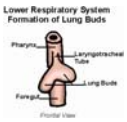
Lung and Upper Respiratory Tract

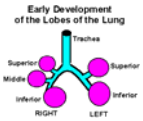
Basic Robbins, Chapter 12

M. E. Bauman, M.D.

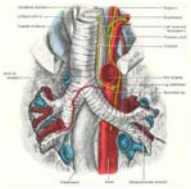
Normal Lung

Embryology, Normal Anatomy (Figures not in text)

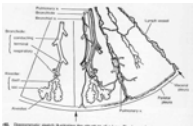




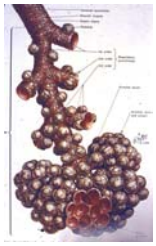
Right vs Left

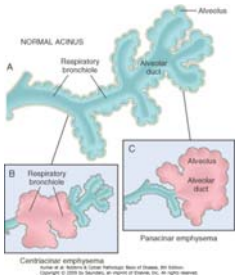


Dual blood supply



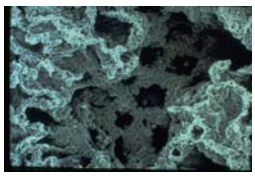
acinus = (Figure 12-6)





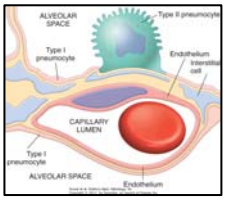
epithelium: vocal cords:

larynx to terminal bronchioles:



alveolar walls: (Figure 12-1)
type I pneumocytes

type II pneumocytes



Pathology

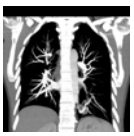
Congenital Anomalies (Section not in Basic Robbins)

Agenesis/hypoplasia

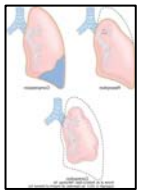
Tracheal/bronchial anomalies

Congenital foregut cysts

Intralobar/extralobar sequestration (Figures not in text)

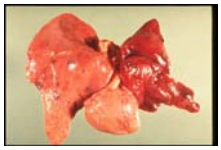


Atelectasis (Figure 12-2)
Definition:



1.

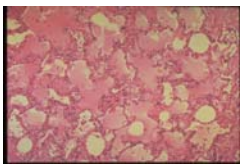
2.



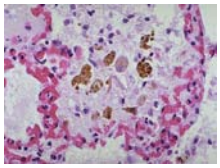
3.

Acute Lung Injury

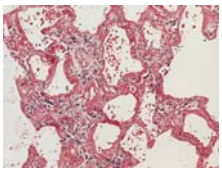
Pulmonary edema (Section not in Basic Robbins. Figures not in text)

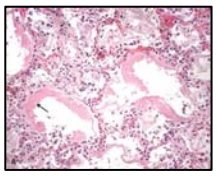


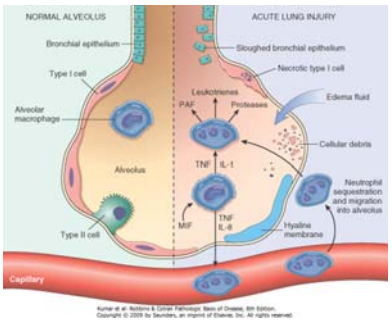
Hemodynamic/hydrostatic pressure



Acute Respiratory Distress Syndrome ARDS (Figures 12-4, 12-3)
Diffuse alveolar damage DAD

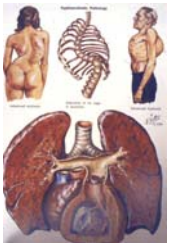






Obstructive vs Restrictive Pulmonary Diseases

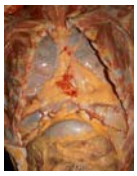
Restrictive:

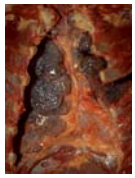


Obstructive:

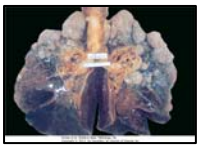
COPD:

1. _____

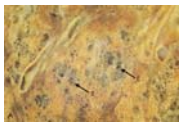




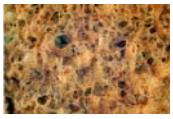
blebs/bullae (Figure 12-9)



vs overinflation

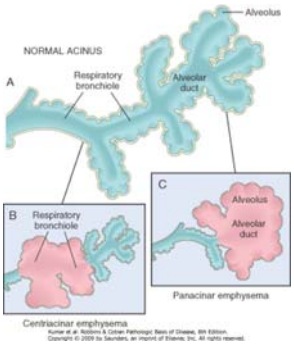


centriacinar (centrilobular) (Figures 12-6, 12-8)

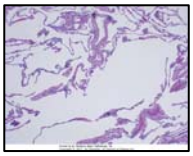


panacinar

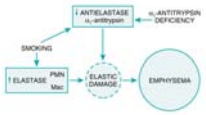
paraseptal



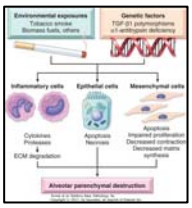
pathogenesis



alpha-1 antitrypsin

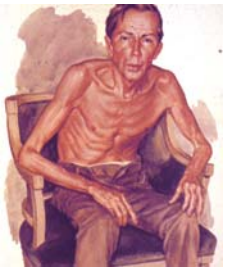


cigarette smoking (Figure 12-7)

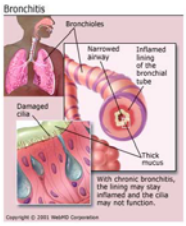


clinical aspects

"pink puffer"

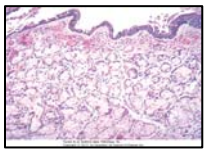


2. _____



Pathogenesis: smoking + infections

histology (Figure 12-10)



"blue bloater"

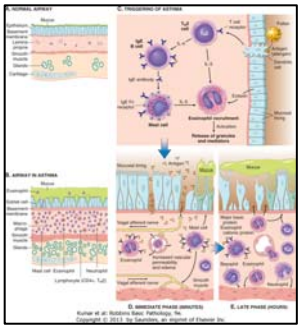
clinical overlap with emphysema

long term consequences

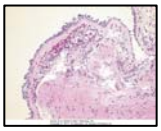
3. _____

Atopic and non-atopic types

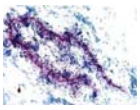
Pathogenesis (Figure 12-11)



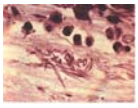
Histology (Figure 12-12)



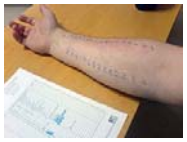
Curschmann spirals

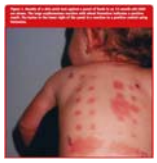


Charcot-Leyden crystals

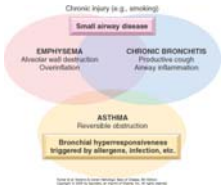


Clinical aspects (Figures not in text)

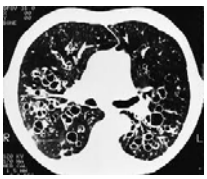


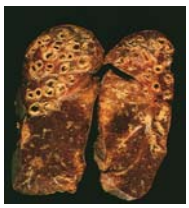


Clinical overlap of COPD types (Figure 12-5)



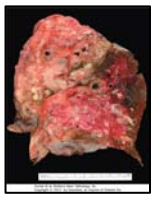
4. _____(Figures not in text)

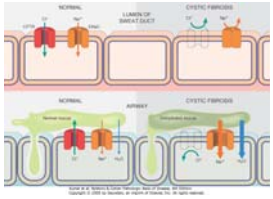




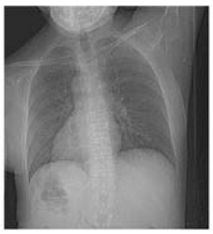
Pathogenesis: obstruction and persistent infection

Cystic fibrosis (Figures 12-13, 6-4)



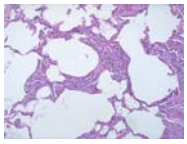


Kartgener syndrome (Figure not in text)

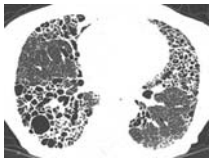


Chronic Interstitial (Restrictive, Infiltrative) Lung Diseases

Interstitial fibrosis



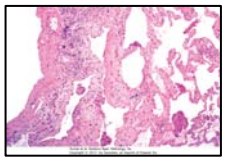
Radiology



Long term sequelae

Fibrosing Diseases

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



Synonyms

Morphology

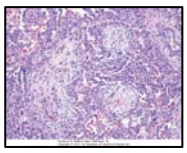
Clinical

Nonspecific Interstitial Pneumonia (NSIP)

Morphology

Clinical

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



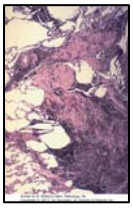
Clinical

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

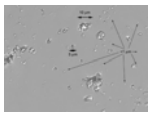
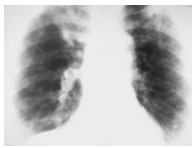
Pneumoconioses (singular = pneumoconiosis)
Definition

Pathogenesis

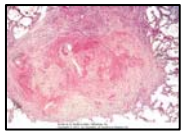
1. Coal worker's pneumoconiosis (CWP)
Anthracosis/simple CWP/complicated CWP-Progressive mass fibrosis



2. Silicosis

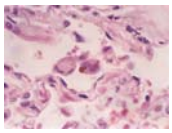
morphology



CXR: eggshells

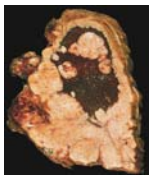
3. Asbestosis

serpentine (chrysotile) and straight (amphobile) fibers



asbestosis bodies (Figure 12-21)

pleural plaques



synergistic effects/malignancies

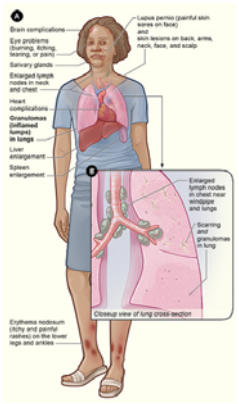
Drug and Radiation-Induced Pulmonary Disease

Drugs

Radiation

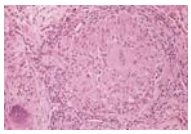
Granulomatous Diseases

Sarcoidosis (Wikipedia image)



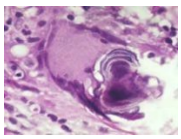
Pathogenesis

Cell mediated response/morphology

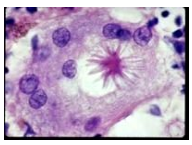


Schaumann bodies

asteroid bodies



Clinical



Sicca syndrome

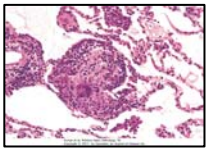
Xerostomia

Mikulicz syndrome

Hypersensitivity Pneumonitis

Synonym

Morphology (Fig 12-24)



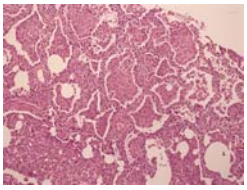
Pulmonary eosinophilia

Acute and chronic eosinophilic pneumonias

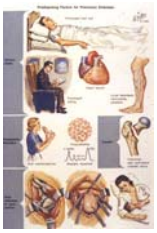
Smoking-Related Interstitial Disease

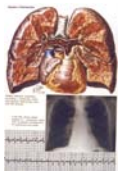
Desquamative Interstitial Pneumonia (DIP) (Figure 1-25)

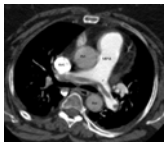
Misnomer

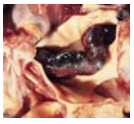


Pulmonary Diseases of Vascular Origin









Pulmonary embolism, hemorrhage and infarction

Thrombus ≠ embolus

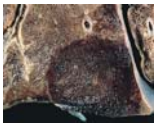
Sources of pulmonary thromboemboli

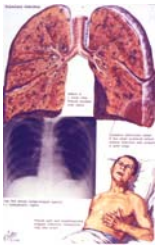
Hypercoagulable states

Saddle embolus

Acute cor pulmonale/acute respiratory distress

Smaller emboli → pulmonary infarcts (Figure 12-27)





Clinical

DX

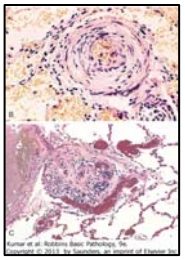
Prophylaxis

Non-thrombotic pulmonary emboli

<u>Pulmonary hypertension</u>

Physiologic/pathologic pressures

Pathogenesis (Figure 12-28)

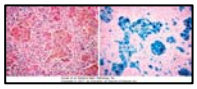


Diffuse Alveolar Hemorrhage Syndromes

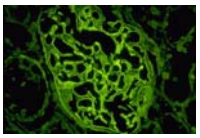
Goodpasture syndrome: simultaneous rapidly progressive glomerulonephritis and a necrotizing hemorrhagic interstitial pneumonitis (Chapter 13)

pathogenesis

morphology (Figure 12-29)



immunofluorescence



clinical

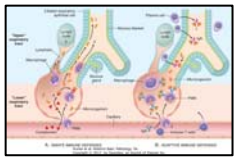
Rx

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

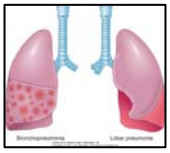
Pulmonary Infections

Pneumonia: an infection of the lung

Lung defense mechanisms (Figure 12-30)

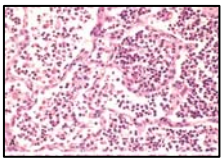


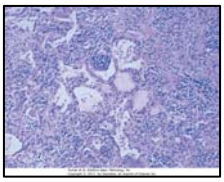
Bronchopneumonia *vis-à-vis* lobar pneumonia

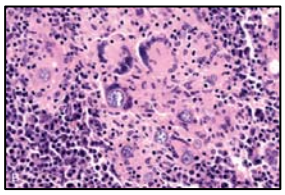


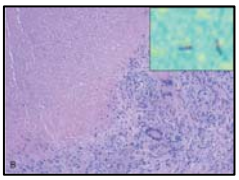
Predisposition to a second infection

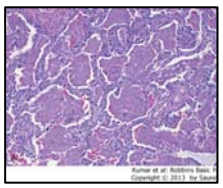
Histologic spectrum of pneumonias (Figures 12-32/34/41/37/42/43)

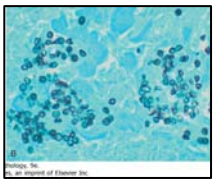


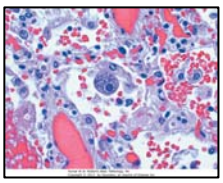












Pneumonias classified by specific agent or by clinical setting

*****Table 12-6*****

<u>Community acquired acute pneumonias</u>

Common organisms

Symptoms

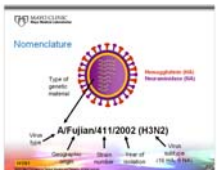
Congestion, red and gray hepatization, resolution

<u>Community acquired atypical pneumonias</u>

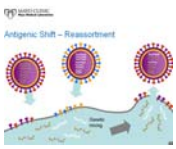
Atypical

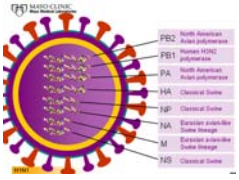
Common organisms

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

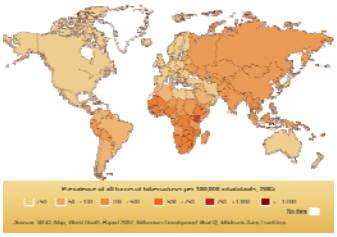
_____ must be excluded in an adult with a pulmonary abscess

Chronic pneumonias

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

Mycobacterium tuberculosis hominis

Epidemiology



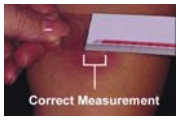
Transmission




Infection *vis-à-vis* disease

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

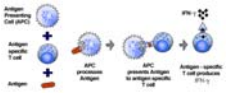
PPD positive



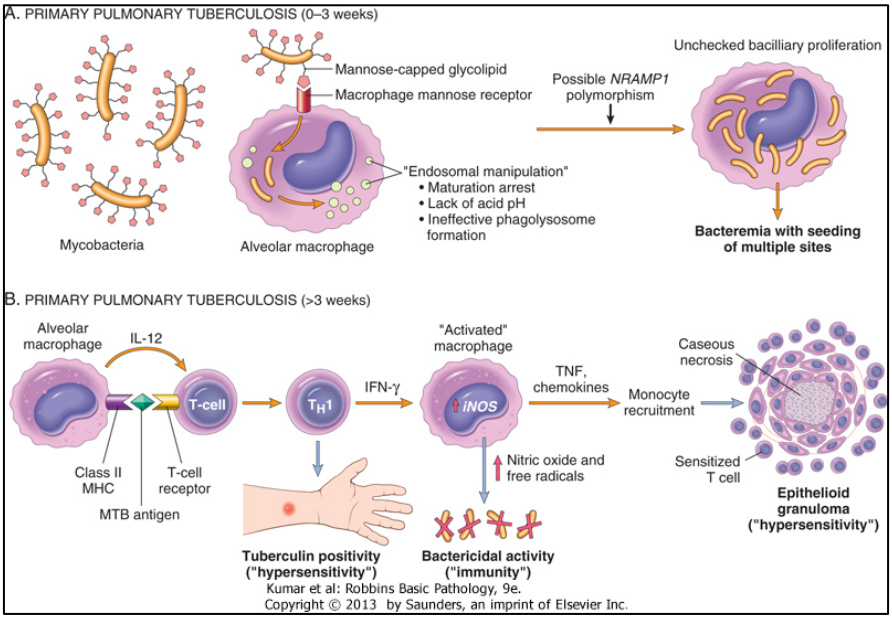
BCG (Bacillus Calmette-Guérin)

PPD negative

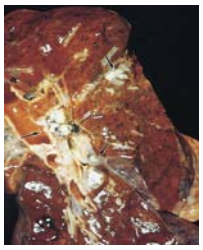
Quantiferon-Tb test (interferon gamma release assay, IFNγ release assay, IGRA)

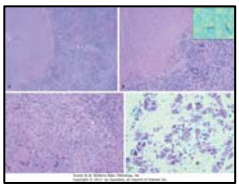
Primary pulmonary Tb (Figure 12-35)



Ghon complex (Figure 12-36)

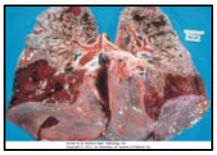


Caseating granulomata/acid fast mycobacteria (Figure 12-37)



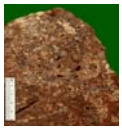
Progressive primary Tb

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

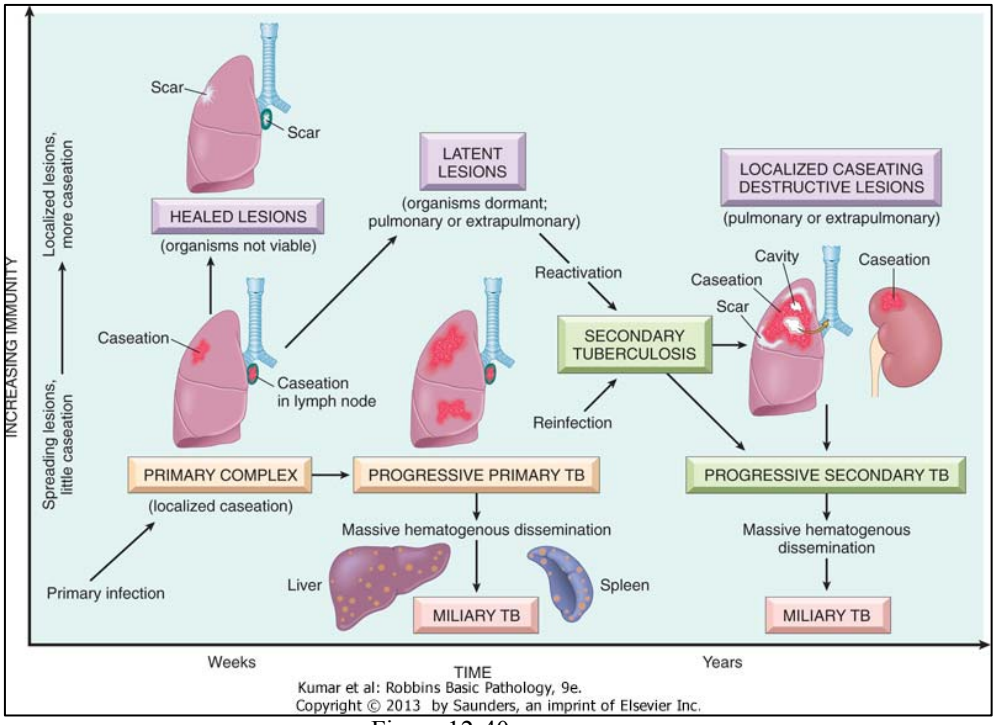


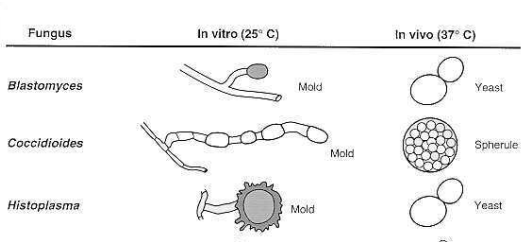
Figure 12-40

Nontuberculous mycobacterial disease

Mycobacterium avium-intracellulare

<u>Histoplasmosis, Coccidioidomycosis, Blastomycosis</u>

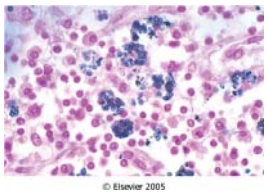
Thermally dimorphic deep mycoses



Room temp/body temp

T-cell mediated immune responses

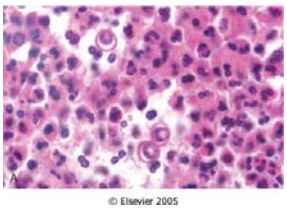
Histoplasmosis (Histoplasma capsulatum)



Region

Morphology

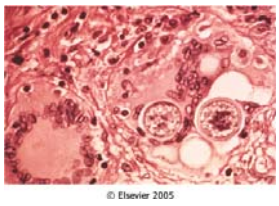
Blastomycosis (Blastomyces dermatitidis)



Region

Morphology

Coccidioidomycosis (Coccidioides immitis)



Region

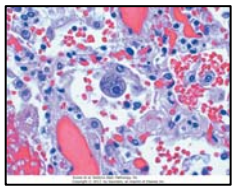
Morphology

Clinical features of deep mycoses

<u>Pneumonia in the Immunocompromised Host</u>

Opportunistic pathogens

Cytomegalovirus (CMV) (Figure 12-42)



Herpes virus family

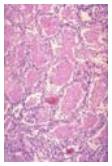
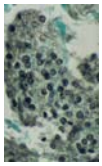
Large nuclear and smaller cytoplasmic inclusions

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

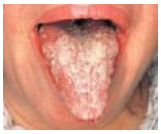
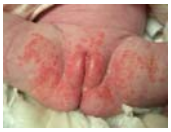



Dx via sputum or bronchoalveolar lavage

Not all infiltrates are infections

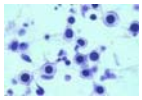
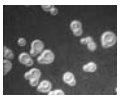
<u>Opportunistic Fungal Infections</u>

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

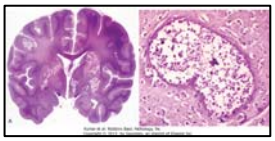





Cryptococcosis (Cryptococcus neoformans)

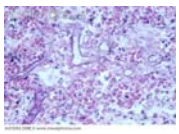
Mucoid encapsulated yeasts: India ink

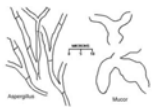



Lungs and especially central nervous system
Meningitis/meningoencephalitis
Perivascular Virchow-Robin spaces: soap bubble lesions

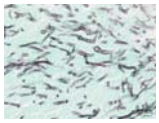


Mucormycosis = fungal infection by fungi in the order Mucorales
Mucor, Rhizopus (genera): rhinocerebral mucormycosis
Nonseptate hyphae, right angle branching
Diabetic ketoacidosis, angioinvasive



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




<u>Pulmonary Disease in HIV Infection</u>

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 = ___%

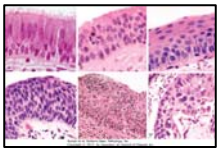
____% of lung cancers occur in active smokers (or recent quitters)

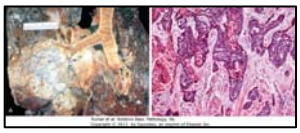
____% of heavy smokers develop lung cancer

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)





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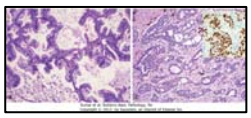
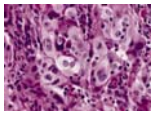
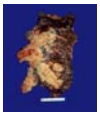


2.



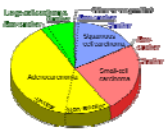
3.



4.

Combined patterns

Clinical distinction



NSCLC/SCLC

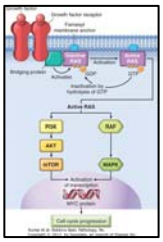
Note: Most of the following material on molecular alterations in lung cancer is not contained in the text.

Integration of histologic and molecular data for classification of lung tumors

Precision medicine/personalized medicine/targeted therapy

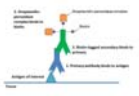
"Approximately 60% of lung adenocarcinomas and 45% of squamous cell carcinomas harbor known driver genomic alterations that are potentially actionable or informative in the clinical setting." L MacConaill. Advancing Personalized Cancer Medicine in Lung Cancer. Arch Pathol Lab Med. 2012;126:1210-1216;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

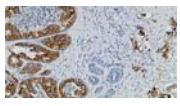
Molecular alterations in NSCLC (Figure 5-19)



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

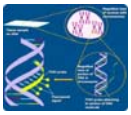
Molecular diagnostic detection techniques

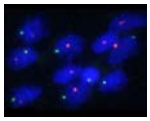




Immunohistochemistry (IHC)

Fluorescence in situ hybridization (FISH)





Copied from Mayo Medical Laboratories' Test menu:

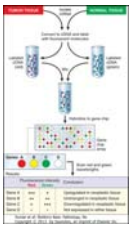
Lung Cancer, ALK (2p23) Rearrangement, FISH, Tissue
Rearrangements of the *ALK* locus are found in a subset of lung carcinomas and their identification may guide important therapeutic decisions for the management of these tumors. The fusion of *EML4* (echinoderm microtubule-associated protein-like 4) 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

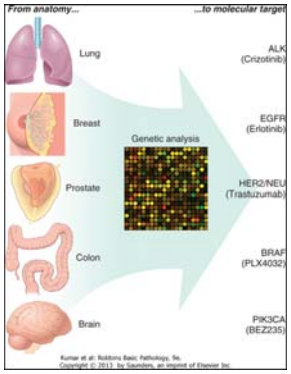
Panel-based profile of tumor DNA for several hundred mutations in several dozen known cancer genes

Microarrays (Figures 5-35, 5-36)



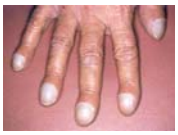
Next-Generation sequencing

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



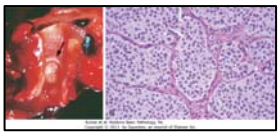
Hypertrophic pulmonary osteoarthropathy

Lambert-Eaton myasthenia syndrome

Pancoast tumor/Horner syndrome

Pancoast tumor/Horner Syndrome

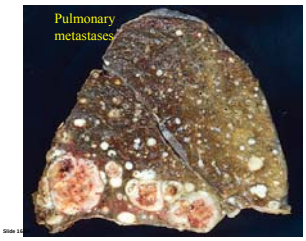
Carcinoid Tumors (Figure 12-49)



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

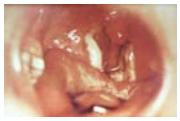
Lesions of the Upper Respiratory Tract

Acute Infections

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

Pharyngitis: β hemolytic streptococci, EBV, Coxsackie A

Epiglottitis: H. influenza



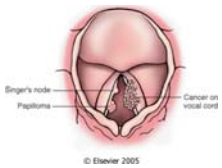
Acute laryngitis: Corynebacterium diphtheria – exudative pharyngitis/grey pseudomenbrane

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