Categories of Pulmonary Disease

I. Obstructive
II. Restrictive
III. Infectious
IV. Neoplasms
V. Pleural
I. Obstructive Diseases

• Characterized by decreased airflow due to:
  - increased resistance (narrowed airways)
  - loss of elastic recoil

Examples: Asthma, COPD, Bronchiectasis

• Decreased expiratory flow
  FEV1:FVC <0.8
  cannot exhale 80% of FVC in 1 second

• FEV1 = forced expired volume in 1 second
• FVC = forced vital capacity (max inspiration to max expiration)
Asthma

- Common (USA: 10% of children, 5% of adults)
- Often in childhood, genetic basis
- Symptoms: dyspnea, cough, wheeze
- Obstruction - bronchospasm, edema, mucus
- Chronic inflammation leads to hyper-responsiveness
- Triggers
  - Extrinsic: Type I hypersensitivity reaction to exogenous allergens
  - Intrinsic: Nonimmune mechanisms - infection, dust & fumes, drugs (aspirin), exercise, cold temp.
Asthma

Pathogenesis

Type 1 Hypersensitivity
Asthma

Dust mite feces - allergen

Pollen
Asthma

- Attack:
  - Duration - hrs
  - Course - subsides or drug relief
  - Status asthmaticus - unresponsive to drugs (bronchodilators)

- Pathogenesis
- Diagnosis
- Treatment
Asthma

Frequent attacks leave little time for repair......
results in chronic inflammation

Figure 8-16
Histopathology of asthma. The lumen of the bronchus contains mucus. The wall is thickened and inflamed and contains hyperplastic smooth muscle cells and bronchial glands.
Asthma - mucoid expectoration
Asthma

Diagnosis

- Patient history, symptoms, lung function tests

Treatment

- Identify/avoid triggers (extrinsic and intrinsic)
- Quick-relief drugs for attack ($\beta_2$-adrenergic receptor agonists: albuterol, terbutaline) relax airway smooth muscle
- Primatene Mist (epinephrine) activates $\alpha_1$, $\alpha_2$, $\beta_1$ and $\beta_2$ receptors......multiple side effects (e.g., change in blood pressure, change in cardiac contractility and rate)
- Anti-inflammatory drugs to prevent attacks (corticosteroids)
Chronic Obstructive Pulmonary Diseases

• COPD: catch-all clinical term for lung diseases characterized by chronic airway obstruction (lungs can’t empty rapidly; poor ventilation)

• 4th leading cause of death

• Patients classified into three broad groups:
  - Emphysema*
  - Chronic bronchitis
  - Bronchiectasis

* may co-exist with chronic bronchitis
Emphysema

- Permanent enlargement of airspace distal to terminal bronchiole and destruction of alveolar walls without scarring. Abnormally enlarged air sacs fill easily (increased compliance) with inspired air but empty poorly (loss of elasticity) with expiration causing small airways to collapse during breathing. Easy filling/poor emptying leads to lung hyperexpansion (barrel-chest)

- Pathogenesis
- Etiology
- Symptoms
- Treatment
Emphysema

Pathogenesis

**Centriacinar (centrilobular)**

- enlargement of respiratory bronchioles in center of a lobule
- most common form of emphysema (associated with smoking)
- remaining respiratory bronchioles can have anthracotic (carbon) macrophages and chronic inflammatory cells
- typically affects upper lobes

**Panacinar (panlobular)**

- enlargement of all airspaces distal to terminal bronchioles
  - characteristic of patients with genetic deficiency of α1-antitrypsin...but may also be linked to smoking
  - typically affects lower lobes
Emphysema

Normal Acinus

Centriacinar

Panacinar
Emphysema

Etiology

• Tobacco smoking is the major cause of ephysema (98%); α1-antitrypsin genetic deficiency (2%)

• Smoking Hypothesis:
  - Increased numbers of neutrophils, which contain serine elastase, are found in BAL fluid of smokers
  - Hepatocytes synthesize and secrete α1-antitrypsin (the major serum antielastase); intrapulmonary cells also express it at a low level. Tobacco smoke oxidizes methionine residues to sulfoxide forms, decreasing α1-antitrypsin activity
  - Unopposed, increased elastolytic activity leads to emphysema
Pathogenesis of emphysema

- Smoking
- Increased elastase
  - PMN
  - Mac
- Decreased antielastase
  - $\alpha_1$-antitrypsin
- $\alpha_1$-antitrypsin deficiency
- Elastic damage
  - Emphysema
Symptoms of emphysema

- Progressive dyspnea, weight loss, barrel-chest (structural change due to lung over-inflation). Patients often hyperventilate and are referred to as "Pink Puffers" (blood oxygenation sufficient to not develop anoxia).

Treatment of emphysema

- Replacement enzyme therapy (α1-antitrypsin purified from plasma; 60 mg/kg/wk; $100,000/yr) for those with genetic form, to slow disease progression
- Stop smoking, bronchodilators, lung volume reduction (20-35%) [allows remaining lung and respiratory muscles to work more efficiently]. Supplemental $O_2$, death by respiratory failure.
Chronic Bronchitis

- Productive cough (lots of mucus, expectoration) for at least 3 consecutive months during 2 consecutive years
- Walls of bronchi/bronchioles thickened, excessive mucus
- Etiology: Smoking (90% of cases); remaining 10% of cases are due to air pollution, toxic fumes, respiratory infections. A single bout of viral pneumonia may predispose an individual to chronic bronchitis later in life. Cessation of smoking improves clinical symptoms
Chronic Bronchitis

• **Symptoms:**
  - Cough, excessive mucus production, and shortness of breath.
  - Right heart failure (*cor pulmonale*: *cor*=heart; *pulmonale*=lung)
  - Chronic hypoxia leads to pulmonary vascular remodeling and vasoconstriction (pulmonary hypertension)
    - May co-exist with emphysema

• **Histological examination:**
  - Evidence of mucous gland hyperplasia, chronic inflammation, and fibrosis
Rat lung

Normoxic

Hypoxic

Bar, 100 um

Crossno Jr. et al., American Journal of Physiology - Lung Cellular and Molecular Physiology Published 11 April 2007 Vol. 292 no. 4, L885-L897
Chronic Bronchitis

- Prolonged coughing bouts accompanied by expectoration of tenacious or purlulent mucus and dyspnea
- Hypoxia may be so pronounced during coughing that patients are commonly referred to as “Blue Bloaters”
### Chronic Bronchitis vs Emphysema

<table>
<thead>
<tr>
<th></th>
<th>Predominantly Bronchitis (&quot;Blue Bloaters&quot;)</th>
<th>Predominantly Emphysema (&quot;Pink Puffers&quot;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest</td>
<td>Normal</td>
<td>Barrel chest</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Cough</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Sputum</td>
<td>++</td>
<td>+/-</td>
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<tr>
<td>Cyanosis</td>
<td>++</td>
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<tr>
<td>Pulmonary hypertension</td>
<td>++</td>
<td>–</td>
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<tr>
<td>Peripheral edema</td>
<td>++</td>
<td>–</td>
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<tr>
<td>Radiographic findings</td>
<td>Densities</td>
<td>Overinflation</td>
</tr>
<tr>
<td></td>
<td>Enlarged Heart</td>
<td>Small Heart</td>
</tr>
</tbody>
</table>

*Remember: Emphysema and chronic bronchitis can co-exist*

**Age (years):**
- 40-45 (bronchitis)
- 50-75 (emphysema)
Bronchiectasis

• Permanent dilation of bronchi & bronchioles due to loss of muscle & elastic support tissue

• Typically affects lower lungs

• Secondary to repeated infection which leads to chronic inflammation and tissue damage

• Frequent infections due to immunodeficiency, and impaired drainage of secretions

• Symptoms: Cough and copious quantities of purulent sputum (often spotted with blood). If diffuse, causes hypoxemia, hypercapnia and pulmonary hypertension
II. Restrictive Lung Disease

- Characterized by reduced lung compliance (i.e., more work to expand lungs)

- Types:
  - Normal lungs but other condition restricts expansion (obesity, neuromuscular disease)
  - Acute or chronic lung disease leading to abnormally rigid alveolar walls (edema, fibrosis)

We will discuss two types of restrictive lung disease:

- Acute (Adult) Respiratory Distress Syndrome (ARDS)
- Chronic Restrictive Lung Disease (Pneumoconiosis)
ARDS

**Adult Respiratory Distress Syndrome**

- Acute, diffuse alveolar & capillary damage and edema
- Symptoms: Severe respiratory distress, shortness of breath, gasping for air, hypoxemia, hypercapnia
- Mechanical ventilation required, mortality high (66%)
- Many causes

**IRDS = Infant Respiratory Distress Syndrome**

- due to deficiency in surfactant (premature baby)
# Box 8-1 Common Causes of Adult Respiratory Distress Syndrome (ARDS)

<table>
<thead>
<tr>
<th>Shock</th>
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<tr>
<td>Trauma</td>
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<tr>
<td>Burns</td>
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<tr>
<td>Acute cardiac failure</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Bacterial</td>
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<tr>
<td>Viral</td>
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<tr>
<td>Toxic lung injury</td>
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<tr>
<td>Toxic fumes</td>
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<tr>
<td>Cytotoxic drugs</td>
</tr>
<tr>
<td>Bacterial endotoxins</td>
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<tr>
<td>Aspiration of fluids</td>
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<tr>
<td>Near-drowning</td>
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</tbody>
</table>
Regardless of the initial injury (epithelial or endothelial), established lesions appear identical and are characterized by fibrin-rich hyaline membranes, ruptured alveolar walls and intra-alveolar edema fluid.
Figure 8-21
Adult respiratory distress syndrome (ARDS). The sequence of events may begin with an endothelial cell or an alveolar cell injury. Regardless of the initial injury, progression of the disease leads to a common pathway and respiratory failure.
ARDS

- Lag phase: lasts 4-24 hours, no symptoms

- Acute phase: lasts ~ 1 week
  - Extensive damage to alveoli and capillaries due to inflammatory response
  - Hyaline membrane formation in alveoli, loss of surface area, lung collapse……appear airless
  - Chemical mediators may enter circulation and cause multi-organ failure

- Repair phase:
  - 1/3 of patients die within days, 1/3 die of pneumonia and heart failure within weeks, and 1/3 recover
  - 40% of patients that recover have permanent respiratory problems related to alveolar wall fibrosis
Chronic Restrictive Lung Diseases

- Interstitial lung disease, interstitial pulmonary fibrosis
- Inflammation of alveolar wall (alveolitis) leads to progressive fibrosis
- Reduced FEV1 and forced vital capacity so, FEV1/FVC not reduced
- Converts lung to mass of air spaces separated by scar tissue e.g. honey comb lung
Chronic Restrictive Lung Diseases

NORMAL LUNG

Honeycomb lung

Honeycomb LUNG
Chronic Restrictive Lung Diseases

• Symptoms: Gradual onset of dyspnea, dry cough, and tachypnea.

• Hypoxia ➔ peripheral capillary swelling and increased connective tissue formation ➔ finger tip clubbing

• Ultimately pulmonary hypertension, heart failure and death

• Treatment: Anti-inflammatory, supplemental oxygen, lung transplant
Pneumoconioses

- Interstitial lung diseases caused by inhalation of dust, fumes, organic and inorganic particulate matter

- Pathogenesis:
  - Particles reaching alveoli ingested by macrophages
  - Induces an inflammatory response and fibrosis
  - Extent of injury depends on the following:
    - Duration of exposure
    - Concentration of particles
    - Particle size, shape and solubility
    - Biochemical composition of the inhaled material
- macrophages killed by ingesting toxic silicon dioxide (1-3 microns in size)

- damaged macrophages release silica crystals, cytokines and growth factors that stimulate fibroblasts to produce collagen

- collagen nodules containing silicon dioxide are prominent along the lymphatics draining toward the hilar lymph nodes

- silicosis rarely occurs in an isolated form.....more common is anthracosilicosis (black nodules).....carbon and silicon

- fibrotic response is incapacitating, but it does not predispose the patient to cancer
Pneumoconioses

Silicosis:

- Collagen fibers
- Cleft-like spaces containing silica particles
- Compressed alveoli
- Capillary congestion
Pneumoconioses

Coal workers lung disease (CWLD):

- “black lung” or anthracosis, macrophages ingest carbon particles leading to inflammation and areas of fibrosis

- particles are deposited in the centrilobular zones of the lung and may be associated with centriacinar emphysema

- no effective treatment

- the disease does not predispose the patient to cancer

- modern well-ventilated mines and the use of protective masks have greatly reduced the incidence of CWLD
Pneumoconiose

Coal workers lung disease (CWLD):

Simple coal worker's pneumoconiosis

Progressive massive fibrosis in a coal miner
Pneumoconioses

- fibers activate macrophages which secrete cytokines and growth factors that induce pulmonary fibrosis and pleural plaques. *May progress to lung cancer or mesothelioma* and smoking increases the risk 50x

Asbestosis:

- fibrous tissue contains beaded bodies with knobbed ends called asbestos bodies which are coated with macrophage-derived proteins that store iron (ferritin and hemosiderin) and appear brown (ferrugenous bodies); only 1 in 10 fibers are iron-coated, so majority of asbestos fibers appear invisible under the light microscope

- presence of asbestos best demonstrated by chemical analysis following incineration of lung tissue
Pneumoconioses

Asbestosis:

Asbestos bodies

Asbestos fiber
Macrophage
Asbestos body
Collagen
Pleura
Interstitial fibrosis
Fibrous plaque
Mesothelioma
Lung cancer
Asbestosis:

There is a mistaken impression that asbestos has been completely banned from use, but millions of asbestos products still remain on auto parts shelves and on vehicles in use today.
III. Pulmonary Infections

- Upper respiratory tract (URI)
- Pneumonia
- Tuberculosis
Upper respiratory tract infections (URIs or URTIs)

- Acute inflammation of nose, sinuses, throat, larynx
- Mostly viral (rhinoviruses cause colds; influenza viruses cause flu)
- Cell infiltrates: lymphocytes, monocytes, plasma cells

Symptoms:
- Congestion, rhinorrhea, sore throat, malaise, fever
- Purulent (neutrophils) discharge and/or sinus/ear pain indicate secondary bacterial infection (typically staphylococcus or streptococcus)

- Resolve spontaneously (few days to 1-2 weeks) unless bacterial complication (requires antibiotics)......*Remember: Streptococcal infections can lead to rheumatic heart disease (review your notes)
Upper respiratory tract (URIs)

* Numerous interconnections...easy spread of infection

**Figure 8-4**
Acute upper respiratory infection typically affects the nose and the nasopharynx, but it may spread into the middle ear, paranasal sinuses, or tracheobronchial tree.
• Inflammation of lungs

• Mostly due to infection, sometimes chemicals

• 6th most common cause of death

• Pneumonia risk factors:
  - immunodeficiency (AIDS, cancer)
  - hospitalization (5/1000 admissions)
  - age (very young and old at risk; “old man’s friend”)

• Organisms contracted via:
  Direct inhalation
  Seepage of secretions from URI
  Circulation
  Aspiration of gastric contents
• Types of pneumonia:

*Bronchopneumonia
- affects specific bronchi and associated alveoli

*Lobar pneumonia
- affects whole lobe and begins with an acute alveolitis
- 4 stages:
  • (Day 1) congestion - blood vessel engorgement, voluminous lung
  • (Day 2-4) red hepatization - resembles liver tissue as airspace fills with red and white blood cells & fibrin
  • (Day 4-6) grey hepatization - still resembles liver tissue but red cells disintegrate
  • (Day 7-9) resolution - exudate is digested by enzymes and cleared by macrophages and/or coughing

*Both characterized by consolidation (solidification)
Bronchopneumonia

*consolidation = filled with liquid rendering the lung hard to the touch

Figure 8-8
Histologic appearance of bronchopneumonia. The bronchus and the surrounding alveoli contain polymorphonuclear leukocytes.
Lobar Pneumonia

- Pulmonary fissure
- Consolidation of whole lobe
- Airways not centre of inflammation
Atypical Pneumonia

- Interstitial
- Inflammation affects alveolar walls (no consolidation)
- Mostly caused by viruses and mycoplasma
- Mycoplasma are very small bacteria lacking a cell wall and hence, are unaffected by common antibiotics (e.g., penicillin)

****NOTE: Mycoplasma should not to be confused with “mycobacteria” which have a thick cell wall and can cause tuberculosis and leprosy
Pneumonia

Clinical manifestations

- **Bacterial**: most serious
  - fever, chills, coughing with expectoration, chest pain, dyspnea, tachypnea

- **Viral**: less serious
  - fever, dry cough, headache, muscle pain, weakness, breathlessness

- **Mycoplasma**: generally mild ("walking pneumonia")
  - violent coughing, sparse whitish mucus, may be associated with longterm profound weakness
Pneumonia

Complications:
- Abscess formation; Empyema (pus in pleural cavity); Fibrosis; Organismal spread leading to meningitis or endocarditis

Bacterial agents (75% of cases):
- *Streptococcus pneumoniae* (causes pneumococcal pneumonia, community acquired, typically lobar)
- *Haemophilus influenzae* (community acquired). Mistaken as the cause of influenza until 1933 when the causative agent was shown to be a virus
- *Pseudomonas aeruginosa* (nosocomial - hospital acquired)
- *Legionella pneumophila* (Legionnaires disease, nosocomial)
Pneumonia

Other agents (25% of cases):

- Viruses: influenza (flu), varicella (chickenpox), cytomegalovirus (herpes)
- Fungi: aspergillus, cryptococcus, candida, *Pneumocystis jirovecii* (old nomenclature: *carinii*) is associated with AIDS
- Mycoplasma: *Mycoplasma pneumoniae*
Tuberculosis (TB)

- Causative agent is *Mycobacterium tuberculosis*.
- 1.7 billion infected, 3 million deaths/year world wide
- Risk factors: AIDS, poverty, over crowding, old age
- Organism is resistant to destruction leading to Type IV hypersensitivity (delayed cell-mediated response not mediated by antibody)

Extensive caseous necrosis and cavitation. Patient is highly infectious.
Tuberculosis (TB)

- **Primary TB**
  - infection occurs in someone not previously exposed to the tubercle bacillus
  
  - “Ghon complex” (Anton Ghon (1866-1936) an Austrian pathologist): Two parts - a) single lesion in the lung parenchyma, usually subpleural and b) a lesion in the hilar lymph nodes draining that part of the lung
  
  - patient is usually asymptomatic; cell-mediated immunity develops over 3-6 weeks
  
  - 90% of patients have spontaneous lesion healing with collagen deposition (viable bacteria may still be present)
  
  - 10% of patients (e.g., immunocompromised patient) exhibit progressive primary TB. Lesion erodes and bacilli spread
Tuberculosis (TB)

**Figure 8-10**
The Ghon complex, typical of pulmonary tuberculosis, consists of a parenchymal focus and hilar lymph node lesions. The detailed section of the diagram shows the typical features of tuberculous granuloma: central caseous necrosis surrounded by epithelioid cells, multinucleated giant cells, and lymphocytes.
Secondary TB

- Reactivation of dormant, endogenous tubercle bacilli or reinfection with exogenous bacilli
- Typically starts at apex of lung
  - Good immune response: limited granuloma formation, spread of organism prevented
  - Poor immune response: large granuloma formation, tissue destruction leads to spread of infection
Secondary Tuberculosis (TB)

**LYMPHATIC SPREAD**
A. Pleural surface  
B. Lung parenchyma  
C. Contralateral lung

**HEMATOGENOUS SPREAD**
Meningitis  
Tuberculosis of urogenital tract  
Bone tuberculosis

**SPREAD THROUGH AIRWAYS**
A. Bronchial spread in the same lung  
B. Spread to the larynx  
C. Aspirated TB swallowed into the esophagus leads to intestinal TB

**Figure 8-11**
Spread of tuberculosis (TB). Reactivated bacilli can spread through the lymphatics, blood vessels, or bronchi. Hematogenous spread usually accounts for tuberculosis in distal sites, such as the urogenital tract or the brain. Expectorated bacilli may be swallowed and cause intestinal tuberculosis.
Symptoms: Dry cough, fever, malaise, night sweats, weight loss. Hemoptysis and dyspnea if wide spread.

Diagnosis: TB skin test (tuberculin protein elicits red induration when sensitized lymphocytes respond), chest X-ray, bacterial sputum test

Treatment: Anti-bacterials (e.g., rifater, rifapentine) for several months. Successful treatment requires complete patient compliance to prevent drug resistance
Tuberculosis (TB) Stages

1) Primary TB occurs in a person lacking previous contact or immune responsiveness; 90% patients heal and recover

2) Progressive primary TB affects ~10% of patients

3) Secondary TB results from reactivation of dormant endogenous bacilli or reinfection with exogenous bacilli

4) Miliary TB is the dissemination of tubercle bacilli to distant organs
IV. Neoplasms

Neoplasm = abnormal tissue mass arising from neoplasia (new growth, abnormal cell proliferation)

- Lung carcinoma is the primary cause of cancer death
- Peak incidence 55-65 yrs
- Causes: smoking (87%), radon gas (12%) and industrial carcinogens (e.g. asbestos (1%))

- 4 Major Types arising from epithelia (70% bronchial and 30% peripheral airway/alveolar)

  Squamous cell carcinoma
  Adenocarcinoma
  Large anaplastic cell carcinoma
  Small-cell carcinoma (oat cell)

  Non-small cell
Most tumors originate from bronchi and are caused by smoking.

- Malignant tumors composed of mucous or ciliated cells are classified as adenocarcinomas.
- Malignant tumors composed of dedifferentiated (anaplastic) neuroendocrine cells; classified as small cell carcinomas.
- Large cell carcinomas originate from stem cells that have never differentiated into any other cell type.
Squamous cell carcinoma

- Accounts for 25-30% of cases and occurs more often in men than women
- Strongly associated with smoking
- Tobacco smoke carcinogen induces bronchial epithelium to become metaplastic and develop squamous epithelium
- Centrally located and associated with pulmonary symptoms of obstruction (collapse, re-current infection, and ulceration)
- Good surgical candidate
Adenocarcinoma

- Most common type, 30-35% of cases
- Most common type in women, non-smokers, <45 yrs
- Associated with smoking but not as strongly as squamous cell carcinoma
- Ciliated or mucus secreting epithelial cells form irregularly shaped glands
- Typically occurs in a peripheral location, particularly at sites of scar tissue
- Grows slowly but metastasizes quickly
Large cell anaplastic carcinoma

- Accounts for approximately 10-15% of cases
- Origin: Have very poorly differentiated large cells which may have derived from metaplastic squamous epithelium or may represent an anaplastic adenocarcinoma
- May have central or peripheral location
- Poor prognosis

Poorly differentiated epithelial lung tumor
Small cell carcinoma

- SCLC or oat cell carcinoma
- Accounts for approximately 20-25% of cases, more often in men than women
- Strongly associated with smoking
- Origin: neuroendocrine cells of bronchial epithelium. Neoplasm has many small dark oval cells resembling oat grains
- Centrally located and so associated with pulmonary symptoms of obstruction
- Highly metastatic
Pulmonary Neoplasms

Genetic abnormalities:

SCLC : loss of Rb-1, p53, activation of myc
Non-SCLC : loss of Rb-1, p53, activation of ras

Rb-1 - retinoblastoma protein (tumor supressor)
p53 - protein 53 (tumor supressor)
myc - transcription factor and its mutation can lead to persistent expression and unregulated gene expression
ras - small GTPase involved in transmitting signals from outside the cell and into the nucleus. Its mutation can lead to persistent and unregulated gene expression
Clinical presentation

- **Pulmonary**: cough, hemoptysis, dyspnea, chest pain, wheezing
- **General**: weight loss, anorexia (loss of appetite), malaise
- **Metastases**: present in 70% patients at diagnosis
  - favored sites: adrenals, liver, brain, bone, kidney
Pulmonary Neoplasms

• Diagnosis: history & clinical presentation, imaging, histological examination of sputum, pleural fluid, needle aspiration biopsy

• Staging

Non-SCLC - TNM system and Staging (I-IV)
SCLC - limited (one lung, lymph nodes on same side) or extensive (both lungs, lymph nodes on both sides, other tissues)
TNM System

Primary Tumor (T)
• TX Primary tumor cannot be evaluated
• T0 No evidence of primary tumor
• T Carcinoma in situ (early cancer, no spread to adjacent tissue)
• T1, T2, T3, T4 Size and/or extent of the primary tumor

Regional Lymph Nodes (N)
• NX Regional lymph nodes cannot be evaluated
• N0 No regional lymph node involvement
• N1, N2, N3 Involvement of regional lymph nodes (number and/or extent of spread)

Distant Metastasis (M)
• MX Distant metastasis cannot be evaluated
• M0 No distant metastasis
• M1 Distant metastasis
Staging

- Stage 0: Carcinoma *in situ* (early cancer that is present only in the layer of cells in which it began)

- Stage I, Stage II, and Stage III: Higher numbers indicate more extensive disease: greater tumor size, and/or spread of the cancer to nearby lymph nodes and/or organs adjacent to the primary tumor

- Stage IV: The cancer has spread to another organ

- Stage Groupings combined with TNM system examples: Stage I - T1N0M0; Stage IV - any M1
Pulmonary Neoplasms

- Treatment: surgical resection, radiation therapy, chemotherapy
- Prognosis (% survival at 5 years)
  - Non-SCLC: 50% (no metastases at diagnosis)
    15% (if metastases at diagnosis)
  - SCLC: 10% limited
    2% extensive
Carcinoma of larynx

• 2% of all cancer cases, men > women, and linked to smoking and alcohol

• Origin: Squamous epithelium of the larynx becomes dysplastic then carcinoma in situ (non-invasive), then carcinoma (invasive)

• Symptoms: Hoarseness for >2 wks, loss of voice, noisy respiration

• Diagnosis: History and clinical presentation, imaging, histology from needle aspiration/biopsy and staged by TNM

• Treatment: surgical resection, radiation, chemotherapy. 75% 5 year survival
V. Pleural Disease

• Pleuritis

- Inflammation of the pleura

- Any fluid accumulating in pleural cavity is referred to as pleural effusion

- If the fluid is very watery then the term hydrothorax is used

- Accumulation of fluid prevents complete lung expansion during inspiration
V. Pleural Disease

• Neoplasms

  - **Mesothelioma**: affects pleural mesothelium. Rare but malignant neoplasm related to asbestos or solvent exposure. Very poor prognosis.

  - **Metastatic tumors** – from ovarian, breast carcinoma
### Obstructive Pulmonary Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Etiology</th>
<th>Symptoms</th>
<th>Pathogenesis</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **Asthma**        | - Obstruction: bronchospasm, edema, mucous   | Dyspnea, cough, wheeze    | - Initial response: vasodilation, vascular leakage, smooth muscle spasm     | - Identify triggers - Quick relief (drugs to relax airway) - Drugs: Beta-2 agonists - Anti-inflammatory drugs (steroids) **No cure, just management! |}
|                   | - Chronic inflam. Leading to hyper-responsiveness |                           | - late-phase: mucosal edema, mucus secretion, leukocyte infiltration, epith. Damage, bronchospasm |                                                                           |
|                   | - Extrinsic (type I hypersensitivity)         |                           |                                                                           |                                                                           |
|                   | - Intrinsic: infection, drugs, etc            |                           |                                                                           |                                                                           |
| **Emphysema**     | - Tobacco (98%) - Genetic (2%)                | Progressive dyspnea, weight loss, barrel chest | 1. Centriacinar (centrilobular) = upper lobe, center of lobule, most common 2. Panacinar (panlobular) = lower lobes, distal & terminal bronchioles, genetic | - Replacement enzyme therapy (only for genetic deficiency) - Stop smoking - Bronchodilators, - LVRS |
| (COPD group)      |                                               | “PINK PUFFERS”            |                                                                           |                                                                           |
| **Chronic Bronchitis** | - Smoking (90%) - Air pollution, toxic fumes, respiratory inf. (10%) - viral pneumonia predispose to chronic bronchitis | Cough, shortness of breath, right heart failure, excessive mucous production, “BLUE BLOATERS” | - walls of bronchi/bronchioles thickened, excessive mucous - histo: evidence of mucous gland hyperplasia, chronic inflame, & fibrosis | - Quit smoking |
| (COPD group)      |                                               |                           |                                                                           |                                                                           |
|                   | (may co-exist w/ emphysema)                   |                           |                                                                           |                                                                           |
| **Bronchiectasis**| - Frequent infections due to immunodeficiency, & impaired drainage of secretions - secondary → repeated infection | - Cough, copious quantities of purulent sputum - if diffuse: cause hypoxemia, hypercapnia & pulmonary hypertension | - permanent dilation of bronchi & bronchioles due to loss of muscle and elastic support tissue - lower lungs | -antibiotics for infections -physical therapy to loosen mucous |
| (COPD group)      |                                               |                           |                                                                           |                                                                           |
Restrictive Lung Disease

- reduced compliance of the lungs

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| **ARDS** (Acute Respiratory Distress Syndrome) | - fibrin-rich hyaline membranes, ruptured alveolar walls and intra-alveolar edema fluid
- diffuse alveolar & capillary damage & edema | Severe respiratory distress, shortness of breath, gasping for air, hypoxemia, hypercapnia         | - Lag phase: 4-24 hrs
- Acute phase: ~ 1wk
- Repair phase: 1/3 die w/n days, 1/3 die w/n wks, 1/3 recover                                      |
| **Chronic Restrictive Lung Disease** (honey comb lung) | - inflammation of alveolar wall (alveolitis) leads to progressive fibrosis
- interstitial lung disease
- FEV1 and FVC reduced but FEV1/FVC normal | - dyspnea, dry cough, clubbing of digits, tachypnea
- pulmonary hypertension, heart failure, death | - Anti-inflammatories
- supplemental oxygen
- lung transplant                                                                                   |
| **Pneumoconioses**          | - occupational & restrictive caused by inhalation of dust, fumes, particulate matter | Induce inflammatory response & fibrosis
- Asbestosis: could progress to lung cancer
- CWLD: simple or progressive (fibrosis) | - CWLD (black lung) no effective treatment, does not predispose patient to cancer                  |
### Pulmonary Infections

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
<th>Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper respiratory Tract</strong></td>
<td>- Acute inflammation of nose, sinuses, throat, larynx</td>
<td>- Congestion, rhinorrhea, sore throat, malaise, fever - purulent discharge = secondary bacterial infection</td>
<td>-Resolves spontaneously (days-wks) - if bacterial inf. requires antibiotics</td>
</tr>
<tr>
<td><strong>Pneumonia</strong></td>
<td>- Inflammation of lungs - due to infection (chemicals) - 2 Types: (both have consolidation) Bronchopneumonia &amp; Lobar pneumonia -Atypical form (no consolidation) → interstitial, caused by viruses &amp; mycoplasma</td>
<td>- <strong>Bacterial: (most serious)</strong> fever, chills, coughing, chest pain, dyspnea, tachypnea - <strong>Viral</strong>: fever, dry cough, headache, muscle pain, weakness, breathlessness - <strong>Mycoplasma</strong>: (mild) violent coughing, sparse white mucus, assoc. w/ long term weakness</td>
<td></td>
</tr>
<tr>
<td><strong>Tuberculosis</strong></td>
<td>- type IV hypersensitivity, chronic inflame., granuloma formation -primary &amp; secondary forms</td>
<td>- <strong>Primary</strong>: <strong>Asymptomatic</strong>, (inf. not previously exposed to organism) - <strong>Secondary</strong>: activation of dormant infection (most common cause) of new infection</td>
<td>- Primary: spontaneous lesion healing w/ collagen deposition, no healing (immunocompromised pat.) - Secondary: w/ good immune = limited granuloma form., spread of organism prevented. Poor immune = large granuloma form., tissue destruction leads to spread of infection</td>
</tr>
</tbody>
</table>
Pulmonary Neoplasms

- Carcinoma of Lung = most common cause of cancer death
- Non-SCLC: 50% 5 yr survival w/ no metastases, 15 % survival if metastases at diagnoses

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<tr>
<td>Squamous cell carcinoma</td>
<td>- 25-30% of cases, men &gt; women&lt;br&gt;- assoc. w/ smoking&lt;br&gt;- Centrally located &amp; assoc. w/ pulmonary symp. of obstruction</td>
<td>- smoke carcinogen induces bronchial epithelial to become metaplastic and dev. squamous epith.</td>
<td>- Good surgical canidate</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>- most common type, 30-35% (women, non-smokers)</td>
<td>- ciliated or mucus secreting cells from irregularly shaped glands&lt;br&gt;- occurs in peripheral locations @ scar tissue</td>
<td>- grow slow → metastizes quickly</td>
</tr>
<tr>
<td>Large anaplastic cell carcinoma</td>
<td>- 10-15% cases&lt;br&gt;- may have derived from metaplastic squamous epith., or may represent an anaplastic adenocarcinoma</td>
<td>- central or peripheral location</td>
<td>- poor prognosis</td>
</tr>
<tr>
<td>Small-cell carcinoma (oat cell)</td>
<td>- 20-25%, men &gt; women&lt;br&gt;- assoc. w/ smoking</td>
<td>- centrally located, assoc. w/ pulmonary symp. Of obstruction&lt;br&gt;- origin: neuroendocrine cells of bronchial epith.</td>
<td>- highly metastatic&lt;br&gt;- worst to get (10% survival rate if 1 lung, or 2% survival w/ both lungs)</td>
</tr>
<tr>
<td>Carcinoma of Larynx</td>
<td>- 2% of all cancer cases&lt;br&gt;- men &gt; women&lt;br&gt;- linked to smoking &amp; alcohol&lt;br&gt;- Origin: squamous epithelium of larynx becomes dysplastic → carcinoma</td>
<td>- hoarseness for &gt;2wks, loss of voice, noisy respiration</td>
<td>- surgical resection, radiation, chemotherapy&lt;br&gt;- 75% 5 yr survival</td>
</tr>
</tbody>
</table>
### Pleural Disease

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</table>
| **Pleuritis** | - inflammation of the pleura  
- any fluid accumulating in pleural cavity = pleural effusion  
- if fluid is watery = hydrothorax | Accumulation of fluid prevents complete lung expansion during inspiration |
| **Neoplasms** | - Mesothelioma: rare but malignant neoplasm, related to asbestos or solvent exposure  
- Metastatic tumors: from ovarian, breast carcinoma | - Mesothelioma: Poor prognosis |