1. Respiratory System I: Slide 1

Respiratory System  
Part 1  
Basic Human Pathology II, 2008

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2. Respiratory System Diseases

Respiratory System Diseases

Part 1  
- Respiratory failure / chronic hypoxemia  
- Atelectasis  
- Vascular and Hemodynamic Diseases  
- Infective disease  
- Infective / obstructive disease  
- Chronic obstructive disease

Part 2  
- Restrictive Pulmonary Disease  
- Neoplastic Disease in Lungs  
- Pathology of the Pleura  
- Lung Disease in Children

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3. Respiratory System

Respiratory System

- Introduction
  - Upper respiratory tract
    - Airways
    - Lungs
  - Main disease causes
    - Infection / inflammation
    - Exposure to environmental agents (e.g., smoke, dust)
    - Carcinoma

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4. Bronchi and Bronchioles

Bronchi and Bronchioles

- Bronchi and bronchioles can be separated histologically by the absence of cartilage in bronchioles

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5. Normal Distal Lung Acinus

Normal Distal Lung Acinus

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6. Normal Microscopic Structure of the Alveolar Wall

Normal Microscopic Structure of the Alveolar Wall

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7. Normal Lung – Cut Surface

Normal Lung – Cut Surface

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8. Normal Alveoli

Normal Alveoli

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9. **Respiratory System**

**Respiratory System**

- **Normal**
  - Blood gases within physiological limits
    - Normal PaO₂ is between 10.7 kPa – 3.3 kPa (80-100 mmHg)
    - Normal PaCO₂ is between 5.7 kPa – 6.0 kPa (35-45 mmHg)
- **Respiratory failure**
  - When PaO₂ falls below 8 kPa (60 mmHg)
  - Types of respiratory failure:
    - Type 1
      - PaO₂ is low but PaCO₂ is within normal range
    - Type 2
      - PaO₂ is low AND PaCO₂ is raised (above 6.7 kPa = 50 mmHg)

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10. **Respiratory System**

**Respiratory System**

- **Respiratory failure - cont’d**
  - Blood gas analysis
    - **Central cyanosis** (PaO₂ less than 6.7 kPa with normal hemoglobin level)
    - **Low PaO₂ alone** means a mismatch between ventilation and perfusion but alveolar ventilation is normal
    - **Hypoxia** (inadequate oxygenation of blood in lung) seen in pulmonary collapse and lung consolidation
    - **Hypoxemia** without hypercapnia because of failure of diffusion of gas due to thickening of alveolar septa

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11. Respiratory System

Respiratory System

- **Causes of respiratory failure**
  - Failure of ventilatory drive
    - e.g. depression of respiratory center
  - Upper airway obstruction
  - Diseases of the lung
    - preventing normal gas exchange
  - Mechanical impairment of ventilation
    - e.g. massive rib fracture, diseases of muscle

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12. Respiratory System

Respiratory System

- **Consequences of chronic hypoxemia:**
  - **Pulmonary hypertension**
    - Pulmonary vasoconstriction $\rightarrow$ increased pulmonary artery pressure and increased work of the right ventricle $\rightarrow$ right ventricular hypertrophy
    - Over time, pulmonary arteries develop intimal proliferation and occlusion of lumina
  - **Polycythemia**
    - Due to stimulation of erythropoietin released from the kidney
    - $\rightarrow$ increased blood viscosity and increased risk of thrombosis

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13. Atelectasis

Atelectasis

- “Collapse of the lung”
- Causes
  - Obstruction of the airway with resorption of air from the lungs distal to the obstruction
  - Compression of the lung when fluid or air accumulates in the pleural cavity
  - Scarring in the lung may cause contraction of parenchyma and collapse
  - Loss of normal surfactant from terminal air spaces leads to generalized failure of lung expansion (i.e., microatelectasis)

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14. Atelectasis

Atelectasis

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15. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- **Pulmonary edema**
  - Due to an increase of fluid in alveolar wall (interstitium)
  - **Main cause is failure of the left ventricle** -> increased hydrostatic pressure in the alveolar capillaries and increased alveolar capillary permeability -> fluid into pulmonary interstitium -> increase fluid flow into pulmonary lymphatics -> increased stiffness of lungs -> subjective dyspnea
  - May remain stable for a long time

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16. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- **Pulmonary edema – cont’d**
  - In severe left ventricular failure, then fluid also leaks into alveolar spaces -> severe acute impairment of respiratory function
  - **Capillary rupture** -> leakage of RBCs into interstitium and alveoli -> hemoglobin phagocytized by macrophages that thus gather iron pigment (aka heart failure cells)

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17. **Pulmonary Edema and Heart Failure Cells**

   - **Pulmonary Edema and Heart Failure Cells**
     - Tense, shiny external surface
     - Alveolar spaces contain macrophages with brown hemosiderin content

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18. **Vascular and Hemodynamic Diseases of the Lung**

   - **Vascular and Hemodynamic Diseases of the Lung**
     - **Pulmonary hypertension**
       - Increased pulmonary arterial pressure -> irreversible structural changes in pulmonary arteries -> increased work of right side of heart and right heart failure (cor pulmonale)
       - Most important causes of pulmonary hypertension
         - Chronic obstructive pulmonary disease (COPD)
         - Fibrosis of the lungs
         - Chronic pulmonary venous congestion
         - Increased pulmonary blood flow
         - Increased blood viscosity

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19. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- Pulmonary hypertension - cont’d
  - Structural changes:
    - Long-standing cases
      - Medial hypertrophy in muscular arteries (increase of smooth muscle) and pulmonary veins (i.e., arterialization)
    - Severe long-standing cases
      - Pulmonary arterial wall produces calcified atherosclerotic plaques in the main pulmonary arteries (e.g., untreated patent ductus arteriosus)

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20. Pulmonary Hypertension Morphologic Changes

Pulmonary Hypertension Morphologic Changes

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A = normal pulmonary muscular artery with internal elastic lamina (IEL) and external (EEL)
B = intimal hyperplasia (arrow) and medial hypertrophy (mild to moderate hypertension)
C = advanced pulmonary hypertension with plexiform lesion (aneurysmal disruption of wall [arrow] with secondary thrombus and recanalization)

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21. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- Pulmonary hypertension – cont’d
  - Net result
    - Occlusion of lumen of pulmonary arteries with prominent heart failure cells
    - Fibrosis of the lung’s interstitium
  - Net clinical effects
    - Breathlessness
    - Development of right-sided cardiac failure

22. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- Pulmonary embolism
  - Most arise as thrombi in deep leg veins and pass in the venous circulation to right side of heart – → lodge in pulmonary arteries
  - Pulmonary infarction
    - Hemorrhagic or ‘red’ infarcts
    - Only about 10% of all emboli result in infarction, because the dual blood circulation to the lungs protects against ischemic necrosis
    - Clinical consequences - variable
      - Asymptomatic
      - Massive coiled pulmonary embolus is impacted in a main pulmonary artery then – → acute right heart failure and death
23. Emolus

Emolus

- Large saddle embolus (arrow) from the femoral vein lying astride the main left and right pulmonary arteries

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24. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- Pulmonary embolism
  - Occurs in clinical settings marked by venous stasis (primary venous disease, congestive heart failure, prolonged bed rest or immobilization, and prolonged sitting while traveling)
  - Rarely due to nonthrombotic particulate material
  - Predisposed by
    - cancer - embolization of clumps of tumor cells
    - fractures - fat, bone marrow emboli
    - childbirth - amniotic fluid embolism
    - foreign material such as bullet fragments

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25. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- **Pulmonary infarction**
  - Gross
    - Hemorrhagic infarcts because of blood entering from the bronchial circulation
    - Wedge-shaped infarcts with associated pleurisy (chest pain)
    - Infarcts → over time → fibrous scar
  - Microscopic
    - Thromboembolism → extravascular blood in a necrotic lung (causes clinical hemoptysis)

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26. Pulmonary Infarction

Pulmonary Infarction

\[ a = \text{Hemorrhagic wedge-shaped infarct with pleurisy (P)} \]
\[ b = \text{Infarct caused by thromboembolism (E) has extravasation of blood into necrotic lung (N)} \]

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27. Hemorrhagic Pulmonary Infarct

Hemorrhagic Pulmonary Infarct

- Small, recent, hemorrhagic pulmonary infarct (roughly wedge-shaped)

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28. Red Infarcts Due to Thromboembolism

Red Infarcts Due to Thromboembolism

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29. Pulmonary Infarction

Pulmonary Infarction
due to thromboembolus

30. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

- Pulmonary vasculitis (angiitis)
  - Cellular infiltration of pulmonary blood vessels leading to necrosis of pulmonary parenchyma
- Examples:
  - necrotizing vasculitis
  - Wegener's granulomatosis (nose, lung, kidney)
  - Churg-Strauss syndrome (eosinophils infiltrate lung)
31. Vascular and Hemodynamic Diseases of the Lung

Vascular and Hemodynamic Diseases of the Lung

❖ Review of key facts
  - Pulmonary edema is most commonly caused by left ventricular failure
  - Pulmonary hypertension causes right-sided heart failure
  - Pulmonary thromboembolism is most commonly from deep leg vein thrombosis
  - Large pulmonary emboli cause acute right heart failure and death

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32. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

• Upper respiratory tract infections are common in western world
  - Nose, pharynx, trachea, bronchi
  - Most minor and transient
• Lower respiratory tract infections are serious cause of morbidity and mortality
  - Bronchus to alveoli

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33. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Infection of bronchi and bronchioles
  - Extremely common
  - Most due to self-limiting viral diseases
    - Examples:
      - influenza - tracheobronchitis with necrosis of lining epithelium
      - respiratory syncytial virus - bronchiolitis in the very young
      - adenovirus and measles virus - severe inflammation of bronchioles
      - fibrosis - permanent oblitative bronchiolitis

- Bacterial diseases - common
  - Precedes development of bronchopneumonia
  - Example:
    - bordetella pertussis (whooping cough) associated with bronchial and bronchiolar inflammation

34. Acute Bronchitis

Acute Bronchitis

- Gross appearance
  - Airway mucosa is red and edematous
  - Overlying mucoid purulent exudate
  - Rarely, destruction and scarring of airways can occur

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35. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Pneumonia
  - Infective inflammation and consolidation of the lung
  - One of the most common infective conditions
  - 5th most common cause of death in U.S.

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36. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Pneumonia - cont’d
  - Classification
    - Pathological - how it spreads
      - Bronchopneumonia
      - Lobar pneumonia
    - Microbiological - what caused it
      - Cause of organism
    - Clinical - circumstances of development
      - Community-acquired
      - Hospital-acquired (nosocomial)
      - Acquired in special environments
      - Immunosuppressed patients
      - Aspiration pneumonia

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37. Infective Disease of the Respiratory System

**Infective Disease of the Respiratory System**

- **Bronchopneumonia**
  - Acute bacterial pneumonia centered on bronchi that spreads --> adjacent alveoli --> filled with acute inflammatory exudate --> affected areas consolidated (first patchy within lung lobules, then if not treated, confluent (lobes))
  - Causative organism depends on circumstances predisposing to infection
    - Staph. aureus, Haemophilus, Klebsiella, and Strep. pyogenes
  - Gross
    - Affected lung is firm, airless, dark red or gray appearance
    - Pus may be present in the peripheral bronchi

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38. Bronchopneumonia

**Bronchopneumonia**

- Bronchopneumonia – cut surface shows pale areas in lower lobe = consolidation

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39. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Bronchopneumonia - cont’d
  - Histology
    - Acute inflammation of the bronchi; alveoli contain acute inflammatory exudate
    - Pleura often involved → pleurisy
  - If treated, then focal organization of lung by fibrosis
  - Common complications
    - Lung abscess
    - Pleural infection (pleurisy – pleuritis) – patchy white fibrinous exudate
    - Septicemia

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40. Bronchopneumonia

Bronchopneumonia

- Bronchopneumonia – cont’d
  - Inflammation centered on bronchi (B) spreads to alveoli (A)
  - Consolidation occurs in dependent parts of the lung

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41. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Lobar pneumonia
  - Acute bacterial pneumonia
  - Occurs when microorganisms widely colonize distal alveolar air spaces rather than bronchi
  - Rapid spread through alveolar spaces and bronchioles causes acute inflammatory exudate into air spaces
  - Especially *Strep. pneumoniae* (Pneumococcus) or *Klebsiella*
  - Gross
    - Entire lobe consolidated and airless
  - Histology
    - Alveoli filled with acute inflammatory exudate which is limited by pulmonary fissures

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42. Lobar Pneumonia

Lobar Pneumonia

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43. Lobar Pneumonia

- **Lobar pneumonia - cont’d**
  - The whole lobe is rapidly consolidated
  - Alveoli are filled with acute inflammatory exudate (E) limited by pulmonary fissures (F)

44. Infective Disease of the Respiratory System

- **Lobar pneumonia – cont’d**
  - Adults - vagrants and alcoholics; poor social and medical care
  - Usually severely ill with associated bacteremia
  - If not treated, (pre-antibiotic era) then 4 phases:
    - (1) Consolidation, (2) red hepatization (fibrinopurulent exudate and RBC), (3) gray hepatization (fibrinopurulent exudate), and (4) resolution
  - Prompt treatment:
    - Many recover with lungs returning to normal structure and function by resolution
    - In others - exudate in alveoli organizes - - -> scarring and permanent dysfunction
  - Common complications
    - Pleurisy, lung abscess, septicemia

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45. Lobar Pneumonia

Lobar Pneumonia

- Lobar pneumonia with gray hepatization; lower lobe uniformly consolidated

46. Anatomic Distribution Comparison

Anatomic Distribution Comparison

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Infective Disease of the Respiratory System

**Community-acquired pneumonia**

- Usually caused by gram-positive bacteria
  - *Streptococcus pneumoniae* - most common (~33% of cases)
  - *Haemophilus influenzae* - in children / > 60 years old / chronic obstructive disease
  - *Legionella* - (5% of cases) middle aged adults with 10% mortality
  - *Mycoplasma pneumoniae* - atypical pneumonia; about 10% of cases in persons between ages 20-60
  - *Chlamydia pneumoniae* - neonates and working adults
  - *Mycobacterium tuberculosis* - socially deprived with poor medical care

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Infective Disease of the Respiratory System

**Community-acquired pneumonia**- cont’d

- Gram-negative cases < 1%
  - *Klebsiella pneumoniae* - lobar patterns; debilitated, poor nourished
- Viral pneumonia - ~ 10%
  - Often bacterial superinfection
  - *Staphylococcus aureus* may cause a very severe pneumonia following viral infection - - - > lung abscesses
- 30% no cause identified
- If bacteremia exists then ~ 25% die

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49. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- **Hospital-acquired pneumonia (nosocomial)**
  - Mainly caused by gram-negative bacteria endotoxins
    - 60% - *Klebsiella, E. coli, Pseudomonas, Proteus, Serratia*
    - Community-acquired organisms can rarely also be involved
      - *Pneumococcus* ~ 5%
      - *Legionella* - air conditioning filters or water supplies

- **Diagnosis**
  - Bronchial lavage better due to contaminated expectorated sputum of the oropharynx

- **Infection occurs two days or more after hospitalization**
  - Incidence is ~ 5% of those admitted esp. if predisposed with old age, serious illness, cigarette smoking, decreased lung defenses (anesthesia, reduced consciousness), and mechanical ventilation in critical care units

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50. Pseudomonas Pneumonia (nosocomial)

Pseudomonas Pneumonia (nosocomial)

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- Extensive destruction of pulmonary parenchyma (arrowhead) with full-thickness fibrinoid necrosis of the arterial wall (arrow)
- Abundant bacteria (blue) invading the blood vessel wall adjacent to the lumen (asterisk)

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51. Infective Disease of the Respiratory System

Infected Disease of the Respiratory System

• Aspiration pneumonia
  – Usually due to regurgitation during episodes of unconsciousness, also due to impaired swallowing due to neuromuscular disease (e.g., stroke, motor neuron disease)
  – Typical organisms involved
    • *Fusobacterium, Bacteroides* – anaerobes
    • *Staphylococcus* and gram-negative – common in hospitals
  – Common complication
    • Lung abscess
  – Gastric acid – → chemical pneumonia – → ARDS
    • Increasing respiratory dysfunction
    • Opacification of the lungs
    • Food material excites a foreign body histiocytic response in the lung

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52. Aspiration Pneumonia

Aspiration Pneumonia

Multinucleated giant cells engulf aspirated foreign material

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53. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- **Atypical pneumonia (acute interstitial)**
  - Inflammation of alveolar septa by chronic inflammation—diffuse and patchy
    - Unlike lobar and bronchopneumonia patterns in which air spaces have inflammatory exudate
  - Causes
    - Several viruses, *Chlamydia, Rickettsia*
    - *Mycoplasma pneumoniae*—most common form; children and young adults
  - Fever, dry cough, dyspnea, no consolidation; more insidious onset; milder clinical course

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54. Normal Microscopic Structure of the Alveolar Wall

Normal Microscopic Structure of the Alveolar Wall

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55. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- **Interstitial pneumonitis**
  - Most caused by viral infection and response by lymphoid cells
  - Severe cases have damage to alveolar lining cells - - - > alveolar exudation of fibrin
  - Types of viral infections:
    - Measles
      - Formation of multinucleated giant cells
      - Inflammation of bronchioles with scarring
      - May be fatal in immunocompromised or poorly nourished
    - Cytomegalovirus
      - Self-limiting; small children; severe in immunocompromised

56. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- **Interstitial pneumonitis - cont’d**
  - Types of viral infections: - cont’d
    - Influenza
      - Rhinitis, pharyngitis, tracheobronchitis, interstitial pneumonitis
      - Usually superinfection with *Staphylococcus aureus*
      - Rarely severe pneumonitis - - - > necrosis of alveolar lining cells - - - > death
      - Causes the most number of annual deaths secondary to viral pneumonia
    - Varicella
      - Chickenpox lung
      - Military small scars in lung parenchyma
      - May be fatal in the immunocompromised
57. Interstitial Pneumonitis

Interstitial Pneumonitis

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Chronic inflammation of alveolar septae

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58. Viral Pneumonia

Viral Pneumonia

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Thickened alveolar walls are heavily infiltrated with mononuclear leukocytes

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59. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Fungal pneumonia
  - Causes destructive inflammation
  - Typically seen in immunosuppressed
    - **Candida**
      - Severe debilitated, acute inflammation; bronchopneumonia pattern
    - **Aspergillus**
      - Extensive necrosis, infarction via vessel wall invasion
    - **Cryptococcal pneumonia**
      - Immunocompromised; granulomatous inflammation with consolidation and cavitation
  - Unusual environmental exposure in healthy patients exposed to agent indigenous to a particular geographic area
    - **Histoplasmosis, coccidioidomycosis, sporotrichosis**
      - Granulomatous inflammation; fibrosis resembling TB

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60. Invasive Candidiasis in Immunocompromised Patient

Invasive Candidiasis in Immunocompromised Patient

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Pseudohyphae and budding yeasts

Organisms within wall of a pulmonary vessel

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61. Aspergillus

Areas of organizing infarction (arrow)

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62. Infective Disease of the Respiratory System

- **Immunosuppressed** – such as AIDS
  - Opportunistic infections
    - Pneumonia
      - Routine bacterial pathogens of community acquired are more severe
      - *Mycobacterium tuberculosis* or atypical mycobacteria
      - CMV, herpes simplex
      - *Candida, Aspergillus, Pneumocystis carinii* (alveoli filled with fine, foam-like material; fungus)
    - Children – lymphocytic interstitial pneumonitis of unknown cause

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63. Pneumocystis Carinii Pneumonia

**Pneumocystis Carinii Pneumonia**

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Alveoli are filled with foamy ‘cotton candy’ exudate (left) and GMS stain demonstrates cup-shaped cyst wall within the exudate (above)

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64. Infective Disease of the Respiratory System

**Infective Disease of the Respiratory System**

- **Pneumonia - key facts**
  - Lobar type spread through alveoli to involve whole lobes
  - Bronchopneumonia develops as spread from tracheobronchial infection
  - Atypical type causes predominantly interstitial inflammation
  - Different sets of organisms cause community-acquired type
  - Most common community acquired infections are due to *Strept. pneumoniae*

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65. Infective Disease of the Respiratory System

Infective Disease of the Respiratory System

- Pneumonia key facts – cont’d
  - Majority of hospital-acquired cases are due to gram-negative organisms
  - Unusual environmental exposure is a factor in psittacosis, Legionnaire’s disease, and fungal pneumonias
  - Aspiration pneumonia results in both chemical and mixed infective damage to lungs
  - Opportunistic infections affect patients with immunsuppression. Main groups include mycobacteria, viruses, fungi, and protozoa

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66. Infective / Obstructive Diseases of the Respiratory System...

Infective / Obstructive Diseases of the Respiratory System

- Bronchiectasis
  - Permanent abnormal dilatation of the bronchial tree (main bronchus, esp. base of the lungs) due to chronic infection with inflammation and necrosis of the bronchial wall
  - Most often involves the lower lobes of both lungs
  - Predisposes to infection
  - Recurrent cough and hemoptysis; expectorate copious quantities of infected purulent sputum; may lead to lung abscess
  - Recurrent episodes of chest infection common
  - Mixed flora including anaerobes

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67. Infective / Obstructive Diseases of the Respiratory System...

Infective / Obstructive Diseases of the Respiratory System

• Bronchiectasis – cont’d
  – Airways typically dilated to 5-6 times normal diameter and may contain purulent secretions
  – Pathogenesis
    • Interference with drainage of bronchial secretions
      – Obstruction by tumor or foreign body
      – Abnormal mucus viscosity (cystic fibrosis)
      – Inamotile cilia syndrome
    • Recurrent and persistent infection weakening bronchial walls
    • Chronic sinusitis with postnasal drip
    • Also idiopathic form

68. Bronchiectasis

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Cross section of lung with dilated bronchi extending almost to pleura

Lower lung lobe surgically resected; large dilated air passages (P)
69. Infective / Obstructive Diseases of the Respiratory System...

**Infective / Obstructive Diseases of the Respiratory System**

- **Bronchiectasis – cont’d**
  - Histology
    - Chronic inflammation in the wall of the abnormal bronchi; epithelium replaced by inflammatory granulation tissue (bleeds and causes hemoptysis) and squamous metaplasia with bronchial mucosa
    - May be fibrous scarring and obliteration → respiratory failure
  - Complications
    - Chronic suppuration
    - Formation of lung abscess
    - Hematogenous spread of infection (esp. brain)
    - Systemic amyloidosis

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70. Infective / Obstructive Diseases of the Respiratory System...

**Infective / Obstructive Diseases of the Respiratory System**

- **Bacterial lung abscess**
  - Cavity, 1-3 cm, containing pus surrounded by fibrosis and organizing lung
  - Predisposers
    - Infection in pulmonary infarct
    - Unresolved acute pneumonia (esp. Staph)
    - Aspiration of gastric contents
    - Bronchiectasis
  - Complications
    - Rupture into pleura → empyema, pneumothorax
    - Bacteremia → central abscess

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71. Lung Abscess – from infected area of infarction

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Cavity of lung abscess (A) filled with pus and a wall (W) of acute inflammatory granulation tissue

* Restricted use. PEIR, Dr. Peter Anderson, University of Alabama at Birmingham, Department of Pathology.

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72. Chronic Obstructive Airway Diseases (COAD)

Chronic Obstructive Airway Diseases (COAD)

• Conditions in which there is chronic limitation to airflow in the lungs
• Flow is reduced due to either:
  – increase in airway resistance (narrowing of airways)
  or
  – reduced outflow (elastic recoil of lungs lost)
• Lung function test results:
  – 1-second forced expiratory volume
    • Marked decrease
  – Forced vital capacity:
    • Decreased or normal
• Main diseases:
  – Asthma (narrowing)
  – Emphysema (loss of elastic recoil)
  – Chronic bronchitis (narrowing)

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Chronic Obstructive Airway Diseases

- COAD often contrasted with restrictive pulmonary disease in which reduced lung capacity is due to:
  - Chest wall or skeletal abnormalities such as kyphoscoliosis
  - Interstitial or infiltrative parenchymal disease

- In restrictive pulmonary diseases lung function test results:
  - 1-second forced expiratory volume
    - Reduced
  - Forced vital capacity:
    - Reduced

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Chronic Obstructive Airway Diseases

- **Asthma**
  - Most common cause of recurrent breathlessness, cough, and wheezing on expiration due to narrowing of airways
    - 5% of adults
    - 10% of children
  - Obstruction of small airways by combination of bronchospasm and mucus plugging
    - Fluctuates with time
    - Frequently partially reversible with bronchodilator drugs
Chronic Obstructive Airway Diseases

- Asthma pathogenesis – cont’d
  - Complex low-grade chronic inflammatory response in bronchial mucosa with a variety of triggers causing acute exacerbations
  - Triggers
    - Allergy – dust mites
    - Infection - viral
    - Occupational exposure
    - Drug-induced – aspirin, Beta-antagonists
    - Irritant gases – sulfur dioxide, nitric oxide, ozone
    - Psychological stress
    - Exertion
    - Cold air

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Chronic Obstructive Airway Diseases

- Asthma – cont’d
  - Most have mild disease with acute episodes of bronchospasm
    - Drug therapy
      - Beta 2 adrenergic receptor agonists and corticosteroids
  - Complications
    - If severe (chronic) then airway obstruction persists despite drug therapy: superimposed infections, chronic bronchitis, and pulmonary emphysema
    - Status asthmaticus
      - Severe, acute asthma that can last for days and does not respond to drug therapy
      - Death possible from acute respiratory insufficiency

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Chronic Obstructive Airway Diseases

- **Asthma – cont’d**
  - **Types**
    - **Extrinsic (immune)**
      - Mediated by type I hypersensitivity response involving IgE bound to mast cells
      - Begins in childhood usually in families with history of allergy
    - **Intrinsic (nonimmune)**
      - Asthma associated with chronic bronchitis, exercise- or cold-induced asthma
      - Usually begins in adult life and not associated with a history of allergy

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Chronic Obstructive Airway Diseases

- **Asthma – cont’d**
  - **Pathogenesis (structural changes)**
    - **Bronchoconstriction**
      - Increased smooth muscle (hypertrophy)
    - **Hypersecretion**
      - Hyperplasia of bronchial submucosal glands and goblet cells with plugging of airways
    - **Mucosal edema**
      - Narrowing of airways
    - **Extravasation**
      - Plasma into submucosal tissues

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79. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- Asthma - cont’d
  - Pathogenesis (structural changes) - cont’d
    - Infiltration of bronchial mucosa
      - Eosinophils, mast cells, lymphoid cells, macrophages
    - Focal necrosis
      - Airway epithelium
  - Deposition
    - Collagen beneath bronchial epithelium
  - Sputum
    - Charcot-Leyden crystals (from eosinophil derived proteins)
    - Curschmann spirals (mucus plugs from small airways with whorl-like accumulations of epithelial cells)

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80. Asthma - Structural Changes

Asthma - Structural Changes

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81. Asthma - Structural Changes

Asthma - Structural Changes

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82. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- Asthma - cont’d
  - Cellular mechanisms
    - Immune mechanisms
      - 80% of cases; type 1 hypersensitivity
    - Mast cells
      - Release histamine but antihistamines not effective in providing relief
    - T-cells
      - Release IL-5 to recruit eosinophils
    - Eosinophils
      - Migrate into the mucosa releasing many inflammatory mediators (e.g., leukotrienes, prostaglandins, thromboxane, PAF)
    - Local peptides released that cause edema and hypersecretion of mucus
    - Inflamed bronchial walls cause airflow restrictions due to surfactant depletion

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83. Normal vs. Abnormal Bronchiole in Asthma

Normal vs. Abnormal Bronchiole in Asthma

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84. Asthma

Asthma

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Immediate Stage of Asthma  Late Stage of Asthma

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Chronic Obstructive Airway Diseases

- **Emphysema**
  - Permanent dilation of any part of the respiratory acinus (air spaces distal to the terminal bronchioles) with destruction of alveolar walls but lack of scarring; strongly assoc. with cigarettes
  - Functionally, loss of elastic recoil in lungs
    - Tissue destroyed \(\rightarrow\) reduced gas exchange area
    - If severe then, reduced oxygen uptake despite increased ventilation \(\text{AND}\)
    - Blood oxygenation maintained by rapid respiratory rate but a feeling of breathless on the slightest exertion and hypoxia occurs, “pink puffer” – overventilate to maintain oxygenation

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Chronic Obstructive Airway Diseases

- **Emphysema – cont’d**
  - If pure condition – “pink puffer”
    - Only in late disease does cyanosis, hypoxia, hypercapnia, respiratory acidosis and cor pulmonale develop
  - Exhalation is normally a passive respiratory function requiring no work, it becomes active in emphysema
    - Clinically increased anterioposterior diameter of the chest (barrel-chest); increased total vital capacity

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87. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- Emphysema – cont’d
  - Pathogenesis
    - (?): Parenchymal destruction by secreted extracellular proteases; normal defensive protease inhibitors (e.g., alpha-1 antitrypsin) being either inactivated or absent - an imbalance between proteases and protease inhibitors
      - Smoking - increases release of proteases (e.g., elastase) from PMN and macro; inactivates \( \alpha_1 \)-antitrypsin
      - Congenital - lack protease inhibitors

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88. Pathogenesis of Emphysema

Pathogenesis of Emphysema

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89. Pathogenesis of Emphysema

Pathogenesis of Emphysema

Proteases destroy lung tissue due to imbalance between proteases and their inhibitors; smoking increases release of proteases as does congenital lack of protease inhibitors.

90. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- Emphysema – cont’d
  - Review of normal anatomy
    - Respiratory acinus distal to the terminal bronchioles consists of respiratory bronchioles, alveolar ducts and terminal acini (alveolar sacs)
  - Two main generalized forms - defined by location of damage in respiratory acinus
    - Centriacinar and panacinar
  - Gross
    - Lungs are voluminous with large dilated air spaces
91. Bullous Emphysema with Apical and Subpleural Bullae

Bullous Emphysema with Apical and Subpleural Bullae

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92. Pulmonary Emphysema

Pulmonary Emphysema

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Marked enlargement of airspaces with thinning and destruction of alveolar septa

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93. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- **Emphysema – cont’d**
  - Centriacinar (centrilobular) form
    - Most common
    - Associated with smoking, chronic bronchitis and inflammation of the distal airways
    - Most often seen in upper part of lobes
    - Pathogenesis
      - Secretion of extracellular proteases by local inflammatory cells
      - Dilatation of the respiratory bronchioles at the center of the respiratory acinus
      - Dilated air spaces are surrounded by normal-sized alveolar ducts

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94. Centriacinar Emphysema

Centriacinar Emphysema

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dilated air spaces (D) surrounded by normal ones

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95. Chronic Obstructive Airway Diseases

Chronic Obstructive Airway Diseases

- Emphysema - cont’d
  - Panacinar form - loss of elasticity
    - Involves dilation of the entire respiratory acinus
    - Commonly associated with smoking
    - Pathogenesis
      - Related to excessive activity of extracellular enzymes secreted by inflammatory cells
      - α-1 antitrypsin deficiency due to smoking or congenital
    - Dilation of the terminal acini (alveolar sacs) and alveolar ducts
    - Later affects respiratory bronchioles and terminal bronchioles
    - Dilated air spaces evident uniformly in all lobes

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96. Panacinar Emphysema

Panacinar Emphysema

dilated air spaces (D) evident in all lobes

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97. Centrilobular and Panacinar Emphysema

**Centrilobular and Panacinar Emphysema**

- Centrilobular emphysema with emphysematous foci (E) abut the arteries but normal alveolar spaces are adjacent to the septa (S).

- Panacinar emphysema with more generalized distribution of the permanently enlarged emphysematous foci.

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98. Chronic Obstructive Airway Diseases

**Chronic Obstructive Airway Diseases**

- **Other emphysemas** = also have dilated air spaces but not the 2 classic forms since scarring present
  - Localized (paraseptal)
    - Probably due to infection, inflammation and fibrosis
      - Localized to distal part of acinus including alveolar ducts and terminal acini (alveolar sacs)
      - Subpleural zones of upper lobes, adjacent to lobular septa, around blood vessels and bronchi
  - Scar
    - Dilated air spaces around scarred lung for whatever reason
  - Focal dust
    - Dilatation of centrilobular air spaces around aggregates of macrophages containing coal dust; no functional disability
  - Compensatory
    - Dilatation of air spaces that takes place in areas around collapsed lung or after surgical lung resection

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99. Chronic Obstructive Airway Diseases

**Chronic Obstructive Airway Diseases**

- **Emphysema complications**
  - Complicated by, or coexistent with, chronic bronchitis
  - May be complicated by interstitial emphysema
    - Air escapes into the interstitial tissues of the chest from a tear in the airways
  - Rupture of a surface bleb \( \rightarrow \) pneumothorax

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100. Chronic Obstructive Airways Disease

**Chronic Obstructive Airways Disease**

- **Chronic bronchitis**
  - A functional clinical disorder in which there is a cough productive of sputum on most days for 3 months of the year for at least 2 successive years
  - Structural changes
    - Secretion of abnormal amounts of mucus \( \rightarrow \) plugging of the airway lumen
    - Hypersecretion associated with hypertrophy and hyperplasia of bronchial submucosal mucus secreting glands
    - Increase of Reid index = ratio of gland:wall thickness in the bronchus
    - Inflammation typically not present but excess mucus can result in coincidental respiratory tract infections with secondary inflammation; squamous metaplasia common

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101. **Chronic Obstructive Airway Diseases**

**Chronic Obstructive Airway Diseases**

- **Chronic bronchitis – cont’d**
  - Airway obstruction due to luminal narrowing and mucus plugging -> alveolar hypoventilation, hypoxemia, and hypercapnia
  - Typically cyanosed but not usually with distressing dyspnea
    - *Blue bloaters* – constantly cyanosed
  - Clearly linked to cigarette smoking
    - Also associated with air pollution, infection, and genetic factors

102. **Chronic Bronchitis**

**Chronic Bronchitis**

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Marked thickening of the mucous gland layer and squamous metaplasia of the lung epithelium

Plugging (P) of the airway lumen with mucus; hypertrophy and hyperplasia of mucous glands (M); squamous metaplasia (S) common if persistent or recurrent superimposed infections

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103. **Chronic Obstructive Airway Diseases**

Chronic Obstructive Airway Diseases

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"Blue bloater"  "Pink Puffer"
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Increase in airway resistance  Reduced outflow
(narrowing of airways)

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104. **Chronic Obstructive Pulmonary Disease [COPD]**

Chronic Obstructive Pulmonary Disease [COPD]

- Frequently, chronic bronchitis, emphysema, and asthma are seen together as a mixed disease
  - Heavy smokers
    - Persistent cough with sputum
    - Breathlessness on exertion
    - Airways obstruction
      - Frequently also have a reversible component to airways obstruction
  - Superimposed acute episodes of infection cause acute decline in lung function and precipitate acute deterioration of chronic cor pulmonale
    - Prophylactic pneumococcal and influenza vaccines advisable
  - **Main risk factors**
    - Lifetime smoking exposure
    - Childhood asthma

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Chronic Obstructive Airway Diseases

**Summary**
- Chronic bronchitis and asthma cause airway narrowing; emphysema causes loss of recoil in lungs.
- Asthma is characterized by a chronic inflammatory response in airways, leading to reversible airways obstruction.
- Muscle spasms, mucus plugging and mucosal edema cause airway obstruction.
- Generalized emphysema is permanent dilatation any part of the respiratory acinus, with destruction of tissue in the absence of scarring.

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Chronic Obstructive Airway Diseases

**Summary – cont’d**
- Emphysema caused by unregulated extracellular protease (secreted from inflammatory cells) activity.
- Two patterns of generalized emphysema: centrilobular and panacinar.
- Chronic bronchitis - airways show mucus hypersecretion with mucous gland hyperplasia.
- May patients with chronic bronchitis have an asthmatic component to obstruction, as well as emphysema.
- Pulmonary hypertension and right-sided heart failure are common in long-standing (i.e., chronic) obstructive pulmonary disease [COPD].

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