Lec1

asthma and bronchiectasis:

Asthma:reversible bronchoconstriction

Types:

1.atopic asthma:due to allergen,family history,associated with allergic rhinitis,eczema ,present in the childhood,diagnosis:skin test with the antigen,radiallergosorbent test (RAST)

2.non atopic asthma:not associated with allergen ,negative skin test,associated with viral infection ,inhaled air pollutant

3.drugs induced asthma:

Aspirin inhibit cycloxygenase,make abnormality in prostaglandin metabolism

4.occupational asthma,farmers ,animal handler,manufacturers of metals ,bakers,food processer ,cotton workers

Pathogenesis:

Allergen is recognized by APC or dendritic cells ,activation helper T cell,release Il13,4 (produce IGE),IL13(produce mucus),IL5 (attract eosinophil),

Reeposure to antigen lead to IGE mediated activation of mast cells:

Early phase reaction:

Release of histamine,prostaglandins ,leukotriens from mast cells lead to bronchospasm,increase vascular permeability(vasodilation), increase mucus production,

Late phase reaction:

Eosinophils produce major basic protein destroys epithelium

Morphology:

Marked mucus accumulation,goblet cells hyperplasia ,submucosal gland hypertrophy, bronchial smooth muscle hyperplasia and hypertrophy, chronic intense inflammation in lamina propria ,plugs called curschman spirals ,eosinophilic derived crystalls (Charcot Leyden crystalls)

Airway remodelling :

Repeated bouts of inflammation will cause changes bronchial wall such as:

1.muscle ,glands hypertrophy

2.deposition of collagen

3.increase vascularity

Symptoms:

Productive cough,_wheezing ,dyspnea

Asthmatic attacks last 1 to several hours,reversible except in advanced severe cases ,treated spontaneouslyor by intervention (bronchodilator,corticosteroid,leukotriene inhibitors)

Status Asthmaticus :severe paroxysm doesn't respond to therapy ,hypercapnea,hypoxia,acidosis , maybe death

……

Bronchiectasis:perminant dilation of bronchi due to severe inflammation with damage to airway walls ,loss of airway tone

Etiology:

***Cystic fibrosis**

***Primary Ciliary dyskinesia:Autosomal reseccive ,causes broncheictasis and sterility in males (infertility)**

***Necrotizing,spurutive pneumonia by Staph aureus,klebseulla spp**

Pathogenesis:secondary to obstruction or necrotizing infections

poor clearance of secretions, inflammatory damage,accumulation of secretions causes irreversible dilation

Symptoms:Cough,rhinosinusitis,hemoptysis ,mucupurulent sputum ,Severe bronchiectasis:hypoxiemia (decrease in o2pressure in blood),hypercapnea, core pulmonale ,pulmonary hypertension

Morphology: affect lower lobes of lungs bilaterally,most severe involvements are bronchi and bronchioles,no complete repair,bronchial,bronchiolar ,peribronchial fibrosis

Microscopically:acute and chronic inflammatory exudate,ulceration,desauamation of epithelium

Lec2

Restrictive diseases:infiltrative

Poroblem in inhalation ,decreasing in lung compliance,volume,capacity,TLC,FVC,FEV,normal ratio

Inflammation ,fibrosis in interstitium,+/-intraalveolar

Sypmptoms:Dyspnea ,tachypnia ,crackles,cyanosis,in x ray : bilateral lesions(small nodules) ,irregular lines, glass shadows,Hypoxia(due to damage of alveolar epithelium and interstitial vasculature)

Diagnosis:Clinical ,histology

Types of chronic interstitial diseases:

Fibrosing:Idiopathic pulmonary fibrosis,non specific interstitial pneumonia,cryptogenic organising pneumonia,CT diseases,pneumoconiosis

Granulomatous:sarcoidosis,hypersensitivity pneumonitis

Smoking related:disquamative interstitial pneumonia,respiratory bronchiolitis

Morphology:End stage lung ,diffuse scarring,honeycomb lung(dilated air spaces surrounded by fibrous connective tissue lined by metaplastic epithelium instead of pneumocytes

Granulomatous diseases:

Sarcoidosis: (activation of helper T cell)systemic disease characterized by non caseating granuloma in multiple organs

Etiology:unknown

Pathogenesis:exposure to unknown antigen by genetic predisposed patient leads to cell mediated immunity driven by CD4+T cells

Hisologyical appearance:shaumann body laiminated concerations(protein and calcium) looks like onion skin,asteroid body (giant cell is engulfing star like structure)

****not required for diagnosis of sarcoidosis**

Can be in

***Lung:90%**

Granuloma in interstitiam ,+/-alveolar lesions around bronchi, blood vessels, along lymphatics

Healing ;different stages of healing and hyalinization

(5-15%) honeycomb lung

***Lymph nodes:painless,discrete , non ulcerative nodes+/-calcification**

***Skin:25%**

Erythromstous nodosum: (Associated with viral infection)red,tender(painful during touch)nodules

Subcutaneous nodules: inflammation in subcutaneous layer

Erythromatous plaques

Flat lesions

***Eye,lacrimal gland:**

Uveitis most common(iritis,irridocyclitis)uni,bilateral

Choroiditis

Sicca (inflammation in lacrimal gland)

Parotitis

Xerstomia

Mikulicz syndrome(uveoparotid)

***Spleen: in ¾. Cases granuloma,10%splenomegaly**

***Liver:granulomas in portal triad,hepatomegaly in 1/3**

***BM:40%**

Hypercalcemia,hypercalceuria: activation of vitamin D by 1-a 25 hydroxylase enzyme VitaminD increases small-bowel absorption of calcium , and reduces renal tubular calcium absorption to make granulomas

Symptoms:asymptomatic or eye involvement ,splenomegaly ,hepatomegaly,respiratory symptoms (dry cough),chest discomfort,dyspnea,)fever,anorexia,night sweat,
Diagnosis: clinical,radiological,histological(noncaseating granuloma,exclusion

Hypersensitivity pneumonitis: activation helper T cell,cupytotoxic T cell more
allergic alveolitis:Ag-Ab reaction,immune mediated interstitial lung disorder,due to prolonged exposure to antigen>300
Numerous diseases:
Farmers lung(humid ,warm hay),hot tub lung(non tuberculous mycobacteria),pigeon breeders lung(bird's feathers) ,humidifier(thermophilic bacteria)
Immunology basics:
CD4+,CD8+ in BAL,Ab aginst ag, complement, immunoglobulins
Morphology:
Interstitial pneumonitis (plasma cells ,Mac,rarely eosinophils,lymphocyte),loose poorly formed granuloma in peribronchial location,no necrosis, upper lobe and bilateral interstitial fibrosis (usual interstitial pneumonia) in severe cases
Acute hypersensitivity pneumonitis:cough,dyspnea,fever,stop exposure to antigen ,complete resolution of symptoms after4-8hours
Chronic hypersensitivity pneumonitis:not stopped by removing the agent ,progressive couph ,dispnea,fever,malaise,wight loss
Diagnosis:
Clinical,radiological (ground glass opacities) ,pathological
……
Lec3
Idiopathic pulmonary fibrosis (usual interstitial pneumonia): also known as cryptogenic Fibrosing alveolitis: patchy, progressive bilateral interstitial fibrosis.

Morphology:
Cobblestones appearance of the pleural surface, due to retraction of scars along the interlobular septa
The cut surface shows fibrosis (firm, rubbery white areas).
Temporal heterogeneity is typical (early and late lesions coexist):
• earliest lesions:Fibroblastic foci are fibroblastic proliferations
• Late lesions: are more collagenous and less cellular and may show honeycomb fibrosis
Sypmptoms:
Non productive cough, progressive daspnea,Velcro or dry like crackles ,cyanosis,corpulmonale
Poor prognosis
Survival :3years
Treatment:
The only definitive treatment is lung transplantation,
Management
we use anti inflammatory,anti fibrotic drugs
Males, Never before 50s
Diagnosis
exclusion, radiologic and histologic pattern are needed, Lower lobe and subpleural regions and along the interlobular septa are mostly affected.

Pathogenesis: unknown etiology
-Repeated cycles of epithelial activation/injury by some unidentified agent, Defective repair of alveolar epithelium, Genetic predisposition (telomerase, surfactant, MUC5B variant).

Nonspecific Interstitial Pneumonia :-Chronic bilateral interstitial lung disease of Unknown etiology,patchy but uniform mild to moderate interstitial chronic inflammation and/or fibrosis.

Symptoms:

Female non smoker in the 6th decade with Dyspnea and cough of several months.

Pathogenesis:unknown etilogy

frequent association with collagen vascular disorders such as rheumatoid arthritis.

Diagnosis:

-Better prognosis than IPF.,lower lobe opacities,

Distinct clinical, radiologic, and histologic features.

Histology:

Cellular pattern: mild to moderate chronic interstitial inflammation, lymphocyte ,few plasma cells

Fibrosing patterning :diffuse ,patchy interstitial fibrotic lesions in the same stage

Cryptogenic Organizing Pneumonia:Uncommon,Unknown etiology

Diagnosis:

chest x-ray: subpleural or peribronchial patchy airspace consolidation.

Microscopically:

Intraalveolar plugs of loose organizing connective tissue.

Symptoms:

Cough and dyspnea

Treatment:

Some patients recover spontaneously while most require treatment, usually with oral steroids.

Pneumoconiosis:

lung reaction to inhalation of mineral dusts, organic and inorganic particulates, chemical fume and vapor.

*The most common mineral dust are induced by inhalation of Coal dust, silica, and asbestos.

*usually related to workplace exposure, except for Asbestos(any one who expose to asbestos in workplace or outside workplace and family members of asbestos worker)

*The reaction depends on amount ,size, shape, solubility, and reactivity of the particles,Particles that are 1 to 5 µm in diameter are the most dangerous.

*The pulmonary alveolar macrophage is a key cellular element of lung injury and fibrosis.

*Tobacco smoking worsens the effects of all inhaled mineral dusts, more so with asbestos .

* PMF is confluent fibrosing reaction in the lung, can be a complication of any one of the pneumoconiosis.

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Lec4

coal worker pneumoconiosis

Asymptomatic anthracosis: pigment accumulates without a cellular reaction, Seen also in urban dwellers and tobacco smokers. - Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages, accumulate in the connective tissue along the pulmonary and pleural lymphatics and in draining lymph node

Simple CWP:

Presence of coal macules and nodules. Coal macules: dust-laden macrophages small amounts of collagen fibers arrayed in a delicate network. accumulations of macrophages with little to no pulmonary dysfunction. centrilobular emphysema can occur

Complicated CEP:pulomonary massive fibrosis

coalescence of coal nodules that develops over many years,multiple, dark black scars >2 cm & up to 10 cm consist of dense collagen and pigment, extensive fibrosis and compromised lung function. increasing pulmonary dysfunction, pulmonary ht, and cor pulmonale,less than 10% of cases of simple CWP progress to PMF

Salicosis:the most prevelent chronic occupational disease

Quartz the most common crystalline form implicated in silicosis.

Amorphous silica is less pathogenic.

When mixed with other minerals, the fibrogenic effect of quartz is reduced, this fortuitous situation is commonplace, as quartz in the workplace is rarely pure

Pathogenesis:

Upper zones of the lungs

-After inhalation, the particles interact with epithelial cells and macrophages, Activating the inflammasome and the release of inflammatory mediators by pulmonary macrophages (IL-1, TNF, fibronectin, lipid mediators, oxygen-derived free radicals, and fibrogenic cytokines.)

Macroscopically:

• early stages are tiny, barely palpable, discrete, pale-to-black (if coal dust is present) nodules.

Microscopically:

• Silicotic nodules: Concentrically arranged hyalinized collagen fibers surrounding amorphous center. With "whorled" collagen fibers.

• Polarized microscopy reveals weakly birefringent silica.

• Nodules may coalesce into hard, collagenous scars, with eventual progression to PMF.

• Fibrotic lesions also may occur in hilar lymph nodes and pleura.

Symptoms:

Asymptomatic: detected as fine nodularity in the upper zones of the lung on routine chest radiographs.

after PMF: Shortness of breath, pulmonary hypertension and cor pulmonale,slowly progressive, impairing pulmonary function to a degree that limits physical activity,-Increased susceptibility to tuberculosis (impaired cell mediated immunity)

relationship with lung cancer is controversial

Asbestosis: -Begins in the lower lobes and subpleurally.

diffuse pulmonary interstitial fibrosis (the first to appear), indistinguishable from UIP.

Microscopically:

-Asbestos bodies: golden brown, fusiform or beaded rods with a translucent center. Formed of asbestos fibers coated with an iron-containing proteinaceous material.

-Pleural plaques: the most common manifestation of asbestos exposure, well-circumscribed plaques of dense collagen containing calcium, on anterior and posterolateral aspects of the parietal pleura and over the domes of the diaphragm

Symptoms:

Progressively worsening dyspnea 10 to 20 years after exposure.

• cough and production of sputum. • static or progress to congestive heart failure, cor pulmonale, and death.

• Pleural plaques are usually asymptomatic.

ASSOCIATED WITH: (1) parenchymal interstitial fibrosis (asbestosis); (2) localized fibrous plaques or, rarely, diffuse pleural fibrosis. (3) pleural effusions (4) Lung carcinomas (5) malignant pleural and peritoneal mesotheliomas (6) laryngeal carcinoma.

OUTCOMES:

• The risk for developing lung carcinoma is increased 5-fold for asbestos workers.

• the relative risk for mesothelioma is more than 1000 times greater than the risk for lung cancer.

• Concomitant cigarette smoking increases the risk for lung carcinoma but not for mesothelioma.

• Lung or pleural cancer associated with asbestos exposure carries a particularly poor prognosis.

-once phagocytosed by macrophages asbestos fibers activate the inflammasome and damage phagolysosomal membranes, release of proinflammatory factors and fibrogenic mediators→1. cellular and fibrotic lung reactions 2. tumor initiator and a promoter mediated by the oncogenic effects of reactive free radicals generated by asbestos fibers on the mesothelium.

-The adsorption of carcinogens in tobacco smoke onto asbestos fibers results in remarkable synergy between tobacco smoking and the development of lung carcinoma in asbestos workers.

- The risk of cancer is increased in family members of asbestos workers and to individuals exposed outside of the workplace.

Smoking related interstitial diseases:

Desquamative interstitial pneumonia (DIP)

accumulation of large numbers of macrophages containing dusty-brown pigment (smoker's macrophages) in the air spaces,Alveolar septa are thickened by sparse inflammatory infiltrate (usually lymphocytes),+/- mild Interstitial fibrosis,good prognosis,excellent response to steroids and smoking cessation, however, some patients progress despite therapy.

respiratory bronchiolitis

presence of pigmented intraluminal macrophages akin to those in DIP, but in a "bronchiolocentric" distribution (first- and second-order respiratory bronchioles),Mild peribronchiolar fibrosis,As with DIP, presents with gradual onset of dyspnea and dry cough,symptoms recede with smoking cessation.

Table 9.4: Summary of Pneumoconioses

ENTITY	EXPOSURE	PATHOLOGIC FINDINGS	COMMENTS
Coal Workers' Pneumoconiosis	Carbon dust; seen in coal miners	Massive exposure leads to diffuse fibrosis ('black lung'); associated with rheumatoid arthritis (Caplan syndrome)	Mild exposure to carbon (e.g., pollution) results in anthracosis (collections of carbon-laden macrophages); not clinically significant
Silicosis	Silica; seen in sandblasters and silica miners	Fibrotic nodules in upper lobes of the lung	Increased risk for TB; silica impairs phagolysosome formation by macrophages.
Berylliosis	Beryllium; seen in beryllium miners and workers in the aerospace industry	Noncaseating granulomas in the lung, hilar lymph nodes, and systemic organs	Increased risk for lung cancer
Asbestosis	Asbestos fibers; seen in construction workers, plumbers, and shipyard workers	Fibrosis of lung and pleura (plaques) with increased risk for lung carcinoma and mesothelioma; lung carcinoma is more common than mesothelioma in exposed individuals.	Lesions may contain long, golden-brown fibers with associated iron (asbestos bodies, Fig. 9.14), which confirm exposure to asbestos

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Lec5

Types of embolism:

1.Thromboembolism:

95% of pulmonary embolism originated from thrombus in deep large veins of leg ex:popletial vein

Risk factors:

Rest,orthopaedic surgery,disseminated cancer, using of contraceptive oral pills,period around the parturition, hypercoagulopathy

Consequences:

Increase in pulmonary artery pressure,Vado spasm,ischemia

Depend on size ,large embolus will olodge main pulmonary artery or major branches,small embolus will obstruct medianm and small arteries and depend on the heart state

Morphology:

Small embolus ……alveolar hemorrhage

Pulmonary infarct:

Morphology:

red blue ares of coagulation necrosis, occluded vessel near the apex of infarcted area

Red cells lysed within 48h……hemosiderin ……fibrosis (white,gray)……scar

Clinical features:
60-80%:silent
5% death due to cardiovascular collapse
10-15%dyspnea
Small ,medium pulmonary arteries occlusion:pulmonary infarction
<3% worsening dyspnea due to pulmonary hypertension,and pulmonary sclerosis
Management:
Prophylactic:walking,elastic stocking,leg exercises
Treatment:
Anticoagulant for massive pulmonary embolism,thrombolytic for pulmonary embolism in hemodynamically unstable patient
2.Non thrombotic pulmonary embolism: uncommon ,lethal
Amniotic fluid ,air ,fat embolism, Foreign body embolism(Iv drug users),BM embolism due to bone infarction secondary or sickle cell anemia
Pulmonary hypertension:
High pressure in the pulmonary circulation (mean arterial pressure=25mmHg)
Etiology:
decrease cross sectional area or increase in blood flow
Classification:
Pulmonary arterial hypertension affects small pulmonary arteriole ,inherited form,ct diseases,HIV virus,congenital heart disease

Pulmonary hypertension due to left side heart disease:systolic ,diastolic dysfunction ,valve diseases

Pulmonary hypertension due to lung disease or/and hypoxia:copd ,interstitial lung disease

Chronic Pulmonary thromboembolic hypertension

Pulmonary hypertension of unclear and multi factorial mechanisms

Morphology:
Muscular hypertrophy

Right ventricular hypertrophy

Pulmonary arterial atherosclerosis

Plexiform lesion :uncommon, web of capillaries span to the lumen of thin walled dilated small arteries extend outside the vessel

Diffuse alveolar hemorrhage syndroms :

1.goodpasture syndrome:autoimmune disease against type4(IV) collagen ,:males>females,active smokers,teens and teenagers
Treatment:
immunosuppressive drugs,plasmapheresis,kidney transplantation
Histology
Fibrous thickening of septa,focal necrosis in alveolar wall,intraalveolar hemorrhage (red ,brown cosolidation),hemosiderin,hypertrophy of type 2 pneumocyte ,IgG,Some times IgM or IgA (seen in alveolar septa)
Granulomatosis and polyangitis:

Lung lesions:Granulomatous inflammation,necrotizing angitis(vasculitis)
Symptoms:like URT symptoms:
Nasal perforation,epistaxis,sinusitis,in lung:cough,hemaptysis,cheesy pain,glumerulonephritis),necrotizing ,cresentic glomerulonephritis
Antineutrophil antibodies (ANCA)in 95%cases

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Lec6+7

Lung cancers:

Squamous cell carcinoma, Small cell lung carcinoma: associated with Smoking, at the Center, paraneoplastic Syndrome.
SCLC all cases metastasised,chemotherapy+/-radiotherapy but recur, no treated by surgery
NSCLC like adenocarcinoma, squamous cell carcinoma poorly response to chemotherapy and radiotherapy,can treat by surgery,better prognosis
Etiology
Accumulation of genetic abnormalities,due to carcinogens
Genetic predisposition
Mutations:
Early:inactivation of Timor suppressor genes located on chromosome 3
LateTP53tumor suppressor gene,KRAS
Mutation activate epidermal growth factor receptor,(adenocarcinoma in non smoker women)

Carcinogens:
Smoking(major cause,ex:pipes smoking, cigars, passive smoking), risk depend on the amount of smoking and pack years of cigarette somking ,env factors(arsenic, asbestos)
When stopping smoking ,lung cancer will not return to the base line level

Adenocarcinoma:most common

•Peripherally ,grow slowly,early metastasised,acinar(gland formation)
Histology:malignant epithelial cells:dysplasia,invasive surrounded by desomblasic reactions(fibrous tissue around the tumor)
Glandular architecture:can secrete mucin (well developed adenocarcinoma)
Immunostains:+ brown in the tumor cells ,so it is lung adenocarcinoma

Atypical adenomatous hyperplasia:
Equal to or less than5mm
No invasion ,single layer of lining epithelial cells shows atypia
Histology:nuclei are dark , atypia,septum is normal ,no break to basement membrane,

Adinocarcinoma in situ
mucinous,nonmucinous,or mixed tumor cells,Alveolar architecture is still preserved ,no invasion ,no desomoblastic reaction
<3cm
Minimally invasive adenocarcinoma:
<3 cm in diameter with an invasive component of <5mm
Invasive adenocarcinoma:
a tumor of any size with an area of invasion >5 mm

Squamous cell carcinoma:

Ranges from Well differentiated SCC showing keratin pearls and intercellular bridges to Poorly differentiated neoplasms with only minimal residual squamous cell features.

Squamous metaplasia:

ciliated pseudostratified columnar
epithelium is replaced by squamous epithelium.

Squamous dysplasia:

presence of disordered squamous epithelium, with loss of nuclear polarity, nuclear hyperchromasia, pleomorphism, and mitotic figures

.Carcinoma in situ (severe dysplasia):

there is full thickness of squamous epithelium showing cytologic atypia, lacking the basement membrane disruption.

Invasive squamous cell carcinoma:

lesions show cytologic atypia and basement membrane invasion.

Association: More common in men -Closely correlated with smoking history
Location:Arise Centrally in major bronchi and eventually spread to local hilar nodes and outside the thorax
Large lesions may undergo central necrosis, giving rise to cavitation.
• the lesion is asymptomatic until reaches a symptomatic stage when it begins to obstruct the lumen of a major bronchus, +/- atelectasis and infection.
• Goblet cell hyperplasia and basal cell hyperplasia are adaptive responses related to smoking.
• Hypercalcemia (secretion of a PTH related peptide).
•If NSCLCs detected before metastasis or local spread,cure is possible by lobectomy or pneumonectomy
•Most common in Males ,related to smoking
•Centrally located : In bronchi spread to hilum,outside the thorax
•Foci of necrosis and cavitation,large lesions
•Preneoplastic lesions: Squamous metaplasia……dysplasia……carcinoma in situ……squamous cell carcinoma
•Asymptomatic until make obstruction in major bronchi,with or without atelectasis and infection

•Adaptive mechanisms: due to injures to fight back ,reversible changes:metaplasia,hyperplasia,hypertrophy,atrophy
Goblet cell,basal cell hyperplasia,squamous metaplasia, squamous dysplasia,carcinoma in situ

•Well differentiated squamous cell carcinoma
1. keratin pearls production
2.Intercellular bridges spikes
3 .desmosomes

Small cell carcinoma

•Pale gray
•Under microscope:small cells,size as lymphocyte,big nucleus,less cytoplasm, granular chromatin like salt and pepper appearance
•Frequent mitosis,area of necrosis, able to fragile (crush artifact)

•nuclear molding(due to tumor cells adjacent to each other having scant cytoplasm,neuroendocrine markers,
•azzopardi effect(Basophilic staining of vascular walls due to encrustation by and from necrotic tumor cells ,accumulation of DNA of necrotic tumour cells)
•Closely correlated with smoking history
•Centrally located with extension into the lung paranchyma
• Early involvement of the hilar and mediastinal nodes. By the time of diagnosis, most will have metastasized to hilar and mediastinal lymph nodes.
• In the 2015 WHO Classification, SCLC is grouped together with large cell neuroendocrine carcinoma.
• Express neuroendocrine markers.
• Secreting hormones > paraneoplastic syndromes:
• Cushing syndrome (production of ACTH),
• Syndrome of inappropriate secretion of ADH
• Acromegaly (growth hormone- releasing hormone (GHRH) or growth hormone (GH)).
• Surgical resection is not a viable treatment.
• Very sensitive to chemotherapy but invariably recur.
• Median survival even with treatment is 1 year.

Large cell carcinoma
***Undifferentiated,large cells,large nucleus , moderate cytoplasm,atypia,no mucin ,no sign of differentiation, Lack cytologic features of small cell carcinoma and have no glandular or squamous differentiation,**
***undifferentiated malignant epithelial tumors**

Mixed patterns 5%
Adnecarcinoma+squamous cell carcinoma(adenosquamous)
Adnecarcinoma+small cell carcinoma

Carcinoid tumors:
composed of cells containing dense- core neurosecretory granules in their cytoplasm and, rarely, may secrete hormonally active polypeptides.
• well demarcated
• Typical carcinoids:
composed of nests of uniform cells
that have regular round nuclei with "salt-and-pepper" chromatin, absent or rare mitoses and little pleomorphism.
Atypical carcinoid:
tumors display a higher mitotic rate and small foci of necrosis.
• grow in one of two patterns:
(1) an obstructing polypoid, spherical, intraluminal mass.
(2) a mucosal plaque penetrating the bronchial wall to fan out in the peribronchial tissue—the so-called collar-button lesion.
•young adults (mean 40 years)
•originate in main bronchi mostly, Peripheral carcinoids are less common
5% of all pulmonary neoplasms. • malignant tumors, low-grade neuroendocrine carcinomas.
• subclassified as typical or atypical; both are often resectable and curable.
• May occur as part of the multiple endocrine neoplasia syndrome (MEN syndrome)
• 5% to15% of carcinoids have metastasized to the hilar nodes at presentation.
• distant metastases are rare.

• Atypical tumors have a higher incidence of lymph node and distant metastasis than typical carcinoids, have TP53 mutations in 20% to 40% of cases
• Rarely induces the carcinoid syndrome.
• Mostly manifest with symptoms related to their intraluminal growth, including cough, hemoptysis, and recurrent bronchial and pulmonary infections.
• 5- and 10-year survival rates: for typical carcinoids are above 85% , For atypical carcinoid 56% and 35%, respectively .
• May be associated with cushing syndrome, acromegaly.

Malignant Mesothelioma

At autopsy, the affected lung typically is ensheathed by a layer of yellow- white, firm, variably gelatinous tumor that obliterates the pleural space.
one of three morphologic appearances:
(1) Epithelial: cuboidal cells with small papillary buds line tubular and microcystic spaces (the most common & confused with a pulmonary adenocarcinoma) .
(2) sarcomatous: spindled cells grow in sheets
(3) biphasic: both sarcomatous and epithelial areas

Rare cancer of mesothelial cells lining parietal or visceral pleura
• Less commonly in the peritoneum and pericardium.
• highly related to exposure to airborne asbestos (80% to 90% of cases).
• Long latent period: 25 to 40 years after initial asbestos exposure.
• begin in a localized area and spread widely, either by contiguous growth or by diffusely seeding the pleural surfaces.
• Preceded by extensive pleural fibrosis and plaque.
• Distant metastases are rare.
• Normal mesothelial cells are biphasic, giving rise to pleural lining cells as well as the underlying fibrous tissue.

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Lec8:
TB:communicable granulomatous disease
etiology:mycobacteria;acid fast staining organism stained by ziel neelsen stain resist decolorizer
Types of mycobacterium:
1.huminis:most cases,by inhalation or exposure to secretions
2.bovis:oropharyngeal,intestinal TB,by contaminated unpasteurised milk
3.avium,less virulent,rarely causes disease in healthy patients

Pathogenesis:

*Before activation cell mediated immunity:
alveolar mac bind to mycobacterium ,bicilliary prolifation,bacteremia
*Initiation of cell mediated immunity:
Exposure to mycobacterium,bind to mannose or complement receptor on alveolar mac,activation of Mac,release IL2,TNF,activate type1helper T cell,release IFY-1,activate Mac,release TNF (monocyte recruitment),iNOS,defensins
**Immune response will cause hypersensitivity and tissue destruction,Defect in this mechanism will cause progression to the disease,reexposure will cause more necrosis rapid defensive mechanism
**95%cell mediated immunity will controls infection

Tuberculin test:
+ : can't didffereniate between disease or infection
_: Loss of hypersensitivity

False _:viral infection ,sarcoidosis,Hodgkin lymphoma,malnutrition,immunosuppresion
False+: atypical mycobacteria

Primary TB:

,limited,fever,pleural effusion,5%can cause progressive disease,dormant for years,develop in unsensitized patient,

Prognosis:

Scarring with viable bacilli can reactivate

Location :lower part of upper lobe ,upper part of lower lobe

Morphology:

Ghon focus:whitish gray inflammatory consolidation,Ghent complex(fibrosis and calcification),caseous necrosis,free bacilli or in phagocyte,**regional lymph node involvement**

Secondary TB:

In previously exposed (sensitized)patients with weakened resistance,<5%from orimaryTB,regional lymph node less evolved than primary,cavitation leading to erosion تآكل,infectivity source

Location :

Initial lesion 1-2cm in the apical pleura ,in the apex of the upper lobes

Morphology:

whitish gray to yellow central cassation ,peripheral fibrosis

Active lesion(bacilli with central cassation),bacilli found in early exhudative and caseative stages,impossible seen in late fibrocalcific stage

Healing :

with fibrosis either spontaneously or during therapy

Progressive TB

More central caseation

Erosion in bronchus evacuate the caseous centre to irregular cavity lined by caseous material

Hemoptysis is:erosion in blood vessels

Stopped by treatment,if it is inadequate lead to progression and dissemination through airway,lymphatic,vascular system

Military pulmonary disease:

Reassemble milett seedsالدخن اسمها نبته بذور,small white yellow consolidation in lung paranchyma,

Causes:Granulmatous lesions ,endotracheal,endobroncheal,layrngealTB

With progressive pulmonary tuberculosis, the pleural cavity is invariably involved and serous pleural effusions, tuberculous empyema(pus accumulation), or obliterative fibrous pleuritis develop

Systemic military TB:

It inmost prominent in,bone marrow,spleen,adrenal glands,meninges, kidneys, fallopian tubes, and epididymis

Isolated organ TB

TB in kidney (renal TB)

Mininges(tuberculous meningitis)

Fallopian tube (salpingitis)

Vertebrae (pott disease)

Lymphadenitis:

Extrapulonray TB,cervical region ,univocal,in HIV patients(have multifocal disease, systemic symptoms, and either pulmonary or other organ involvement by active tuberculosis).

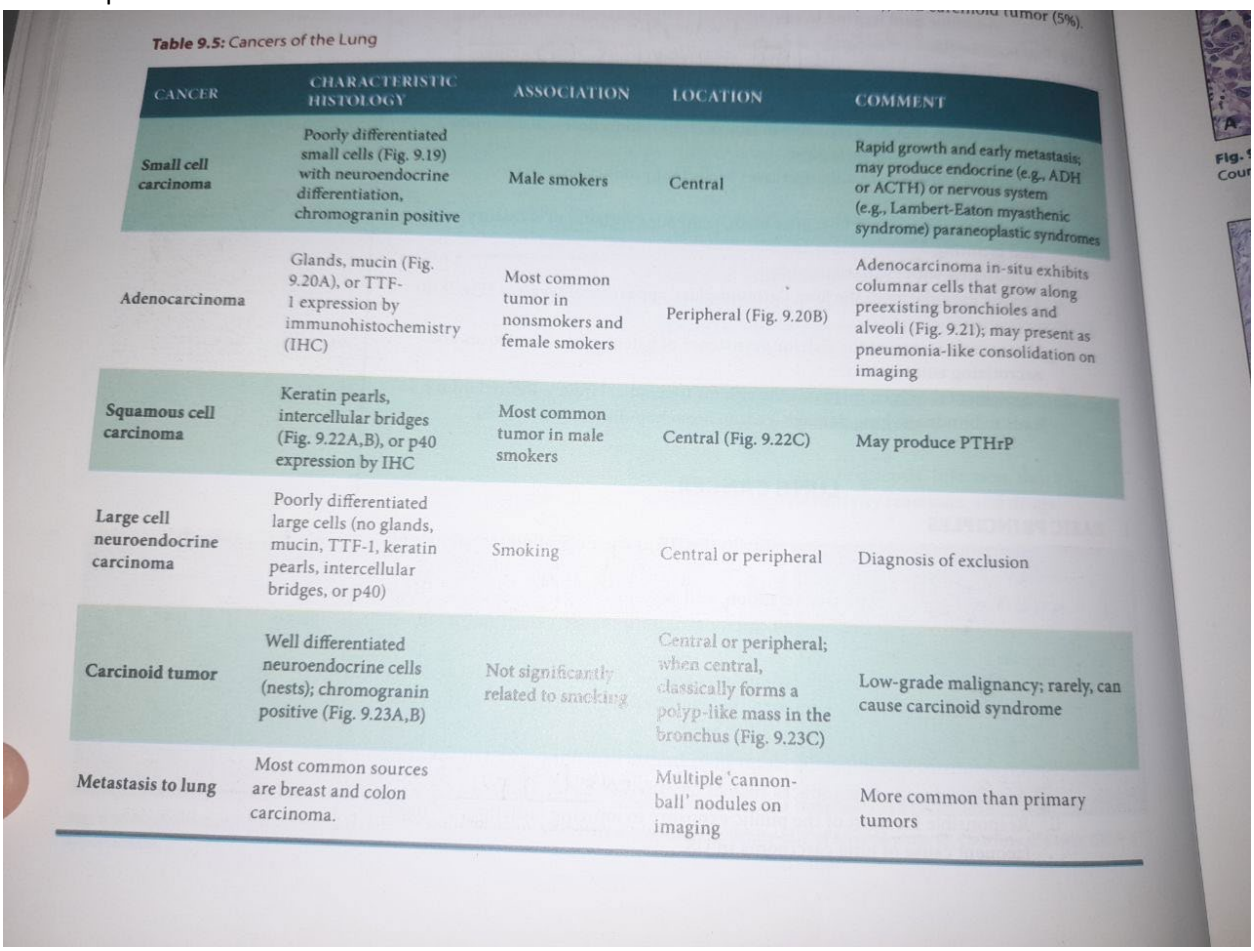
Asymptomatic

Systemic:remittent and lower grade fever(lower or higher than normal), night sweats WL,malaise,anorexia

Pulmonary:mucoid sputum(early),purulent(later)sputum with bacilli,hemoptysis,cavitation,pleuritic pain

Extrapulmonary manifestations:
infertility, headache, neurologic deficits, back pain and paraplegia.
Diagnosis:
Physical,history ,radiology
TB must be identified by:
***culture(10weeks)(standard)**
***Liquid media based radio metric assay(2weeks)**
***PCR**
***Fluorescent auramine rhodamine**
Prognosis:
Extent of infection
Sensitivity of organism or Ab
Immunity state

From pathoma



carcinoid tumor (5%).

Table 9.5: Cancers of the Lung

CANCER	CHARACTERISTIC HISTOLOGY	ASSOCIATION	LOCATION	COMMENT
Small cell carcinoma	Poorly differentiated small cells (Fig. 9.19) with neuroendocrine differentiation, chromogranin positive	Male smokers	Central	Rapid growth and early metastasis; may produce endocrine (e.g., ADH or ACTH) or nervous system (e.g., Lambert-Eaton myasthenic syndrome) paraneoplastic syndromes
Adenocarcinoma	Glands, mucin (Fig. 9.20A), or TTF-1 expression by immunohistochemistry (IHC)	Most common tumor in nonsmokers and female smokers	Peripheral (Fig. 9.20B)	Adenocarcinoma in-situ exhibits columnar cells that grow along preexisting bronchioles and alveoli (Fig. 9.21); may present as pneumonia-like consolidation on imaging
Squamous cell carcinoma	Keratin pearls, intercellular bridges (Fig. 9.22A,B), or p40 expression by IHC	Most common tumor in male smokers	Central (Fig. 9.22C)	May produce PTHrP
Large cell neuroendocrine carcinoma	Poorly differentiated large cells (no glands, mucin, TTF-1, keratin pearls, intercellular bridges, or p40)	Smoking	Central or peripheral	Diagnosis of exclusion
Carcinoid tumor	Well differentiated neuroendocrine cells (nests); chromogranin positive (Fig. 9.23A,B)	Not significantly related to smoking	Central or peripheral; when central, classically forms a polyp-like mass in the bronchus (Fig. 9.23C)	Low-grade malignancy; rarely, can cause carcinoid syndrome
Metastasis to lung	Most common sources are breast and colon carcinoma.		Multiple 'cannon-ball' nodules on imaging	More common than primary tumors

Past papers:

1) Which of the following is wrong regarding chronic bronchi﷽s:
A) Caused by air pollutants
B) May be manifested by wheezing
C) Obstructive bronchitis manifest as blue bloaters
D) Significant airway obstruction results in almost always complicated by chronic bronchiolitis
ANS: D

2) Which of the following is correct about TB :
A) Primary TB is not infective
B) Regional lymph nodes are less involved in secondary TB
C) 80% of primary TB becomes secondary
ANS: B

3) Which of the following is correct about TB (again):
A) Secondary TB is localized in the lower lobe
B) Mycobacterium Bovis causes oropharyngeal TB
C) Mycobacterium Avium Complex causes disease in 3% of AIDS pa﷽ents
ANS: B

4) Which of the following is true regarding pulmonary embolism:
A) The more peripheral the embolic occlusion the lower the risk for infarction
B) 40% of them are silent
C) Consequences are only determined by the size of the embolus
D) Small emboli cause alveolar hemorrhage
ANS: D

5) Which of the following is true about Goodpasture syndrome:
A) Autoimmune disease that affects the lungs only
B) IgG granular deposition in the lung is diagnostic
C) Results in necrotizing hemorrhage interstitial pneumonitis
D) Predominance in females

ANS: C

6) Choose the true sentence:
A) Hyalinized collagen fibers are found in silicosis
B) asbestos bodies are golden brown rounded structures
C) pleural plaques contain Ca++ and iron
ANS: A

7) Mass that contains large cells, with large nuclei and prominent nucleoli, and show no glandular or squamous differentiation , what is the diagnosis?
A) Squamous cell carcinoma
B) Large cell carcinoma
C) Carcinoid tumor
D) Small cell carcinoma
ANS: B

8) True about sarcoidosis:
A) Higher prevalence in smokers
B) Mainly occupational disease
C) In liver it manifests as granulomas surrounding central veins D) In more than 50%, it causes granuloma in spleen
ANS: D

9) True about adenocarcinoma:
A) Forms large masses
B) Centrally located
C) It has a wide range of metastasis in a short ?me
ANS: C

10) True about lung tumors:
A) They have good prognosis
B) Adenocarcinoma is the most common in smokers
C) Women are more susceptible to carcinogens in tobacco than men

ANS: C

11) Long case of a tumor that begins centrally in a localized area and spread widely to the pleura (pleural cell proliferation), this case is associated with?
A) Distant metastasis
B) Adenocarcinoma
C) Extensive pleural fibrosis
ANS: C

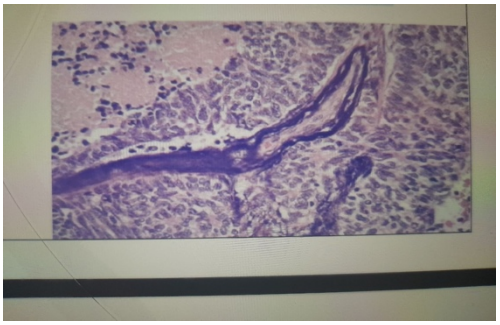
12) Interalveolar fibrosis with patchy air space consolidation:
A) Cryptogenic Organizing pneumonia
B) Carcinoid syndrome
C) Nonspecific interstitial pneumonia
ANS: A

13) 51-year-old patient presented with right chest pain that increases with inspiration which one is the less likely diagnosis:
A) Pneumonia
B) Pulmonary embolism
C) MI
D) Pneumothorax
ANS: C

14) What's specific about sarcoidosis?
A) Non-caseating granuloma
B) Schaumann bodies
C) Asteroid bodies
D) None of the above
ANS: D

15) Case about man, heavy smoker, presented to the clinic with nausea, vomi  ng and malaise. A clinical history and physical examinaon and lab results revealed

signs and symptoms consistent with the syndrome of inappropriate an�diure�c hormone. A chest X-Ray showed an ill-defined 5 cm mass involving the le� hilum of the lung, lung biopsy was performed and captured in the figure below, based on your diagnosis, which of the following statement is CORRECT?
A) Surgery is a curative treatment
B) It's an asbestos related tumor
C) Early involvement of lymph nodes
D) It's an undiffereniated tumor
E) This tumor never metastasizes



ANS: C

16) A 40-year-old man, non-smoker, presented with increasing dyspnea for the past 5 years, the disease involves mainly the lower lung lobe, pulmonary func�on test showed an obstructive patern, A lung biopsy showed enlarged air spaces and destruction of alveolar wall without fibrosis, what is the most likely cause of this disease?
A) Type-1 IgE mediated hypersensitivity reaction
B) Genetic abnormality resulting in primary ciliary dyskinesia
C) Reduced anti-elastase activity
D) Mucus hypersecretion and outflow obstruction
E) poorly differeniated adenocarcinoma
ANS: C

17) Regarding bronchiectasis, one of the following statements is CORRECT:
A) It's a primary inherited pulmonary disease

B) considered as reversible obstruc﷽ve pulmonary disease C) Alveolar sacs are the most involved part
D) Heals with complete resolu﷽on and no fibrosis
E) patient present with cough and purulent sputum
ANS: E

18) Regarding lung tumors, one of the following is CORRECT:
A) Small cell carcinoma is the most common type
B) Lung hamartomas are classified as developmental anomalies
C) Squamous cell carcinoma are the most common tumors in women D) Most carcinoids are peripherally located in the lung
E) Mesothelioma can be epithelial, sarcomatous, or mixed
ANS: E

19) Regarding pneumoconiosis, one of the following is CORRECT:
A) Coal worker pneumoconiosis is associated with increased risk of lung cancer
B) Pleural plaques are the most common manifestaion of asbestos exposure
C) pneumoconiosis is defined as chronic restrictive lung disease with unknown etiology
D) Pulmonary anthracosis is associated with progressive dyspnea and cough
ANS:B

20) Case about man with chronic cough and weight loss, clopping of fingers, X-Ray shows sub-pleural proliferaton, lung biopsy shows glandular formation, TTF-1 immune stain is positive, what is your diagnosis?
A) Adenocarcinoma
B) Squamous cell carcinoma
C) Small cell carcinoma
D) Large cell neuroendocrine carcinoma
E) Sarcomatous mesothelioma
ANS: A

21) Regarding sarcoidosis one of the following is CORRECT:

A) hypercalcemia in sarcoidosis isn't related to bone destruc□on
B) the presence of non-casea□ng granuloma in lung biopsy is diagnos□c
C) Asteroid bodies are laminated concre□ons that contain calcium
D) The non-caseating granulomas are centered within the alveolar spaces
E) Corneal opacification are the most common presenta□on of eye involvement
ANS: A

22) Regarding pulmonary embolism, which statement is correct:
A) Large saddle PE are associated with no histologic altera□on B) Most PE arise from thrombi in the heart ventricle
C) Pulmonary infracts are usually in the upper lobe
D) The most common symptom of PE is progressive dyspnea E) Bone marrow embolism is common in IV drug abusers
ANS: A

23) Case about man with increasing dyspnea, smoker for 25 years, physical examination shows decreased breathing sound aver the upper lung, radiography shows hyperventilaton, pulmonary function test shows obstructive patern, which structure is mostly affected by this disease?
A) Main bronchi
B) Terminal bronchioles
C) Respiratory bronchioles
D) Alveolar duct and sack
E) Pleural lining
ANS: C

24) Which of the following is associated with slowly progressive restric□ve lung disease showing whorls of concentrically arranged hyalinized collagen bundles surrounding amorphous center?
A) Coal dust
B) Tobacco smoke
C) Mushroom
D) Crystalline silica
E) Asbestos

ANS: D

25) Regarding the pathogenesis of atopic asthma one of the following statements is correct:
A) the initial response upon first exposure is associated with type-1 helper lymphocyte activation
B) IL-4 & IL-5 are secreted from alveolar macrophages during the early phase response
C) phago-lysosomal maturation arrest is essential in the pathogenesis during early phase
D) Eotaxin is a potent chemoatractant and activator of eosinophils in late phase
E) early phase is triggered by antigen induced crosslinking of IgG bound to receptor on mast
cells
ANS: D

26) Which of the following diseases affect the lower lung lobe?
A) Distal acinar emphysema
B) Silicosis
C) Bronchiectasis
D) Coal worker pneumoconiosis E) Hypersensi�vity pneumoni�s
ANS: C

27) Regarding primary pulmonary TB which is correct?
A) T-cell mediated immune response develops within the first 30 minutes after exposure
B) Bacteremia is usually asymptomatic or associated with mild symptoms
C) The first step after mycobacteria entry is the activation of phagolysosome killing
D) TNF mobilizes antimicrobial defensins against the mycobacteria
E) IL-12 stimulate expression of inducible nitric oxide synthase to produce ni�c oxide
ANS: B

28) Regarding TB, one of the following is correct?

A) Mycobacterium avium complex is associated with intestinal TB
B) Pulmonary TB is associated with extensive lymph node involvement
C) 95% of primary TB causes develops a progressive disease
D) Apical lung involvement is characteris�c of secondary TB
E) Lung cavitation is more common during primary disease
ANS: D

29) Regarding cobble stone appearance of the pleural surface which statement is correct?
A) Associated with usual interstitial pneumonia patern (UIP) of fibrosis
B) Characteristic of pleural involvement by malignant mesothelioma
C) Happens due to lung hyperinflation and air trapping
D) Associated with miliary pulmonary tuberculosis
E) Characteristic of non-specific interstial pneumonia (NSIP)
ANS: A

30) Regarding pneumoconiosis which is correct?
A) The most dangerous mineral dust par�cle range in size between 5-10 µm
B) Tobacco smoking worsens the effect of all inhaled minerals dust except for asbestosis C) Simple coal worker pneumoconiosis is associated with centre-acinar emphysema
D) The pure form of quartz is less fibro-genic and toxic than mixed form
E) Asbestosis is associated with increased risk of primary tuberculosis
ANS: C

31) Which of the following is true:
ANS: coal worker's pneumoconiosis is found in the upper lobes of the lung, so are silicosis nodules

32) Which of the following is true:
ANS: Adenocarcinoma is the most common lung tumor

33) Which of the following is wrong about emphysema:

ANS: Usually in the lower lobes

34) Which of the following is wrong about ARDS:
ANS: In most patients, after the acute phase pulmonary function is restored in a year or two

35) Which of the following is wrong about the lungs:
ANS: Obstructive over inflaton is due to complete destruc﷽on of affected area

روابط أسئلة من كتب :لا تخافوا

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ولا تنسوا تدعوا لأخواننا في غزة العزة وأهلنا بالسودان وإدلب وباقي بلاد المسلمين بالنصر والرحمة للشهداء وأن يربط على قلوبهم ويلهمهم الصبر والسلوان وحسبنا الله ونعم الوكيل