Lung and Upper Respiratory Tract
Basic Robbins, Chapter 12
M. E. Bauman, M.D.

Normal Lung

**Embryology, Normal Anatomy** (Figures not in text)

Right vs Left

Dual blood supply

acinus = (Figure 12-6)

epithelium: vocal cords:

larynx to terminal bronchioles:
alveolar walls: (Figure 12-1)
  type I pneumocytes
  type II pneumocytes

**Pathology**

**Congenital Anomalies** (Section not in Basic Robbins)

Agenesis/hypoplasia

Tracheal/bronchial anomalies

Congenital foregut cysts

Intralobar/extralobar sequestration (Figures not in text)

**Atelectasis** (Figure 12-2)

Definition:

1.

2.
3.

**Acute Lung Injury**

Pulmonary edema (Section not in Basic Robbins. Figures not in text)

Hemodynamic/hydrostatic pressure

Acute Respiratory Distress Syndrome ARDS (Figures 12-4, 12-3)
Diffuse alveolar damage DAD
**Obstructive vs Restrictive Pulmonary Diseases**

**Restrictive:**

Obstructive:

**COPD:**

1. ______________________

blebs/bullae (Figure 12-9)

vs overinflation

centriacinar (centrilobular) (Figures 12-6, 12-8)

panacinar

paraseptal

pathogenesis
alpha-1 antitrypsin

cigarette smoking (Figure 12-7)

clinical aspects

“pink puffer”

2. __________________________

Pathogenesis: smoking + infections

histology (Figure 12-10)

“blue bloater”
clinical overlap with emphysema

long term consequences

3. Atopic and non-atopic types

Pathogenesis (Figure 12-11)

Histology (Figure 12-12)

Curschmann spirals

Charcot-Leyden crystals
Clinical aspects (Figures not in text)

Clinical overlap of COPD types (Figure 12-5)

4. __________________________(Figures not in text)

Pathogenesis: obstruction and persistent infection

Cystic fibrosis (Figures 12-13, 6-4)
Kartgener syndrome (Figure not in text)

**Chronic Interstitial (Restrictive, Infiltrative) Lung Diseases**

Interstitial fibrosis

Radiology

Long term sequelae

**Fibrosing Diseases**

Idiopathic Pulmonary Fibrosis (IPF) (Figure 12-15)

Synonyms

Morphology

Clinical
Nonspecific Interstitial Pneumonia (NSIP)

Morphology

Clinical

Cryptogenic Organizing Pneumonia (COP) (Figure 12-17)
Synonym: BOOP =

Clinical

Pulmonary Involvement in Collagen-Vascular Diseases
SLE, RA, Systemic Sclerosis, Dermatomyositis

Pneumoconioses (singular = pneumoconiosis)
Definition

Pathogenesis

1. Coal worker’s pneumoconiosis (CWP)
   Anthracosis/simple CWP/complicated CWP-Progressive mass fibrosis
2. Silicosis

morphology

CXR: eggshells

3. Asbestosis

serpentine (chrysotile) and straight (amphibole) fibers

asbestosis bodies (Figure 12-21)

pleural plaques

synergistic effects/malignancies

Drug and Radiation-Induced Pulmonary Disease

Drugs

Radiation
Granulomatous Diseases

Sarcoidosis (Wikipedia image)

Pathogenesis

Cell mediated response/morphology

Schaumann bodies
asteroid bodies

Clinical

Sicca syndrome
Xerostomia
Mikulicz syndrome

Hypersensitivity Pneumonitis

Synonym

Morphology (Fig 12-24)
Pulmonary eosinophilia

Acute and chronic eosinophilic pneumonias

Smoking-Related Interstitial Disease
Desquamative Interstitial Pneumonia (DIP) (Figure 1-25)
Misnomer

Pulmonary Diseases of Vascular Origin

Pulmonary embolism, hemorrhage and infarction

Thrombus ≠ embolus

Sources of pulmonary thromboemboli

Hypercoagulable states

Saddle embolus

Acute cor pulmonale/acute respiratory distress
Smaller emboli $\rightarrow$ pulmonary infarcts (Figure 12-27)

Clinical

DX

Prophylaxis

Non-thrombotic pulmonary emboli

Pulmonary hypertension

Physiologic/pathologic pressures

Pathogenesis (Figure 12-28)
Diffuse Alveolar Hemorrhage Syndromes

Goodpasture syndrome: simultaneous rapidly progressive glomerulonephritis and a necrotizing hemorrhagic interstitial pneumonitis (Chapter 13)

pathogenesis

morphology (Figure 12-29)

immunofluorescence

clinical

Rx

Wegener granulomatosis (Pulmonary angiitis and granulomatosis)  
Chapter 9 Blood Vessels  
Necrotizing granulomatous vasculitis of upper airway and lungs  
Crescentic glomerulonephritis  
PR3-ANCA

Pulmonary Infections

Pneumonia: an infection of the lung

Lung defense mechanisms (Figure 12-30)
Bronchopneumonia vis-à-vis lobar pneumonia

Predisposition to a second infection

Histologic spectrum of pneumonias (Figures 12-32/34/41/37/42/43)
Pneumonias classified by specific agent or by clinical setting

***Table 12-6***

Community acquired acute pneumonias

<table>
<thead>
<tr>
<th>Common organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

Symptoms

- Congestion, red and gray hepatization, resolution

Community acquired atypical pneumonias

Atypical

<table>
<thead>
<tr>
<th>Common organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

Seasonal H1N1 *vis-à-vis* Novel H1N1

Antigenic drift *vis-à-vis* Antigenic shift
Hospital-Acquired Pneumonias  
Nosocomial  
VAP  
Common organisms  

Aspiration pneumonias  
Clinical  

Chemical irritation from gastric acid  
Mixed aerobic/anaerobic organisms  
Lung abscess: cavitary focus of suppurative necrosis  
Etiologies  

Anaerobes  

Embolization of septic material to meninges and brain  

_______________ must be excluded in an adult with a pulmonary abscess  

Chronic pneumonias  

Note: The order of material below differs from the text and contains some material not in the text.  

Mycobacterium tuberculosis hominis  

Epidemiology
Transmission

Infection *vis-à-vis* disease

PPD test (purified protein derivative, Mantoux test, TST-Tuberculin skin test)

PPD positive

BCG (Bacillus Calmette-Guérin)

PPD negative

Quantiferon-Tb test (interferon gamma release assay, IFNγ release assay, IGRA)
Primary pulmonary Tb (Figure 12-35)

Ghon complex (Figure 12-36)

Caseating granulomata/acid fast mycobacteria (Figure 12-37)

Progressive primary Tb
Secondary Tuberculosis (Reactivation Tb)

Cavitation

Miliary disease

Pott disease

Intestinal Tb

DX:

Sputum acid fast stain/fluorescent auramine rhodamine

PCR amplification

Conventional cultures

MDR

XDR
Nontuberculous mycobacterial disease

Mycobacterium avium-intracellulare

Histoplasmosis, Coccidioidomycosis, Blastomycosis

Thermally dimorphic deep mycoses

Room temp/body temp

T-cell mediated immune responses
Histoplasmosis (Histoplasma capsulatum)
Region
Morphology

Blastomycosis (Blastomyces dermatitidis)
Region
Morphology

Coccidioidomycosis (Coccidioides immitis)
Region
Morphology

Clinical features of deep mycoses

Pneumonia in the Immunocompromised Host

Opportunistic pathogens

Cytomegalovirus (CMV) (Figure 12-42)
Herpes virus family
Large nuclear and smaller cytoplasmic inclusions
Congenital (transplacental), perinatal (vaginal secretions at birth, breast milk), respiratory, iatrogenic (tissue transplant, blood transfusion)
Pneumonitis, colitis, retinitis
Dx via tissue sections, viral culture, antibody titer, PCR
Pneumocystis jiroveci (formerly P. carinii)
  Pneumonitis
  
  Dx via sputum or bronchoalveolar lavage

Not all infiltrates are infections

Opportunistic Fungal Infections

Candidiasis (Candida albicans)
  Mucocutaneous and deep: thrush, diaper rash, vaginitis, esophagitis

Cryptococcosis (Cryptococcus neoformans)
  Mucoid encapsulated yeasts: India ink
  Lungs and especially central nervous system
    Meningitis/meningoencephalitis
    Perivascular Virchow-Robin spaces: soap bubble lesions

Mucormycosis = fungal infection by fungi in the order Mucorales
  Mucor, Rhizopus (genera): rhinocerebral mucormycosis
    Nonseptate hyphae, right angle branching
    Diabetic ketoacidosis, angioinvasive

Aspergillus (genus)
  Septate hyphae, acute angle branching
  Pulmonary aspergilloma

Pulmonary Disease in HIV Infection
Lung Tumors

Estimated 220,000 new cases in 2011; 156,000 deaths in 2011 in the USA

5 year survival of all stages of lung cancer = ___%

___% of lung cancers occur in active smokers (or recent quitters)

___% of heavy smokers develop lung cancer

Exposure to asbestos increases the risk for lung cancer ____ times in nonsmokers.

Smokers exposed to asbestos have a ____ times greater risk for lung cancer than nonsmokers not exposed to asbestos.

Histologic types (Figures 12-45, 12-46, 12-47)

1.

2.

3.

4.

Combined patterns
Clinical distinction

NSCLC/SCLC

Note: Most of the following material on molecular alterations in lung cancer is not contained in the text.

Integration of histologic and molecular data for classification of lung tumors

Precision medicine/personalized medicine/targeted therapy

“Approximately 60% of lung adenocarcinomas and 45% of squamous cell carcinomas harbor known driver genomic alterations that are potentially actionable or informative in the clinical setting.” L MacConaill. Advancing Personalized Cancer Medicine in Lung Cancer. Arch Pathol Lab Med. 2012;126:1210-1216; doi: 10.5858/arpa.2012-0244-SA

Molecular alterations in NSCLC (Figure 5-19)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Description</th>
<th>Frequency</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>Epidermal Growth Factor Receptor</td>
<td>15% NSCLC</td>
<td>erlotinib, gefitinib</td>
</tr>
<tr>
<td>KRAS</td>
<td>Kirsten rat sarcoma viral oncogene homolog</td>
<td>22% NSCLC</td>
<td>panitumumab, cetuximab</td>
</tr>
<tr>
<td>(EML4)-ALK</td>
<td>Echinoderm microtubule associated proteinlike-4/Anaplastic Lymphoma Kinase (fusion oncoprotein)</td>
<td>3-5% NSCLC</td>
<td>crizotinib</td>
</tr>
<tr>
<td>ERBB2 (HER2)</td>
<td>Erythroblastic leukemia viral oncogene, homolog 2</td>
<td>2% NSCLC</td>
<td>lapatinib, trastuzumab</td>
</tr>
<tr>
<td>PIK3CA</td>
<td>Phosphoinositide-3-kinase, catalytic, alpha polypeptide</td>
<td>2% NSCLC</td>
<td>Clinical trials for drugs</td>
</tr>
</tbody>
</table>

Molecular diagnostic detection techniques

Immunohistochemistry (IHC)
Lung Cancer, ALK (2p23) Rearrangement, FISH, Tissue

Rearrangements of the ALK locus are found in a subset of lung carcinomas and their identification may guide important therapeutic decisions for the management of these tumors. The fusion of EML4 (echinoderm microtubule-associated protein-like 4) gene with the ALK (anaplastic large cell lymphoma kinase) gene results from an inversion of chromosome band 2p23. The ALK- EML4 rearrangement has been identified in 3% to 5% of NSCLC with the majority in adenocarcinoma and younger male patients who were light or nonsmokers. Recent studies have demonstrated that lung cancers harboring ALK rearrangements are resistant to epidermal growth factor receptor tyrosine kinase inhibitors, but may be highly sensitive to ALK inhibitors, like Xalkori (crizotinib). The drug Xalkori works by blocking certain kinases, including those produced by the abnormal ALK gene. Clinical studies have demonstrated that Xalkori treatment of patients with tumors exhibiting ALK rearrangements can halt tumor progression or result in tumor regression. This FISH assay is a FDA-approved companion diagnostic test for the Xalkori, which the FDA recently approved to treat certain patients with late-stage (locally advanced or metastatic), non-small cell lung cancers that harbor anaplastic lymphoma kinase (ALK) gene rearrangements. It can be used to identify patients who will benefit from Xalkori therapy.

Polymerase Chain Reaction (PCR)

PCR/Mass spectrometry genotyping

Panel-based profile of tumor DNA for several hundred mutations in several dozen known cancer genes

Microarrays (Figures 5-35, 5-36)

Next-Generation sequencing

Ultra-high throughput DNA sequencing
Whole-Exome (the coding sequence of the human genome, 1-2% of the genome) ($2500)
Whole-Genome sequencing (3.1 billion DNA base pairs of an individual’s entire genome) ($7500)
Paraneoplastic syndromes
   ADH
   ACTH
   Parathormone
   Calcitonin

Hypertrophic pulmonary osteoarthropathy

Lambert-Eaton myasthenia syndrome

Pancoast tumor/Horner syndrome

Carcinoid Tumors (Figure 12-49)

Primary vs. metastatic lung tumors
   central vs peripheral
   single vs multiple
**Pleural Lesions**

Effusions: hydrostatic pressure, vascular permeability, osmotic pressure, lymphatic blockage

Pneumothorax: spontaneous, traumatic, therapy related

Mesothelioma: see above

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**Lesions of the Upper Respiratory Tract**

**Acute Infections**

“Common cold”: rhinoviruses, coronaviruses, RSV, parainfluenza, influenza, adenoviruses, enteroviruses.

Pharyngitis: β hemolytic streptococci, EBV, Coxsackie A

Epiglottitis: H. influenza

Acute laryngitis: Corynebacterium diphtheria – exudative pharyngitis/grey pseudomenbrane

Croup: parainfluenza

---

**Nasopharyngeal carcinoma**

EBV associated
High incidence in China
Histologic variants: keratinizing and nonkeratinizing squamous cell carcinomas, undifferentiated carcinoma
Laryngeal Tumors

Benign
Vocal cord nodules/singer’s nodes
Laryngeal papillomas: HPV 6 and 11

Carcinoma
Squamous cell carcinomas
Associated with smoking, 15% HPV association