ill-appearing, high gd fever, rigors, chest pain, purulent sputum
  - Consolidation, rales
  - Leukocytosis
  - CXR: airspace filling, lobar infiltrate
- **Atypical Pneumonia: think mycoplasma or Chlamydia pneumonia**
  - Indolent onset, less ill-appearing, low-gd fever, malaise, HA, dry cough
  - Rales W/OUT consolidation
  - No/mild leukocytosis
  - CXR: patchy, interstitial infiltrates
MORE CAP’n’HAP PNEUMONIA, JAZZERCISED:

When a Gm Stain/culture may be useful from Sputum:
- Large number of single morphology bacteria, in the setting of ↑↑PMNs, w/ few/no squamous epithelial cells
- Sample obtained prior to antibiotic Tx
- When a non-colonizer [mycobacteria, PCP, Legionella] is present

When the sputum stain/culture is not useful:
- Flora misinterpreted as pathogen
- Dry cough
- Shoddy specimen collection and handling, read medical student
- Prior antibiotic
- Legionella, mycoplasma, Chlamydia, viruses

Assessment of Severity & Principles of Tx:
- Older than 60? Are there co-morbidities?
- Is the pt in a severely compromised state
  - Le, RR>30, 40<Temp?<35, HE>125?
- Hypoxemic?, acidotic?,
- Multi-lobar? Fluminant infxn?
- Tx: is often empiric, consider the risk factors for pneumonia in the patient’s environment
  - **Aerobic GN bacilli:** Alcoholism, nursing home, cardiopulmonary disease
  - **Anaerobes:** Loss of consciousness (alcohol, seizure), swallowing dysfunction, poor dental hygiene, airway obstruction
  - **H. influenzae:** COPD, smoker
  - **S. aureus:** Nursing home, post-influenza, IVDA, bronchiectasis
  - **P. aeruginosa:** Structural lung disease (bronchiectasis, CF), recent broad spectrum antibiotics, malnutrition, chronic steroids
  - **DRSP:** Age > 65; β-lactam therapy within 3 months; exposure to child in daycare; underlying medical co-morbidities

Four Tx groups:
- The outpatient w/o comorbidities think Staph pneumonia, H. influenza
  - Use antipneumococcal or macrolide
- Outpatient w/ comorbidities: think aerobic Gm- bacilli, DRSP
  - Use 2nd/3rd gen cephalosporins+macrolide or antipneumococcal
- Inpatient w/o ICU: think aerobic Gm-, DRSP, legionella
  - IV 3rd gen Cephalosporin + macrolide or antipneumococcal [fluoroquinilone]
- Inpatient w/ ICU: think severe; Staph aureus, Pseudomonas, legionella, aerobic Gm- bacilli
  - IV 3rd gen cephalosporin+macrolide, or anti-pneumococcal, Vanc for MRSA, PRSP

HAP:
- Riskfactors: IV/urinary catheters, staff hand washing, etc… being intubated…
- Dx Based upon:
  - Fever, leukocytosis
  - New, worsening infiltrates
  - New or increased respiratory secretions
  - Not based solely on a new culture result
- DDx:: May be hard to distinguish from:
  - CHF
  - pulmonary emboli
  - pulmonary hemorrhage
  - ARDS
- Common pathogens: P. aeruginosa, Enterobacter, E. coli, Klebsiella, Proteus, Serratia, S. aureus, Acinetobacter, and anaerobes
- HAP more likely to be polymicrobial
- Risks based on immune state:
  - Neutropenia: bacteria, aspergillus, candida
  - Splenectomy: encapsulated organisms
  - T-cell number (HIV) or function (immunosuppressives): fungi, mycobacteria, viruses (CMV, EBV), bacteria
- Risks in AIDS pts dep on CD4 counts:
  - <500, think MTB, other bacterial; <200, think P. aeruginosa; <50, think MAC
- Treatment of P. carinii in AIDS: TMP-SMX, IV pentamidine, Corticosteroids: for pO2 < 70 mmHg or A-a grad >35 mmHg
Pneumonia: Viral

Etiology & Epi
@ infxn of lung parenchyma by any number of viral agents
•referred to as atypical pneumonia also
•Influenza virus often the etiologic agent
•dx often presents in immunocompromised pts
•thought to be 86% of the hospitalized adult pneumonia cases in the US
Incidence is age-related and seasonal:
•Influenza: peaks @ age 5; most severe in infants and >65yo; winter for fluA
•RSV: young children is peak, but throughout life; winter and spring
•Adenovirus: young children, adult military recruits; endemic
•Measles: young adults, older children, with failed vaccinations [5%]; year round
•Varicella: adults; spring
•CMV: neonatal though adult; think immunocompromised patient; year round

DDx:
DDx: bacterial pneumonia, other causes of atypical pneumonia [Chlamydia, mycoplasma, Legionella], ARDS, Pulmonary Embolus

Labs/Workup
Sputum: gram stain —; a few PMNs, few bacteria
ABGs: hypoxemia may be profound
WBC: variable from penic to leukocytosis
PCR: for viral nucleic acids
Monoclonal Abs tests for fluA and fluB, and RSV
•open lung Bx required for definitive CMV pneumonia
Dx
CXR: spectrum of findings, patchy interstitial infiltrates

Si/Sx
Variable: but may see
•fever
•tachypnea
•dry cough
•wheezes and rales
CMV: notable for occasional hemoptysis with dry cough

Pathophysiology
Histopath: interstitial lymphocytes
CMV: large "megalic" cells, w/ enlarged nuclei, singular basophilic inclusion
Measles: multinucleated giant cells, w/ nuclear inclusions
Varicella: nuclear eosinophilic viral inclusions, multinucleated
HSV: necrotizing tracheobronchitis, w/ DAD and similar viral inclusions to varicella
Pathophysiology/genesis: will present as a more diffuse patchy interstitial infiltrate, which in advanced stages can enter the alveolar space

Therapy [Tx]
Non-pharmacologic:
•isolation, prevent communal transmission
•↑rest, push hydration,
•flu vaccine, yearly, maeasles vaccine
Pharmacologic:
•Influenza: amantadine, rimantadine
•RSV: ribavarin aerosol
•Adenoviral: none
•Varicella: IV ACV
•measles: none
•CMV: ACV, GCV and focarnet
Prognosis: generally good with supportive Tx. Morbidity is often associated with a coexisting bacterial superinfection.
**Etiology**

@ infxn of lung parenchyma by the small free-living prokaryote, mycoplasma
⇒ common cause of acute self-limiting pneumonia nad tracheobronchitis
⇒ highly transmissible
• 15-20% of pneumonias in developed countries
• most often affects 5-20y/o
• prevalent in temperate climates and in the fall to early winter
• a freq cause of CAP

**synonyms:** walking pneumonia, Eaton’s pneumonia, primary atypical pneumonia

**DDx:**

DDx: C. pneumonia, C. psittaci, Legionella, Q fever, Pneumococcal pneumonia, Pulmonary embolism, infarct

**NOTES:**

Erythema multiforme

---

**Labs/Workup**

<table>
<thead>
<tr>
<th>WBC: elevated above 10K in 1/4th</th>
<th>Sputum: often not produced; but if stained see polyps w/o organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cold agglutinins seen in ½</td>
<td>CXR: predilection for lower lobe involvement; hilar adenopathy in 1/4th</td>
</tr>
<tr>
<td>• rare hemolysis</td>
<td></td>
</tr>
<tr>
<td>• culture is difficult and few perform</td>
<td></td>
</tr>
</tbody>
</table>

**Si/Sx**

| • nonexudative pharyngitis | • muscle tenderness in 50% |
| • rhonci, rales w/o consolidation | • lymphadenopathy, splenomegaly, sometimes |
| • skin rash in 1/4th of pts, most common is morbilliform, multiforme | • ↑ sweat, chills |

**Pathophysiology**

**HistoPath:** patchy consolidation, mononuclear infiltrate; LOWER LOBE predominant
• sparse lymphocytic interstitial inflammation

**Pathophys/genesis:** infxn is spread from droplet infxn from resp tract secretions

**Therapy [Tx]**

• most often resolves w/o Tx

Pharmacotherapy:
• wks of erythromycin, azithromycin, or clarithromycin
⇒ Tx only reduces Sx, the dz itself is self-limiting

Disposition: clinical improvement almost always in 10d; death is rare; X-ray resolution of infiltrates often complete by 8wks in all pts
**Pneumonia: *P. carinii***

foamy macrophage exudate

**Etiology & Epi**

- A serious resp infxn caused by the fungal/protozoal buggar, *Pneumocystis carinii*.
- Seen primarily in the setting of AIDS
- ⇒ seen in 11/100 pts w/ CD4 counts <100
- **AGE:** <2y, or 20-40y

**etiology:** often a reactivation of a dormant infxn; extrapulmonary involvement is rare

**DDx:**

⇒ occurs exclusively in the setting of depressed cellular immunity

**DDx:** TB, histoplasmosis, Cryptococcus; bacterial/viral pneumonia, mycoplasma pneumonia

**NOTES:**

**Whole Body Gallium Scan**

Silver Stain Showing Cysts

**Labs/Workup**

- ↑ LDH in many cases
- HIV Ab screen, if status unknown
- Imaging: diffuse uptake on Gallium scan is suggestive, but not Dx

**Sputum:** for presence of cysts and exclusion of other bugs

**BAL:** if sputum not enlightening, again looking for PCP cysts

**Si/Sx**

- fever
- cough
- SOB
- lungs often clear on auscultation

• cyanosis and tachypnea prominent in sev cases
• see associated spontaneous pneumothorax

**Pathophysiology**

**Histopath:** see PCP cysts on silver stain, see **foamy macrophages** on H&E stain

**Pathophys/genesis:** Dz process is often a reactivation of a dormant infxn in an immunosuppressed individual

**Therapy [Tx]**

**Non-pharmacologic:**

- supp. O2, ventilatory support [as needed], thoracotomy if pneumothorax

**Pharmacologic:**

- TMP-SMX; PO, IV
- Pentamidine, IV

⇒ add prednisone to either one, PO

**Lifelong Prophylaxis:** TMP-SMX
### Etiology & Epidemiology

@ a small Gm^-^- bacillus, that thrives in aquatic environments and causes Legionnaire’s dz and Pontiac Fever.
- seen in isolated cases or local outbreaks
- predisposition: fat, overweight, smoker, male

**DDx:**

### Labs/Workup

<table>
<thead>
<tr>
<th><strong>DFA:</strong> direct fluor Ab staining</th>
<th>quite Dx, done on sputum or BAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Culture:</strong> requires special growth media</td>
<td></td>
</tr>
<tr>
<td><strong>CXR:</strong> often presents a more morbid picture than dz state truly is.</td>
<td></td>
</tr>
<tr>
<td><strong>CBC:</strong> ↑ WBC</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Si/Sx</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• acute onset:</td>
</tr>
<tr>
<td>• malaise, fever, pneumonia, myalgias, abdominal pain, diarrhea; chills, cough</td>
</tr>
<tr>
<td>• may hear fine crackles on auscultation</td>
</tr>
</tbody>
</table>

### Pathophysiology & Pathogenesis

**Pathology:** bronchopneumonia w/ multiple lobes involved
**Histology:** alveoli **filled with fibrin and inflammation mediators**

**Pathophysgenesis:** transferred through the respiratory system from a contaminated water storage system; person-person resp transfer has yet to be proven

### Therapy [Tx]

**Pharmacologic:**
- **1st line** = erythromycin or quinolone [ciprofloxacin]
- **2nd line** = rifampin

**overall mortality rate = 15%**
RARE BACTERIAL PNEUMONIA AGENTS:

**Actinomycetes:**
- *Actinomyces israelii:* most common
  - Gm+, normal flora, mouth, nose
  - Aspiration is mode of infxn
  - Can cause some nasty lung abscesses which contain colonies known as **sulfur granules**

![Sulfur Granule](image1)

**Nocardia:**
- *Nocardia asteroides:* most common
  - Gm+, weakly acid fast
  - Think pneumonia and abscesses in the immunocompromised pt
  - Granulomatous reaction to nocardia

![Granulomatous reaction to nocardia](image2)
### Primary Tuberculosis

#### Etiology & Epi

@ an infxn of the lung and sometimes, the surrounding structures, due to the bacterium *Mycobacterium tuberculosis*

**EPI:** US incidence is @ its lowest in history  
- only 10% of pts w/ PPD conversion will develop TB, most w/in 1-2y  
- new cases show increased incidence in racial and ethnic minority communities  
- 36% of new cases are from new immigrants  
- **AGE:** 25-45y/o reflects booming AIDS population  
- HIV+ pts are at the highest risk  
- 90% of Sx dz is due to reactivation of latent dz

#### DDx:

**DDx:** necrotizing pneumonia, histoplasmosis, melioidosis, coccidioidomycosis, sarcoid, silicosis

### Labs/Workup

<table>
<thead>
<tr>
<th>PCR: more sensitive than AFB smear</th>
<th>PPD: single positive not helpful, per Dx; useful if proof of reactivation conversion ⇒ neg PPD never rules out acute TB</th>
</tr>
</thead>
</table>
| Sputum SMEAR: acid-fast staining bacilli  
⇒ consider Bx if smear negative  
DNA fingerprinting: also possible, using RFLPs | **CXR:** 1º TB reflected in calcified peripheral lung nodule w/ calcified hilar node  
⇒ reactivation by: necrosis, cavitation, interstitial infiltrates, military pattern |

#### Si/Sx

- primary TB generally aSx  
- reactivation is often the Sx case showing:  
  ⇒ fever, cough, night sweats, hemoptysis, scanty nonpurulent sputum, weight loss  
  ⇒ sometimes hear rales accentuated following cough

- Progressive dz can lead to TB pleurisy:  
  ⇒ pleuritic chest pain, fever, SOB, due to effusion

**Boards Crap:** dz can sometimes lead to a massive, suffocating, fatal hemoptysis, from pulm artery erosion, called Rasmussen’s aneurysm

### Pathophysiology & Pathogenesis

**Histopath:** look for AFB on smear, beaded-rod appearance  
⇒ **caseous necrotizing granulomas**  
⇒ **Ghon complex [focus+node]:** periph focus of infxn, a granuloma basically, found often in lower lobe and hilar node granulomatous infxn

Pathophys/genesis” the progression of the dz is due to tissue dmg from inflammation and immune response  
⇒ Mtb ingested by m.phages in alveoli, transported to regional lymph nodes  
⇒ Mtb may sometimes reach blood stream for spread  
⇒ primary TB is essential an intracellular infxn  
⇒ local/disseminated contained by a T-cell response; see recruitment of monocytes, lymphocytes, m.phages, resulting in a contained granuloma  
⇒ buggars live in m.phages called Langhans’ giant cells  
⇒ progressive dz: leads to necrotizing pulmonary infiltrates, cavitation, hemoptysis, effusions, pleural seeding

### Therapy [Tx]

- **Non-pharmacologic:** bed rest, ↑ nutrition, isolation in a room that “sucks”
- **Pharmacologic:** compliance is the chief determinant of success;  
  - always use 2-3 different drugs @ once  
  ⇒ **INH and rifampin** are the drugs of choice  
  ⇒ **DOT Tx** has best results  
  =>= isoniazid+ethambutol+pyrazinamide; 3X/wk, 6mo

Don’t let the pts out till there are THREE consecutive negative AFB smears.  
- Screen all contacts w/ PPD, during 3mo post-exposure

**MDRTB:** is a concern in pts:  
- previously treated, homeless, AIDS, prisoners, IV druggies
Secondary tuberculosis: from reactivation or infxn of sensitized host
- **Si/Sx:** very Sx versus 1ºTB; fever, fatigue, weight loss, night sweats, hemoptysis
- **Pathology:** numerous caseating granulomas most common in **upper lobes** [highest aeration]  
  - ⇒these may calcify and heal, but may also erode and lead to a tuberculosis cavitation

complications of tuberculosis:
- **Miliary TB:** multiple smalle granulomas in many organs  
  - caused by hematogenous spread  
  - affects kidneys, adrenals, BM, spleen, liver lymph nodes
- **Hemoptysis:** erosion of the pulmonary artery
- **Bronchopleural fistula:** erosion 2º to inflammation, opening into the pleural space causing an TB empyema
- **Tuberculosis laryngitis:** from the old favorite cough and swallow mechanism
- **Intestinal tuberculosis**

Other mycobacterial dz:
- **mycobacterium avium-intracellulare:** found in soil, water, 70% of population exposed  
  - think immunocompromised folk
- **mycobacterium kansasii:** associated with hairy cell leukemia [HCL]
- **mycobacterium bovis:** infxn from bad milk; pasteurize to prevent
**Histoplasmosis**

@ fungal inxn caused by *Histoplasma capsulatum*
- found in the soil of the river valley region (Ohio, Mississippi river valleys)
- dimorphic fungus
- infected dust, or bird droppings
- exists as a mold @ ambient temps
- Occupational: construction, outside; street cleaners, spelunkers, aviary folk

SEX: male:female = 4:1

**Chronic Pulmonary Histoplasmosis [CPH]**
- most common in men older than 50 w/ a Hx of COPD

**DIAGNOSIS:**
- Travel/occupational Hx is key to Dx
- DDx: MTb, other CAP, other fungal inxn

**NOTES:**
- Labs/Workup
  - **Periph Smear:** Wright-Giemsa stain, showing oval yeast in PMNs or m.phages
  - **Serology:** complement fixing [CF] Abs
  - **CXR:** APH= single or patchy infiltrates, esp in the lower lung fields; hilar or mediastinal adenopathy
  - **CPH=** see upper lobe dz w/ cavitation, sometimes w/ 2º fungus ball; pre-existing calcification of the hilum w/ peribronchial streaking

**Si/Sx**
- **Acute 1º pulm histoplasmosis [APH]:**
  - often aSx, but may show fevers, malaise, HA, non-prod cough, and weight loss
  - **In immunocompromised:**
    - see disseminated dz affecting liver, lungs, adrenals, intestines

**Pathophysiology & Pathogenesis**
- **Histopath:** see yeast phagocytosed by m.phages; and tiny yeast; often see the oval yest inside PMNs on W-G stain of peripheral smear
- **Pathophysgenesis:** the conidia are deposited in the alveoli, fungus converted to yeast in initial focus and then spreads to regional node, and then on to other organs, esp liver and spleen via the lymphatics
  - similar to Ghon complex presentation of 1º TB
  - on spread can lead to meningitis
  - 7-18d post-onset host response forms discrete granulomas around the yeast, in attempts to contain; can become caseating
  - in nl host; the granulomas will undergo contraction and fibrosis, +/- calcification

**Therapy [Tx]**
- For APH & CPH: no Tx if aSx
  - if Sx: ketoconazole or itraconazole
  - give amphotericin B if Sx more severe
Coccidioidomycosis

**Etiology & Epidemiology**

- @ INH of *Coccidioides immitis*
- dimorphic fungus
- large, thick walled, sporangia filled w/ endospores
- endemic to SW US, mainly San Joaquin valley, CA; limited to western hemisphere
  ⇒ NM, Arizona, Nevada, Texas, Mexico
- SEX: males ages 25-55

**DDx:**

Travel/occupational Hx is key to Dx

**DDx:** CAPs, granulomatous dzs, other fungal dzs

**NOTES:**

- Labs/Workup
  - CBC: eosinophilia
  - IgE: ↑ serum levels
  - Culture: makes the Dx
    ⇒ best yield w/ pus, sputum, synovial fluid
    ⇒ requires pulm Bx in AIDS pts
  - Serologic: ↑ CFA
    - latex agglutination
    - coccidioidin Ag detection
  - CXR: unilateral infiltrates, hilar adenopathy
    - areas of fibrosis containing solitary thin-walled cavities

**Si/Sx**

- often aSx or non-specific URTI
- if Sx, see:
  ⇒ cough, malaise, fever, chills, night sweats, anorexia, weakness, arthralgias

- skin rashes
- scattered rales on auscultation

**Pathophysiology & Pathogenesis**

**HistoPath:** see UL image; sporangia w/ endospores

**Pathophys/genesis:** often characterized by a pulmonary focus w/ infrequent progression to a disseminated state

- possible bronchiectasis
  ⇒ windswept arthrospore deposits in alveoli via INH ⇒ converts to thick walled spherule ⇒ internal spores released ⇒ parasitic cycle

- fungus incites a granulomatous reaction, often w/ caseous necrosis

- MSK involvement: joint swelling, bone pain
- meningeal involvement: focal deficits, nuchal rigidity

**Therapy [Tx]**

- supportive and draining of pus
- Pharmacologic: only in severe states
  - fluconazole: 1st line
  - itraconazole:
  - amphotericinB: for disseminated dz, extraneural

- immunocompromised pts are more likely to have disseminated dz and higher mortality and morbidity
• Cryptococcosis •

Etiology & Epidemiology

@ caused by INH of spores of *Cryptococcus neoformans*
• mucinous capsule
• reservoir is pigeon droppings
• a dz almost exclusively of the immunocompromised

DDx:

DDx: Acanthamoeba, Basal Cell Carcinoma, Histoplasmosis, Lipomas, Molluscum Contagiosum, Pneumocystis Carinii Pneumonia, Syphilis, Toxoplasmosis, Tuberculosis

NOTES:

India Ink stain

Pathophysiology & Pathogenesis

HistoPath: special stain [mucin & India ink] for capsule is often Dx; well-formed granulomas ARE NOT present

Pathophys/genesis: lung is the common port of entry, and the CNS is the common presenting site, but can also involve the skin, heart, liver, kidneys, muscles, bone, adrenals

⇒ transmits via the respiratory route and not from one human to another. After inhaling C neoformans, the alveolar macrophages ingest the yeast⇒ encapsulated organisms are more resistant to phagocytosis [cryptococcal polysaccharide capsule has antiphagocytic properties and may be immunosuppressive]⇒ The antiphagocytic properties of the capsule block recognition of the yeast by phagocytes and inhibit leukocyte migration into the area of fungal replication.

• characterized by little to no necrosis or organ dmg till late in dz process

⇒ dmg is often due to local deformation of tissue 2º to fungal mass

• in the lung may produce a solid mass, *cryptococcoma*

Therapy [Tx]

Pharmacologic:
• fluconazole
• itraconazole
• amphotericinB

⇒ for severe dz= amphotericinB + flucytosine

Labs/Workup

CSF, BAL & Bx: mucin staining and India ink stains shows the capsule well ⇒ mucicarmine +

Serology: latex agglutination test for cryptococcal Ag

Si/Sx

Variable pulmonary presentation from aSx to:
• fever, malaise, cough w/ scant sputum, pleuritic pain, weight loss

In immunocompromised pt:
• fever, dyspnea, headache, weight loss, and often CNS Sx
# Blastomycosis

## Etiology & Epidemiology

- Caused by inhalation of fungal spores from soil contaminated by *Blastomyces dermatitidis*
- Large dimorphic fungus, with broad based budding
- Found in wood and soil
- Think Mississippi and Ohio River Valleys
- Less common than other fungal dz
- Presents most often immunocompromised

### DDx:

DDx: other fungal infxn, large size helps in delineation amongst fungal etiologies

## Labs/Workup

### Culture:
- Sputum: with special stains
- Skin Bx if available

### CXR:
- Nodules or cavitation
- Pneumonia

### Si/Sx:
- Pulm involvement may be aSx; but often spreads to skin, bone, & UG system
- If Sx: cough w/ brown/bloody sputum, SOB, fever, fatigue, weight loss, skin lesions, muscle and joint stiffness

## Pathophysiology & Pathogenesis

### HistoPath:
- Much larger yeast than crypto or histoplasma

### Pathophys/gensis:
- Dz is often contained to the lungs, causing a mixed granulomatous and suppurative inflammation

## Therapy [Tx]

### Pharmacologic:
- AmphotericinB, fluconazole, or itraconazole

### Disposition:
- W/ Tx @ early Sx dz, prognosis is good, but left untreated can be lethal
- Complications: often see abscesses, drug resistance, recurrent infxn
## Aspergillosis

### Etiology & Epidemiology

- **@ talkin’ about yeast ball**
  - septate hyphae w/ acute angle [45°] branching
  - found in soil and decaying plant material

### DDx:

- Aspergilloma: cough, hemoptysis, chest pain, SOB, weight loss, fever
- ABPA: wheezing, SOB, mild fever
- Invasive: cough [dry-productive], SOB, fever, acute weight loss

### NOTES:

- Invasive Aspergillosis: seen exclusively in immunocompromised hosts
  - see invasion of the pulm vasculature, causing infarction, thrombosis, exsanguinations
  - a fulminate dz

### Labs/Workup

<table>
<thead>
<tr>
<th>Aspergilloma</th>
<th>ABPA</th>
<th>Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum culture</td>
<td>Bronch &amp; BAL</td>
<td>Serology: detecting</td>
</tr>
<tr>
<td>Aspergillus Abs</td>
<td></td>
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</tr>
<tr>
<td>ABPA: see bronchiectasis</td>
<td></td>
<td>Invasive: CBC shows</td>
</tr>
<tr>
<td>CXR: fungus ball shows mass and air w/in a cavity</td>
<td>Chest HRCT</td>
<td>PMNs</td>
</tr>
<tr>
<td>Si/Sx</td>
<td></td>
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<td></td>
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</tr>
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</table>

### Pathophysiology & Pathogenesis

- **HistoPath:** septate hyphae, 45° branching
- **PathoPhysgenesis:** pulm parenchymal infxn can lead to sever dz states, those being:
  - **Aspergilloma:** “fungus ball”, which will grow in a pre-existing cavity, often from TB; prognosis is least serious, though
  - **Invasive Aspergillosis:** seen exclusively in immunocompromised hosts

### Therapy [Tx]

- **Aspergilloma:** Surgical removal is most effective, occasionally antifungals are used
- **ABPA:** corticosteroids + bronchodilators, NO antifungals!
- **Invasive:** antifungals [itraconazole, voriconazole, and capsofungin], bolster immune system, ie NO corticosteroids; give GCSF;

### Disposition:

- Aspergilloma: good w/ clean resection
- ABPA: good with allergic control
- Invasive: poor, difficult to cure, causing multiple organ damage
**Mucormycosis [Zygomycosis]**

**PAS stain**

**Etiology & Epidemiology**

@ INH of spores of several fungi found in soil, food, decaying veggies
  • NON-septate
  ⇒ often seen in DIABETICS
  ⇒ in US the dz is rhinocerebral and pulmonary

**DDx:**

**NOTES:**

HP stain

**Labs/Workup**

**Si/Sx**

**Pathophysiology & Pathogenesis**

**Histopath:** broad, non-septate hyphae w/ 90º branching; have hollow appearance of mucor

**PathoPhys/genesis:** infxn leads to vascular invasion, septic infarction, hemorrhage

**Therapy [Tx]**
## Primary Ciliary Dyskinesia (PCD)

### Etiology & Epidemiology

- **@ Immotile ciliary Syndrome (ICS)**
  - characterized by abnormal ciliary motion, w/impaired mucociliary clearance
- **Genetic:** appears to follow an autosomal recessive inheritance pattern
- **Incidence:** 1:16,000 live births

### DDx:

- **DDx:** CF, consider immunodeficiency

### Notes:

- **Hx** often shows chronic otitis, rhinorrhea, anosmia, halitosis.

### Kartagener’s Syndrome:

- **TRIAD:**
  - situs inversus
  - chronic sinusitis
  - bronchiectasis

### Labs/Workup

| **ABGs:** | hypoxia |
| **CXR:** | may show dextrocardia |
| **Bronchoscopy:** | shows situs inversus, mucosal inflammation |
| **Mucociliary Clearance Study:** | expect a delayed or absent response |

### Si/Sx

- **Situs inversus**
  - **Hearing:** hearing loss, inflammation of TM
  - **Nose/Sinuses:** nasal polyps, nasal mucopurulent congestion, nasal obstruction; mouth breathing & halitosis
- **LRT:** retractions, crackles, wheezes
- **Dextrocardia:** apex beat and heart sounds on right side
- **Cyanosis:** w/recurrent LRTI's
- **Infertility:** often seen in males w/ ICS/PCD

### Pathophysiology & Pathogenesis

- **Pathology/Histology:** see cilia with missing outer dynein arm and missing inner dynein arm

- **Pathophys/genesis:** the ciliary defect causes abnormal motion and impaired mucociliary clearance;
  - leads to recurrent sinopulmonary infxns
  - leads to male infertility

### Therapy (Tx)

- **Non-pharmacologic:**
  - Chest PT, to promote clearance

- **Pharmacologic:**
  - bronchodilators for increased clearance
  - immunize
  - antibiotics for recurrent infxns; Augmentin, etc.
  - glucocorticoids: for inflammation; Beclamethasone

- **Surgery:**
  - Typanostomy: for chronic OM
  - polypectomy: to remove nasal polyps for increased clearance; promotes drainages and improves nasal breathing
  - lobectomy: in severe cases of bronchiectasis
AIRWAY DEFENSES:

TAKE HOME MESSAGES:

1. Normal host-defense requires coordination of many individual components of lung defense. The importance of the individual components is recognized as a result of acquired or genetic defects, i.e., “in vivo mutational analysis”.

2. **Proximal conducting airways** (and nose)
   a) Primary Components: cilia, liquid/mucus, submucosal gland secretions (mucus, slgA, lysozyme, lactoferrin)
   b) “Surveillance” Defense: mucociliary clearance and secretory dimeric IgA (non-opsonic)

3. **Distal airways/alveoli**
   a) No cilia or submucosal glands (although distal region indirectly protected by these components).
   b) “Surveillance” Defense: Alveolar macrophage (phagocytosis; microbicidal; produce chemotactic factors and cytokines) and IgG (opsonic)

4. **Secondary defense mechanism throughout the lungs**: neutrophils (and other immune cells)
   a) Acute: bacteriocidal, but proteolytic enzymes (including elastase) do not usually damage lungs
   b) Long-term: human neutrophil elastase contributes to bronchial damage (bronchiectasis) and alveolar septae destruction (emphysema)
   c) Anti-proteases (α1-antitrypsin) inhibits the destructive activity of elastase.
• Pulmonary Artery Thromboemboli

big ass PE, w/ signs of beginning recanalization or preparation artifact

Etiology & Epidemiology

@ a PE is the lodging of a thrombus or other embolic material from a distant site in the pulmonary circulation.

•650,000 cases of PE un US per yr, w/ 50,000 resulting in death; 8-10% die w/in 1st hour

•most emboli are clinically silent

•90% of PEs originate in the deep venous sys of the lower legs

Risk Factors for PE:

•prolonged immobilization, and long flights

•post-op

•lower extremity trauma

•estrogen birth control pills

•prior DVT, PE Hx

•CHF

•pregnancy

•adv age

•obesity

•hematologic dz predisposition [FV Leiden’s, lupus. ATIII def]; ie hypercoagulable states

•COPD

•Diabetes

DDx:

DDx: MI, pericarditis [friction rub], pneumonia, oneuemothorax, GI abnormalities, CHF, Anxiety DO, asthma, aortic dissection

NOTES:

•remember no single test is non-invasive and has BOTH high sensitivity and high specificity for PE

⇒L note obstruction on contrast cath

⇒R note the blockade on 2D Doppler ECHO

Labs/Workup

Lung Scan: for confirmation studies; good for ruling out

•V/Q mismatch is suggestive

•local V/Q goes to ∞

Pulmonary angiogram: can be Dx also [gold standard]

ABGs: may show ↓PaCO2, ↓PaO2, ↑pH

↑d-dimer: good for ruling out

↑ troponin: since many PE cases show R-sided dilation

CT angiography: less invasive, less costly, tells us info about other intrathoracic dz, accurate

⇒Drawbacks: not helpful for the subsegmental emboli

A-a gradient: increased

CV: ↑P2 sound, tricuspid murmur [insuff]; RV heave, R-sided S3; tachy

Spiral CT: good for ruling out PE

CXR: variable; classic rare eponym finding:

•Hampton’s Hump: wedge-shaped opacification @ distal lung border, from infarction, often middle-lower lobe

•more common to see atelectasis

ECG: sinus tach most often: rarely non-specific ST-segment or T-wave changes, and signs of RV strain

Si/Sx

Most common= DYSPNEA, and TACHYPNEA

•chest pain, if pleuritic indicates infarction

•syncope [massive PE]

•fever, diaphoresis, DOOM!

•swollen, painful leg

•hemoptysis, cough

•sinus tachycardia

Pulm: may hear rales, wheezing, friction rub

•JVD due to ↑SVP

•cyanosis, edema

Pathophysiology & Pathogenesis

HistoPath: often see occluded artery surrounded by region of parenchymal infarct w/ hemorrhage leading to atelectasis

•may see frank necrosis

Pathophys/genesis: vessel occlusion⇒ ↓perfusion⇒ infarct

•hypocapnea: occurs due to reflex hyperventilation

•see other notes

Therapy [Tx]

Non-pharmacologic: address risk factors

Pharmacologic:

•acute: tPA thrombolysis [in massive PE, or hemodynamically unstable], heparin

⇒embolectomy: possible, but requires quick presentation, rapid Dx and action; indicated in pt w/ massive PE, and refractory hypotension

•prevention: IVC filter, LMW heparin Tx, coumadin

LUNG VENTILATION

Posterior

LUNG PERFUSION

*note the loss of perfusion in the RUL
MORE PATHOPHYSIOLOGY & PATHOGENESIS

- The V/Q mismatch is caused by the bronchoconstriction of the small airways not involved in the embolism
  - This constriction is secondary to chemical mediator release
  - This is a probable cause for the hypoxemia seen in PEs
- The synthesis of surfactant is compromised in the alveoli affected by the emboli
  - This leads to ↑risk for atelectasis and fluid leaking into the alveolar space
    - Take ~24hrs before the adverse effect is seen
- secondary bronchoconstriction occurs:
  - due to hypocapnea in the dead regions
  - causes increased lung volume loss or atelectasis
- disturbance of the metabolism of bioactive substances is disturbed
- infarction and PEs:
  - generally thought to require a loss from 2 sources of supply to cause an infarct

MORE EPONYMS

- Westermark’s sign: rare localized area of decreased perfusion on CXR, compared to baseline
- ECG: nonspecific and uncommon finding
  - The S1Q3 pattern w/ R-heart strain
  - This is really only seen in massive PEs

DVT:

- Dx tests for DVT: Doppler Flow study is cheap and reliable; Duplex Scanning is also another good option for detection of DVTs
- THERAPY:
- When to use long-term anti-coagulation [coumadin]:
  - Underlying hypercoaguable state; recurrent PE; lupus anticoagulant; uncontrolled CA
- When to use IVC Filters: #1 is the patient who is contraindicated to anti-coagulation
  - Large “floater” thrombus
- Absolute CI’s for heparin Tx:
  - Recent cerebrovascular accident
  - Recent CNS-related surgery; eyes,brain,spine
- Histological SI of DVT: lines of Zahn: alternating red/white stripes
### Pulmonary Artery Hypertension

Note: medial hypertrophy and marked intimal hyperplasia of this muscular pulmonary artery

#### Etiology & Epidemiology

@ the elevation of intravascular pressure w/in pulm circulation, w/ systolic pressures above 30mm considered elevated

Primary Pulmonary HTN: is RARE, 2 in a million
- sporadic form is idiopathic
- PPH is more common in men than women
  - [1.7:1]
- AGE: 3rd-4th decade
- probable familial relation: autosomal dominant

Possible Etiologies: ↓PGIS[dilator], ↑endothelin[strictor], ↓eNOS, ΔBMPR2

Secondary pulmonary HTN: more common than
- from underlying pulmonary or cardiac conditions
  - COPD, interstitial lung dz, collagen-vascular dz [SLE, systemic sclerosis], LV failure from CAD, AS, cardiomyopathy, valvular dz, congenital heart dz
- often leads to cor pulmonale

#### DDx:

DDx: includes all the causative agents of secondary pulmonary hypertension

#### Notes:

Factors contributing to pulmonary hypertension:
- alveolar hypoxia
- acidosis
- thromboemboli [PE]
- scarring or destruction of alveolar walls [COPD, infiltrative dz]
- primary thickening of the arterial walls occurs in PPH

#### Labs/Workup

<table>
<thead>
<tr>
<th>CBC:</th>
<th>often nl, may show 2° polycythemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABGs:</td>
<td>↓PO2, ↓O2 sats</td>
</tr>
<tr>
<td>CXR:</td>
<td>shows incr central arteries w/ RAPID tapering of distal vessels</td>
</tr>
<tr>
<td>V/Q Scan:</td>
<td>for ruling out PE</td>
</tr>
<tr>
<td>Cardiac Cath:</td>
<td>for direct measurement of pressures, and to detect any shunting</td>
</tr>
</tbody>
</table>

#### Diagnosis & Symptoms

PPH: insidious
- progressive [exertional] dyspnea = common
- syncope, chest pain[from RV ischemia]
- JVD
- peripheral edema

#### ECG:

- prominent parasternal RV impulse
- loud P2
- R-sided S4
- holosystolic tricuspid regurg murmur, ↑on inspiration
- hoarseness, hemoptysis

#### Pathophysiology & Pathogenesis

Histopath: see medial hypertrophy, intimal proliferation & intimal fibrosis ⇒ plexiform vascular lesions [slit-like arborizations of the single lumen as the walls invade and occlude the lumen]

Pathophysiology: the muscular arteries become the resistance vessels

#### Therapy [Tx]

Non-pharmacologic: O2 Tx for incr alveolar O2 flow; avoid exercise; Chest PT

Pharmacologic: PPH
- diuretics: dyspnea, edema
- digoxin: improve cardiac performance
- vasodilators[prostacyclins]: ↑exercise capacity
- endothelin-receptor antagonist [bosentan]: markedly ↑exercise capacity

Chronic Tx:
- anticoagulation, PPH = ↑risk for thromboses; Tx shown to ↑survival

Lung Transplant indicated in end-stage dz

### Disposition:

PPH, class II, III have a mean survival of 3.5y

- note strong central marking w/ rapid tapering
PULMONARY ARTERY HYPERTENSION: continued

PHYSIOLOGY:
• Pulmonary circulation is a low pressure, low resistance system
• Systolic/diastolic pressures tend to be ~25mm/10mm
• Recall the gravity effects on perfusion of the lung; w/ the basic 3 Zone schema, ignoring the 4th zone
  o Zone 1: apical region: PA > Pa > PV; alveolar pressure collapse the vessels
  o Zone 2: middle: Pa > PA > PV; arterial greater than alveolar for most part allowing perfusion
  o Zone 3: base: Pa > PV > PA; most flow since arterial and venous pressures are greater than alveolar pressure
• 2 methods for preventing ↑pulmonary vascular resistance: recruitment [unperfused capillaries] and distension [thin walled vessels]
• Lung Volume & Pulmonary vascular Resistance:
  o @ RV = higher resistance, lower volumes allows for alveolar collapse; higher resistance seen in the extra-alveolar vessels
  o @ TLC = higher resistance; of the alveolar vessels

Pulmonary Vascular Resistance:
• $R = \frac{\text{change in pressure across system [pulm artery pressure -left atrial pressure]}}{\text{FLOW}}$
• Measure LA pressure w/ Schwan-Ganz catheter

Pulm vascular response to hypoxia: hypoxia @ alveoli considered <60-70mm
• See vasoconstriction in response to alveolar hypoxia;
• In localized hypoxia, this constriction diverts flow to the ventilated regions, in an attempt to prevent excessive V/Q mismatch
• Overall pulm vasc resistance does not change markedly
• In generalized hypoxia, 2nd to lung dz, high altitude; this vasoconstriction is also generalized
• Leads to marked ↑pulm vasc resistance, and ↑pulm artery pressure
• Etc.
• Low pH in blood also promotes vasoconstriction

More mechanisms of secondary pulmonary HTN:
• Hyperkinetic flow states: VSD, ASD
• Occlusive: chronic PE
• Obliterative: emphysema [COPD], vasculitis, sarcoidosis, interstitial lung dz
• Vasoconstrictive: hypoxia and sclerodoma

Pulmonary Venous HTN:
• Seen commonly as a cause of pulmonary HTN
• Major causes are L-sided atrial or ventricular heart dz
• Think mitral stenosis
• Or L-sided valvular dz
• Consider external compression of the central pulmonary veins; in fibrosis, adenopathy, tumors

Chronic Pulmonary Venous HTN:
• Leads to fibrosis of the interstitium
• Extravasation of RBCs into the pulmonary parenchyma
• Hemosiderin-laden m.phages

CXR Si:
• Redistribution of blood flow to upper lung zones [cephalization]
• Interstitial and alveolar edema
• Kerley’s B lines: represent the thickening of lymphatic vessels or fluid engorgement of them in the interlobular septa
• Seen extending to the pleura @ the bases
**Etiology & Epidemiology**

@ a multisystem dz; classic triad:
- necrotizing granulomatous lesions in URT or LRT
- focal necrotizing vasculitis involving BOTH arteries and veins
- focal glomerulonephritis of the kidneys

Incidence: 0.5 in 100,000
AGE: mean onset is 40y
ETIOLOGY: an autoimmune response to the granule component of PMNs known as proteinase 3 [PR3]

**DDx:**
- critical to Dx correctly; pt dies if you don’t
  - other granulomatous lung dz [ie churg-strauss, sarcoid, etc]
  - neoplasms
  - goodposture’s syndrome
  - bacterial/fungal sinusitis

**Labs/Workup**

| c-ANCA | look for ↑ ANCA levels, in a cytoplasmic pattern |
| CBC | anemic, leukocytosis |
| Urinalysis | RBC casts, hematuria, proteinuria |
| ESR | ↑ |
| ↓CREAT CL, ↑serum CREAT |

**Si/Sx**

- Lung: cough, hemoptysis, pleuritis
- URT: persistent nasal stuffiness, sinus infxn; nasal septal perforation, mastoiditis
- EAR: chronic OM, chronic OM,
- Kidney: renal insufficiency
- Mouth: chronic ulcerative lesions
- Joints: polyarthritis
- Eyes: retinal and optical nerve vasculitis; proptosis

**Pathophysiolog & Pathogenesis**

HisotPath: daFunk says: **multisystem necrotizing granulomatous vasculitis**
- see elastica disruption w/ elastin stain; this leads to vascular injury
- ANCA in a cytoplasmic staining pattern [c-ANCA]
- may see non-specific hemosiderin-laden m.phages

**Therapy [Tx]**

Non-pharmacologic: ensure airway drainage, nutrition
Pharmacologic:
- perdnisone + cyclophosphamide: for clinical Sx
- TMP-SMX reduces the risk for relapse

Disposition: 80%+ 5y survival w/ Tx; <20% 2yr survival w/out Tx

Necrotizing Granulomatous inflammation of lung
**Goodpasture’s Syndrome**

**Etiology & Epidemiology**
- Idiopathic recurrence of alveolar hemorrhage and rapidly progressive glomerulonephritis, defined by the TRIAD:
  - glomerulonephritis
  - pulmonary hemorrhage
  - antibodies to basement membrane protein
  - anti-GBM

EPI: affects predominantly young, white, male, smokers
- Male:female = 6:1

**Etiology:**
- Anti-body formation against glomerular basement membrane protein leads to a cross-reactive condition affecting the alveolar basement membranes also
- Ab deposition leads to basement membrane damage and pulmonary hemorrhage and glomerulonephritis

**DDx:**
- Wegener’s, SLE, drug-induced renal-pulmonary dz [see w/ penicillamine]

**Labs/Workup**
- CBC: anemic due to iron loss in hemorrhage;
- ABGs: hypoxemic
- PFTs: restrictive pattern
- ↑ serum α-GBM
- ↑ CREAT, ↑ BUN
- CXR: fluffy alveolar infiltrates and hemorrhage

**Si/Sx**
- Dyspnea, cough, hemoptysis
- Pallor, fever, arthralgia
- Hematuria, proteinuria, red cell casts and renal failure

**Pathophysiology & Pathogenesis**
- **Histopath:** hemorrhage into alveolar space
  - linear deposition of IgG and complement along basement membranes of alveoli and glomeruli
  - do stain/immunofluor for α-GBM on Bx

- **Pathophys/genesis:** repeated bouts of hemorrhage and hemoptysis
  - A **cytotoxic antibody** against glomerular and alveolar basement membrane is responsible for the injury.
  - Targets a typeIV collagen
  - By **activating complement**, the antibody causes damage to glomerular and alveolar basement membrane.
  - A **respiratory viral infection is believed to initiate production of the antibody.** [flu]

- Antigenic similarity between kidney and lung basement membrane accounts for the clinical picture.

**Therapy [Tx]**
- **Pharmacologic:**
  - Steroid in high doses controls pulmonary hemorrhage
  - Nephrectomy with dialysis is necessary in some patients
  - Combination of plasmapheresis and immunosuppressive therapy provides the best results.

**NOTES:**
- Hyaline Droplets in the Kidney
**Acute Respiratory Distress Syndrome**

- Acute Respiratory Distress Syndrome •

  note hyaline deposition [pink gum]

### Etiology & Epidemiology

@ ARDS is a form of non-cardiogenic pulmonary edema that results from **acute** damage to the alveoli.
- characterized by:
  - acute diffuse infiltrative lung lesions, causing **interstitial and alveolar edema**
  - severe hypoxemia
  - respiratory failure

**AECC definition:**
- acute onset
- bilateral infiltrates on CXR
- PAWP ≤ 18 or NO evidence of LA HTN
- PaO2/FiO2 ≤ 300: acute lung injury [ALI]
- PaO2/FiO2 ≤ 200: ARDS

**Epi:** up to 100,000 cases per year in US

**Etiology:** several causes
- **Sepsis:** >40% of cases
- **Aspiration:** drowning, gastric acid, >30%
- **Trauma:** >20%
- noxious INH of toxic gas
- **pneumonia:** common
- post-cardiopulmonary bypass
- burns
- pancreatitis
- Hx of chronic alcohol abuse ↑risk for ARDS later in life

### DDx:

**DDx:** cardiogenic pulmonary edema, viral pneumonitis, lymphangitic carcinomatosis

### Notes:

- Having maximal alveolar fluid transport is associated with lower mortality in ARDS.

### Labs/Workup

**ABGs:** respiratory alkylosis, acidosis[sepsis] • ↓PCO2,
- widened A-a gradient
- hypercapnia in progressive dz

**PFTs:** ↓FRC, ↓pulmonary compliance
- ↑pulmonary vascular resistance
- **SHUNTING**
- so may not be totally responsive to O2 Tx
- V/Q mismatch
- alterations in surfactant function

**Blood and Urine Cultures:**
- for infxn
- BAL: see ↑PMNs, presence of ↑eosinophils has Tx significance; they respond to corticosteroids
- CXR: bl infiltrates w/in 24h, prominent @ the bases and periphery
- ⇒ in adv stage; see “white-out” of both lungs

### Hemodynamic monitoring:

- rule out cardiogenic
- common signs:
  - + pulmonary edema
  - ↑↑ cardiac output
  - ↓↓ PAWP

### Si/Sx

- **Dyspnea**
- **chest discomfort**
- **cough**
- **anxiety**
  - **tachypnea**
  - **tachycardia**
  - **hypertension**
  - coarse crepitations, bilateral
  - fever, is part of underlying etiology

### Pathophysiology & Pathogenesis

**HistoPath:** DAD;
- dmg to type I alveolar epithelial cells
- type II pneumocyte hyperplasia
- areas of atelectasis
- interstitial and alveolar edema
- inflammatory cell infiltrate

**hyaline membranes lining distended alveolar ducts**
- fibrosis & pulmonary vascular changes

**PathoPhys/genesis:**
- Early: **exudative phase [ARDS]:** fluid seen in alveolar interstitial septum; see Fibrin-rich hyaline membranes
- **Mid:** proliferative phase: 1-2wks post; see typell alveolar epithelial cell hyperplasia
- Late: **fibrosis:** damaged parenchyma can go unrepaired and is left as a scar; see changes in pulmonary vasculature, like remodeling and compromise of the lumen of small vessels by intimal proliferation and microthrombi

### Therapy [Tx]

- Non-pharmacologic: ventilatory support w/ Auto-PEEP
  - repositional; lateral decubitus; improving perfusion distribution
  - nutritional support, to maintain oncotic pressure
- Pharmacologic: treat precipitating factor[s]
  - antibiotics, only if sepsis determined
  - low dose dopamine may be indicated if PCWP ↑↑,
  - dopamine causes natriuresis and maintain adequate renal flow

**Prognosis:** overall mortality rates of 40-60%; death often attributed to sepsis or multi-organ dysfunction
ARDS: continued

Physiology Pertinent to ARDS

Starling Equation: describes the effects of the factors maintaining fluid transport across the pleural space

- Fluid = K\left(\text{HPc - HPis}\right) - \text{perm.coeff}\cdot\left(\text{COPc} - \text{COPis}\right)

Fluid normally moves from the pulmonary capillaries to the interstitial space and then is resorbed by the lymphatics to prevent accumulation

Mechanisms of Fluid Accumulation

Cardiogenic or hydrostatic pulmonary edema
- Pc increased due to LV failure or from mitral stenosis; as a consequence of elevated left atrial and/or left ventricular pressures
- Since the permeability barrier is intact: protein is not lost en masse, so the fluid is low-protein
- Tx: often can be resolved w/ diuretics or removing the causative clot

Non-cardiogenic pulmonary edema:
- Due to disruption of the permeability barrier
  - Damage can be to the alveolar epithelium or the capillary endothelium, or both
- ARDS is in this class
- Since the barrier is broken down; the fluid is high-protein
- Tx: takes days to mend, since the membrane has to be rebuilt

Ion and Water Transport in the distal airways

- Type II cells: allow for Na and water transport; have ENAC
- Type I cells: have multiple aquaporin channels
- β-agonists stimulate active fluid reabsorption; 3 fold incr; this mechanism helps you from drowning in your lungs @ high altitudes
- ENAC -/- mice can’t clear fluid @ birth; but architecture is intact; death by drowning

ARDS Secondary to Sepsis: Tx considerations

- Activated Protein C has been shown to have a positive impact on survival in pts w/ sepsis/shock
- Acute organ dysfunction must be assessed in the pt w/ sepsis
  - Si/Sx of Sepsis:
    - CNS: delirium, confusion, psychosis
    - Liver: ↑ liver enzymes, ↑ PT, jaundice
    - Resp: hypoxia, tachypnea
    - Cardiac: tachycardic, hypotensive, ↑ CVP
    - Kidney: oliguria, anuria, ↑ ↑ CREAT
    - Hem: thrombocytopenic, ↓ protein C, ↑ D-dimers
- Path to shocky-town: inflammatory cytokines released ⇒ NO released from vasc endothelium ⇒ ↓ systemic vasc resistance ⇒ HIGH CO & hypotension ⇒ wide pulse pressure & ↓ urine output ⇒ brisk cap refill & decr mental status ⇒ hyperdynamic heart & lactic acidosis
- Progression of definitions: Systemic Inflammatory Response Syndrome [SIRS]: systemic response, w/ fever, tachypnea, tachycardia, leucocytosis. ⇒ Sepsis: infxn PLUS ≥ 2 SIRS criteria ⇒ Severe Sepsis: sepsis + organ dysfunction. ⇒ Septic Shock: sepsis + hypotension, despite fluid resuscitation. ⇒ MODS: altered organ function, homeostasis unable to be maintained w/out intervention

RDS of newborn: RDS is also known as hyaline membrane dz

- Main Pathology: inability to immature lung to produce adequate surfactant
  - This leads to atelectasis ⇒ hypoxia/acidosis ⇒ epithelial necrosis
    - Uncontrolled diabetes in mother cold lead to hyperinsulism of the fetus and ↓ surfactant production
    - Labor also ↑ surfactant; so C-sections could also contribute
  - Si/Sx: premature; tachypnea, intercostals m. retraction, hypoxemia
  - RAD: diffuse alveolar filling w/ air bronchograms
  - Pathology of RDS may be partially due to poor ability to generate Na absorption strong enough to pull fluid/water out the lungs
  - ENAC channels play a role in the proper response
  - Steroids upregulate surfactant, so women expected to give birth to preemies are often treated w/ steroids to minimize adverse conditions at birth

Ventilator-Induced Lung Injury: due to overinflation the lungs; why we must ventilate on small tidal volumes and faster breathing rates

Alveolar Hemorrhage Syndrome: Capillary injury, intra-alveolar hemorrhage, and hemoptysis secondary to autoimmune diseases (Wegener’s, SLE, and Goodpasture’s).
- All present with the TRIAD: of hemoptysis, anemia, diffuse alveolar dmg
### Etiology & Epidemiology

**Etiology:**
- **Kids:** Foreign bodies
- **Adults:** Gastric acid, food; mineral oil laxatives, or nasal drops

Exogenous lipoid pneumonias often occur as repeated, subclinical aspiration events in patients using mineral oil as a laxative, or in patients with structural esophageal disease or neurological disease, both of which predispose to aspiration. Lipoid pneumonias also occur in infants with feeding difficulties.

**DDx:**
- Endogenous lipoid pneumonia; bacterial pneumonia, cancer

### Labs/Workup

<table>
<thead>
<tr>
<th>CT: showing fat in the consolidation is highly telling</th>
<th>RAD: focal alveolar pattern, typically of the RLL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Si/Sx:</strong></td>
<td>a resultant pneumonitis may have different radiographic manifestations such as multifocal scattered consolidation, chronic segmental or lobar consolidation, or focal masslike opacities.</td>
</tr>
<tr>
<td><strong>DDx:</strong></td>
<td>• may be aSx</td>
</tr>
</tbody>
</table>

### Pathophysiology & Pathogenesis

**HistoPath:** Large droplets of lipoid material in alveolar AND interstitial macs
- Fibrosis and a granulomatous response are common

**PathoPhys/genesis:** Often an aspiration
- Depending on the type of lipid ingested and the degree of inflammation that occurs, damage to the lung can be little to none or can fulminate to necrosis and hemorrhage

⇒ Gastric acid leads to DAD
⇒ FB leads to foreign body giant cells

⇒ The lesions are characterized at an early stage by a hemorrhagic bronchopneumonia followed by
⇒ An infiltrate of lipid-laden macrophages within the air-spaces.
⇒ A fibroblastic proliferation with bands of collagen occurs subsequently.

### Therapy [Tx]

- Remove the offending material/exposure
- Corticosteroids may help
- Whole lung lavage may help
Endogenous lipoid pneumonia

Etiology & Epidemiology
Synonyms: post-obstructive pneumonitis, cholesterol pneumonia, golden pneumonia

DDx:
DDx: exogenous pneumonia, bacterial pneumonia, cancer

NOTES:
Alveolar spaces are filled with large, pale macrophages that contain finely dispersed lipid droplets. Note the type II cell hyperplasia and the mild thickening and chronic inflammation of alveolar walls.

Labs/Workup

| Bx: often Dx | RAD: peripheral infiltrates w/w/out central mass |

Si/Sx
progressive shortness of breath

Pathophysiology & Pathogenesis

HistoPath: finely vacuolated [small droplets] m.phages fill the alveolar spaces; when lymphatic clearance is obstructed
• see ↑ # of foamy macs, w/w/out cholesterol clefts

General Pathophys/geneis:
• Endogenous lipoid pneumonia may result from inadequate clearance of lipid-containing cellular debris and surfactant materials distal to a bronchial obstruction, at the edge of tumors, and around inflammatory masses; e.g. Wegener’s granulomatosis. Other types of endogenous lipoid pneumonia include lipid storage diseases and pulmonary alveolar lipoproteinosis.

Therapy [Tx]
• resect any localized masses
• whole lung lavage
• treat causative dz process
**Pulmonary Edema: cardiogenic**

### Etiology & Epidemiology
@ often synonymous w/ cardiogenic pulmonary edema.

**Etiology of cardiogenic edema:**
- acute MI
- exacerbation if CHF
- valvular regurg
- VSD
- Mitral stenosis

**DDx:**
- non-cardiogenic pulm edema; exacerbation of COPD or asthma, viral pneumonitis

**cardiogenic edema** will have a PCWP>15, non-cardiogenic will not
- if the PCWP is < 12, then the cause is non-cardiogenic [ARDS]

### Notes:
- Labs/Workup
  - **ABGs:** resp and metab acidosis; ↓PaO2; ↑PCO2, ↓pH
    ⇒ this may be predicated by a resp alkyllosis, 2º to hyperventilating
  - **CXR:** pulm congestion, w/ Kerley B lines
    - common descriptor is the finding of **butterfly distribution**
    - bilateral alveolar infiltrates
    - pleural effusions
    - incr vascular markings
  - **ECHO:** for ruling in cardiogenic
  - **Si/Sx**
    - **dyspnea, w/ rapid shallow breathing**
      - diaphoresis; peripheral cyanosis, perioral cyanosis
      - pink, frothy sputum
    - **pulm congestion, w/ Kerley B lines**
      - moist bilateral rales
      - ↑P2, S3 gallop
      - bulging neck veins
      - stiff, small lungs
  - **Pathophysiology & Pathogenesis**
    - **HistoPath:** see **transudate** in the interstitium and alveolar airspaces
      ⇒ venous and capillary congestion
    - **PathoPhys/genesis:** short and sweet is LV failure or mitral stenosis leading to backup and congestion into pulmonary vasculature ⇒ pulm HTN promotes transudation.
  - **Therapy [Tx]**
    - **Non-pharacologic:**
      - sitting upright, w/ legs off side of bed for improved breathing and ↓venous return
    - **Pharmacologic/Acute response:**
      - 100% O2
      - furosemide bolus: to establish rapid diruesis
      - vasodilator Tx
      - nitrates: for chest pain
      - nitroprussides: for afterload reduction in HTN pts
      - morphine: ↓venous return, ↓systemic vascular resistance, ↓anxiety
      - ACE inhibitors: ↓afterload [Captopril]
    - **PEEP:**
      - helps prevent airway collapse
      - ↑ FRC
      - ↓ shunting
      - expands alveoli for better diffusion
  - **Disposition:** mortality for cardiogenic pulmonary edema is 60-80%
Etiology & Epidemiology
@ non-cardiogenic presents in an ARDS manner
Etiology of noncardiogenic pulm edema:
• sepsis
• GI aspiration
• trauma
• toxic gas INH

DDx:
DDx: cardiogenic pulm edema; exacerbation of COPD or asthma, viral pneumonitis, GERD
• cardiogenic edema will have a PCWP > 15, non-cardiogenic will not
• if the PCWP is < 12, then the cause is non-cardiogenic [ARDS]

NOTES:

Labs/Workup

| ABGs: resp and metab acidosis; ↓ PaO2; ↑ PCO2, ↓ pH  
| = this may be predicated by a resp alklylosis, 2nd to hyperventilating |
| CXR: pulm congestion, w/ Kerley B lines  
| = common descriptor is the finding of butterfly distribution  
| = diffuse bilateral alveolar infiltrates  
| = pleural effusions  
| = incr vascular markings |

Si/Sx

| dyspnea, w/ rapid shallow breathing  
| = diaphoresis; peripheral cyanosis, perioral cyanosis  
| = pink, frothy sputum  
| = moist bilateral rales  
| = P2, S3 gallop  
| = bulging neck veins  
| = stiff, small lungs |

Pathophysiology & Pathogenesis

HistoPath: see exudate in the interstitium and alveolar airspaces
⇒ venous and capillary congestion
PathoPhysgenesis: short and sweet is the edema is due to capillary leak
⇒ exudative phase: due to endothelial damage; see hyaline membrane, type II hyperplasia, fibroblast proliferation, inflammation
⇒ proliferative phase: interstitial fibrosis, alveolar destruction, incr angiogenesis and organization of the exudate
• will lead to obliteration of alveoli and bronchi following resolution; if not treated appropriately

Therapy [Tx]

Non-pharmacologic:
• sitting upright, w/ legs off side of bed for improved breathing and ↓ venous return
Pharmacologic/Acute response:
• 100% O2
• furosemide bolus: to establish rapid diruesis
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• morphine: ↓ venous return, ↓ systemic vascular resistance, ↓ anxiety
• ACE inhibitors: ↓ afterload [Captopril]

PEEP:
• helps prevent airway collapse
• ↑ FRC
• ↓ shunting
• expands alveoli for better diffusion

Disposition: mortality for cardiogenic pulmonary edema is 60-80%
RESPIRATORY FAILURE

Alveolar Gas Equation
• \( p_{A02} = FiO2 \cdot (P_{ATM} - pH2O) - pACO2/R.Q. \)
  • consider R.Q. = 1 for simplification; but actually closer to 0.8
    o a relation of the amount of CO2 produced in relation to the amount of O2 consumed
  • pH2O = 47 in most cases
  • Patm = 747 often @ sea level
⇒ Respiratory Failure: PO2 < 60 torr, or PCO2 > 50 torr

Gas Exchange Failure Si/Sx:
• Dyspnea, impaired mental status, headache, Tachycardia, Papilledema[HyperCapnea], variable finding in lung examination, cyanosis[in sev hypoxemia]

Hypoxemic: due to inadequate O2 delivery
• will have normal to low pCO2
• think ARDS, or pneumonia
• think LUNG failure

Physiological causes:
  • V/Q mismatch is the major player [V/Q is variable]
    ▪ Correctable w/ supp oxygen
    ▪ Rem: Dead Space: V/Q = ∞, no direct effects on O2
    ▪ Rem: Physiologic Shunt: V/Q=0, point when ventilation it totally impeded
      • [ie airway completely filled with fluid]
  • R→L shunt [V/Q=0]
    ▪ Refractory to supp oxygen
  o Decr PiO2 [high altitude, suffocation]
  o Diffusion limitation [typically seen only during exercise induced hypoxemia]
• ↓ VA [caused by increased pACO2 or ↓pAO2]

Therapy: treat the primary cause
• Hypoxemia can lead to death, so treat the patient
• Supp oxygen therapy usually helps

Hypercapneic/Hypoxemic Type: unable to adequately ventilate enough to eliminate CO2 efficiently
• considerations are the minute ventilation and the amount of alveolar space to dead space [Vdead/Vtotal]
  • this is normally 0.25-0.30 @ rest
• Ventilatory Assessment:
  • \( V_A = V_E \cdot (1 - V_D / V_T) \)
  o \( V_E \) is nl 6000ml[BTPS]/min @ rest; 12breath/min x 500ml/breath
  • \( PaCO2 = 863 \cdot VCO2/V_A \)
  o \( PaCO2 = 863 \cdot VCO2 / V_E \cdot (1 - V_D / V_T) \)
• pH must show signs of inadequate metabolic compensation for the respiratory acidosis

CAUSES:
• Depression of central nervous system respiratory control
  • narcotic overdose
• Dz of the respiratory BELLOWS; chest wall or neuromuscular mechanics responsible for thoracic expansion
  • Kyphoscoliosis, flail chest
  • Cervical cord trauma
  • Guillain-Barre Syndrome, Myasthenia-gravis, muscular atrophy
  o Clinical Si/Sx of respiratory muscle weakness:
    • Tachypnea, ↓ vital capacity, ↓ maximum inspiratory force, ineffective cough
    • Hypercapnea is a LATE sign: support ventilation prior to failure!
  o Or a chronic obstructive lung dz [often contributes to a hypoxemic condition also]
    • COPD, asthma
  o Upper airway obstruction
• Precipitants of acute on chronic respiratory failure
  o RTI
Drugs; sedatives, narcotics
CHF
Less commonly: pulmonary emboli, pollutants

- **Therapy:** 1st **TREAT HYPOXEMIA** and then Dx and try to treat underlying etiology
  - 2nd consider resp stimulants
    - Naloxone: opioid antagonist; often come back abruptly
    - Controlled hypoxemia [rare and under proper clinical settings]
    - Chemicals: rarely work
  - 3rd assistive devices
  - 4th: if severely acidotic; think PEEP or tracheal intubation
    - other assistive devices: CPAP, BiPAP, Cuirass ventilator
      - CPAP, BiPAP have the advantage of being non-invasive
    - REM: with mechanical ventilation one can control the tidal volume and respiratory rate on multiple levels, or it can be partially patient-regulated
  - **Why PEEP?**:
    - helps prevent airway collapse
    - ↑ FRC
    - ↓ shunting
    - expands alveoli for better diffusion [↑PaO2]
  - **ADVERSE effects:** Barotrauma, ↓ venous return, ↓ cardiac output
  - 5th: mech ventilation chronic Tx⇒ QOL issues?

**Goals for supportive therapy of gas-exchange:**
- arterial O2 sat > 90%; PO2 > 60 torr
- Hb > 10g/dL; HCT>30%
- NI to near nl cardiac output

**Indications for Mechanical Ventilation:** *when the PCO2 has risen high enough to cause:*
- ↓↓ pH; pH ≤ 7.30
- impaired mental status

**Maintenance of Oxygenation:**
- in the mixed bag patient; w/ acute on chronic resp failre; the contributory hypoxemia can often be counterbalanced w/ supplemental oxygen, w/out absurdly high FIO2 levels
- in the **chronic hypercapneic patient** things may be a little different
  - giving supp oxygen may in fact increase the hypercapnea
    - if the PCO2 shoots through the roof; move them to mechanical ventilation
    - this rarely happens with attentive monitoring and judicious thinking

**Indications for Mechanical Ventilation:**
- PO2 ≥ 60 torr cannot be maintained on 40-60% O2

**BENEFITS of mechanical ventilation:**
- Improved oxygenation
- REDUCED work of breathing
MORE ON GAS EXCHANGE AND ASSESSMENT

Poor Man's Rules of Thumb:
- w/ ACUTE respiratory Acidosis:
  - the $\text{HCO}_3^-$ will rise by 1mEq/L for each 10mmHg of PCO2
- w/ CHRONIC Respiratory Acidosis:
  - the $\text{HCO}_3^-$ will rise by 4mEq/L for each 10mmHg of PCO2

• Stretch receptors in the lungs and chest walls are strong promoters of the respiratory drive.

THE BRAIN AND RESPIRATION
• abnormal respiratory patterns are indicative of the region of the brain damaged
  - Forebrain damage:
    - Apraxia for deep breathing and breath hold
    - Post hyperventilatory apnea [abnormal pause after hyperventilation]
    - Cheyne-Stokes Respiration
      - Crescendo-decrescendo breathing
      - Variations in amplitude of ventilation
      - Considered a hyperventilatory state on avg
      - Often due to CNS or heart failure
  - Midbrain or Hypothalamus damage:
    - Central Reflex Hyperpnea: just breathing rapidly all the time
  - Lower Pontine damage:
    - Cluster breathing: periods of rapid breathing separated by pauses
    - Apneustic breathing: think post-inspiratory pause; indicative alone of pontine dmg
    - Ataxic breathing: w/out any pattern
  - Medullary damage:
    - Ataxic breathing
    - Ondine's Curse: stop breathing as soon as you fall asleep
    - Loss of autonomic breathing control, w/ preservation of voluntary control

SLEEP & RESPIRATION
• The respiratory pattern is different for each stage of sleep
  - Sleep onset shows occasional pauses
  - Stage3-4 sleep show regular monotonous breathing
  - REM sleep: is periodic and variable; see ↓CO2 and ↓O2 sensitivity
**Etiology & Epidemiology**

@ repetitive episodes of diminished air flow associated w/ O2 desaturation or arousal

- Main Types:
  - central, obstructive, mixed-type,

**Risk Factors:**

- ↑neck size, HTN, loud snoring,
- all pts w/ unexplained daytime sleepiness should be assessed, doh!
- ↑incidence in hypothyroidism

**Obstructive Sleep Apnea:** common; affecting 9% of adult males, 3% of females

- sometimes referred to as **Pickwickian Syndrome**

**OSA risk factors:**

- obesity, smoking, alcohol, narrow airway, GERD, heart/brain dz, ADHD?

**DDx:**

DDx: narcolepsy, CHF, COPD, GERD, seizure do, parasomnias

**NOTES:**

In the primary care setting, patients with high risk for sleep apnea meet two of the following criteria:

- snoring
- persistent daytime sleepiness or drowsiness during driving
- obesity
- hypertension

ALSO, any child that snores

<table>
<thead>
<tr>
<th>Labs/Workup</th>
<th>CBC: often shows erythrocytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• refer for sleep study</td>
<td>⇒ polysomnography</td>
</tr>
<tr>
<td>⇒ airflow, EKG, O2 sats, chest, abdomen motion all monitored</td>
<td></td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Si/Sx</th>
<th>HTN</th>
</tr>
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<tbody>
<tr>
<td>daytime sleepiness</td>
<td>tachycardic</td>
</tr>
<tr>
<td>large neck</td>
<td>arrow airway</td>
</tr>
<tr>
<td>edema: late sign</td>
<td>may see mixed Cheyne Stokes breathing also</td>
</tr>
<tr>
<td>depression, HA, irritability</td>
<td></td>
</tr>
</tbody>
</table>

**Pathophysiology & Pathogenesis**

**Pathophys/genesis:**

**Obstructive:** upper airway muscles relax and close off the airway

- will make a + ventilatory effort, but no airflow, since blocked
- event often ends w/ arousal
- site of obstruction in obese is often the pharyngeal passageway

**Central:** lower resp muscles relax

- no effort is made to breath
- pt may have no arousals; often REM-related
- often seen in the Obese, as part of Obesity Hypoventilation Syndrome

**Therapy [Tx]**

**Obstructive:**

- Non-pharmacologic:
  - weight loss
  - CPAP during sleep
  - surgical resection of neck tissue
  - surgical: removal of uvula, nasal septoplasty, mandible advancement

**NOTE:** OSA increases the 5-10y risk for mortality by 40-60%

- therapy of the epileptic patient often shows a >50% reduction in sz frequency

- one mode of therapy is the **mandibular advancement device**
- shows effectiveness in improving sleep in up to 2/3rd's of patients