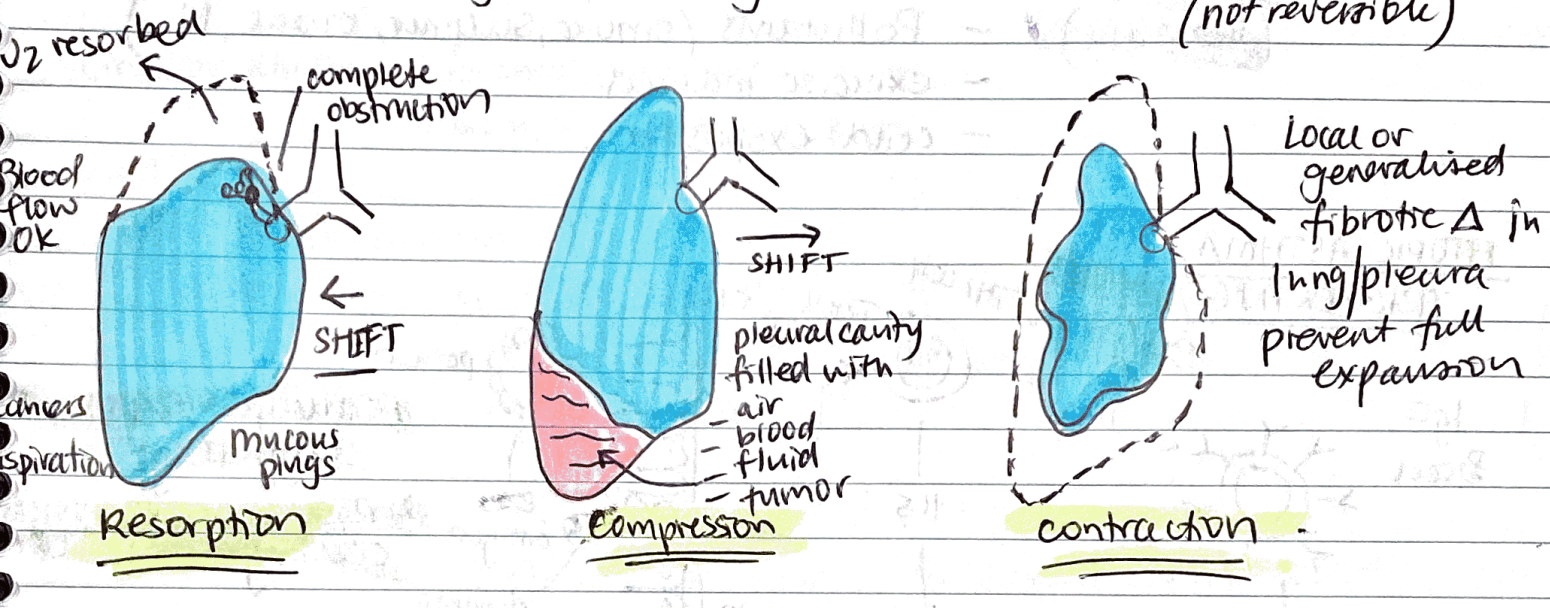
Pathology week 10 - Resp 2.

1. What is atelectasis?

→ incomplete expansion (i.e neonatal atelectasis)

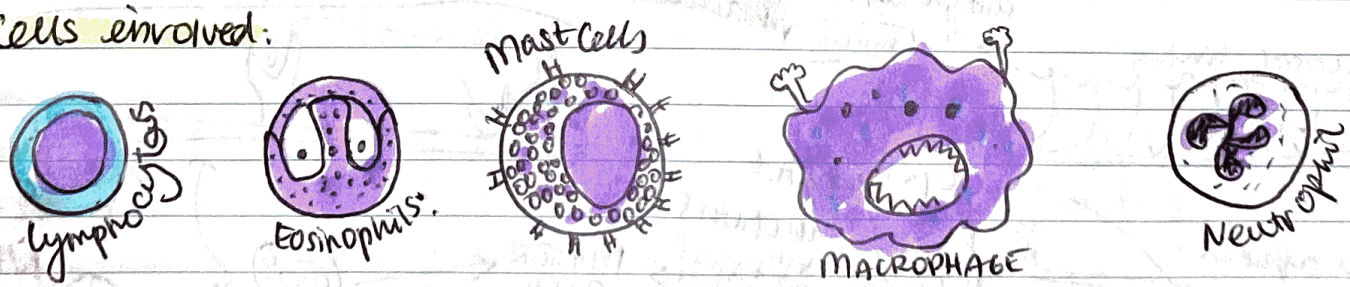
→ collapse of previously inflated lung



2. Pathogenesis + morphology of asthma (4) ↑airway responsiveness

ASTHMA = disorder of conducting airways caused by immunological reaction. marked by episodic bronchoconstriction due to airway sensitivity to a variety of stimuli, inflammation of bronchial walls, ↑mucus secret°.

Cells involved:



Types of asthma:

ATOPIC - most common, IgE (type 1) hypersens rxn, TH2 mediated. 2 phases: immediate (bronchoconstriction) & late (inflammation phase)
cytokines IL-4, IL-5, IL-13 important. Environmental triggers.

NON ATOPIC - no allergen (neg skin test) FHx rare, viral URTI triggers

Drug induced i.e aspirin

Occupational i.e fumes from epoxy, chemicals, wood dust,

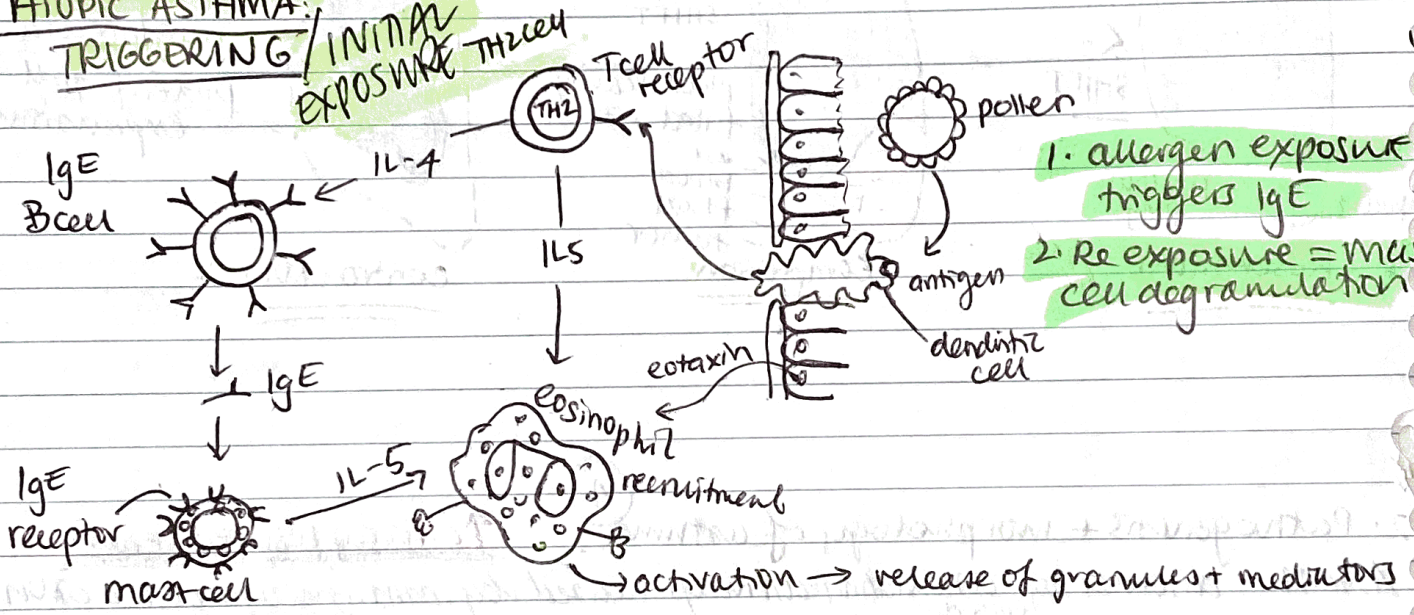
Triggers

ATOPIC
- environmental (pollen/dust/food/animal dander)
- pro-inflam cofactors i.e URTI

NON-ATOPIC (less clear)
- Viral URTI (rhino/RSV/para flu)
- Pollutants (smoke, sulphur, ozone, N_2)
- exercise induced
- cold exposure.

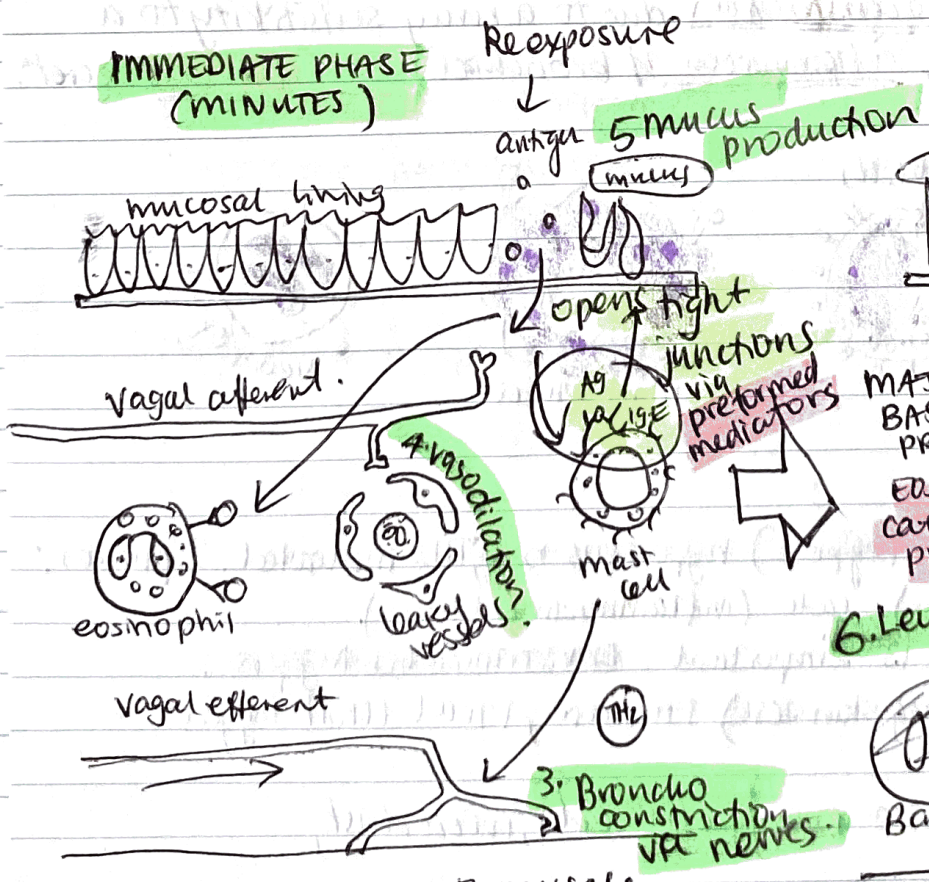
ATOPIC ASTHMA:

TRIGGERING/INITIAL EXPOSURE



1. allergen exposure triggers IgE
2. Re exposure = mast cell degranulation

IMMEDIATE PHASE (MINUTES)



LATE PHASE/HOURS

ASTHMA NOTES:

Drug induced asthma — occurs in older people
- sensitivity to a drug.
- Aspirin + NSAIDs can cause.
- ACE inhibitors can cause cough.

Circadian Rhythm = maximal constriction at 6am
maximal dilation at 6pm.

VIVA QS.

What is bronchiectasis?

Disease characterized by permanent dilatation of bronchi & bronchioles caused by destruction of muscle + elastic tissue by chronic neutrophilic infections.

What factors can predispose to bronchiectasis?

Congenital — cystic fibrosis, ciliary dyskinesia, immunodeficiency
Infections — Staph, TB, haemophilus
Bronchial obstruction — tumour, foreign body
Other: RA, SLE
Idiopathic: 25-50%.

Emphysema: a chronic lung condition characterised by irreversible enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of alveolar walls without fibrosis.

Pathogenesis:
- loss of homeostasis from exposure to toxic substances → mild chronic inflammation.
- ongoing inflammation, epithelial cell death, ECM proteolysis
- neutrophils, macrophages, lymphocytes release elastases, cytokines (IL-8) and oxidants → epithelial injury + oxidant-antioxidant imbalance; proteolysis "protease – antiprotease imbalance"
- destruction of walls without fibrosis.
- Reactive oxygen species. ABUNDANT

1% pts α1AT deficiency

Phenotypes: dyspnoea, dry cough, occasional infections, hyperinflated in small heart, not cyanotic, prolonged expiration with pursed lips, normal gas exchange until late in disease.

Complications of emphysema:
- bullous lung disease
- expiratory airflow limitation
- infection
- respiratory failure
- pneumothorax
- cor pulmonale / CHF

95% centriacinar / upper lobes + apices = smoking b/c distribution of smoke particles impacted in small airways. assoc w chronic bronc

Panacinar = α1AT deficiency + chronic low level destruction from neutrophils in lung circulation. Lower basal zones.

also – distal acinar (paraseptal) → causes spontaneous pneumothorax in young adults.
irregular – airspace enlargement with fibrosis
- compensatory emphysema – i.e after lobe resection
- senile emphysema
- bullous emphysema – subpleural blebs
- interstitial emphysema – air into connective tissue
- obstructive overinflation – partial blockage, air trapping
- paraseptal / ductal – spontaneous pneumothorax, near to pleural edge

NB: α1-antitrypsin → major inhibitor of proteases secreted during inflammation. Allele on ch 14 → polymorphic.
↓ expression = unchecked proteases.

Chronic Bronchitis: persistent cough ± sputum production for >3months in 2 consecutive years in the absence of other cause.

Pathogenesis: Longstanding irritation by inhaled substances i.e tobacco smoke, dust from grain / silica / cotton.
Hypersecretion of mucus & hypertrophy of glands.
↑ goblet cells of bronchi + bronchioles
Sputum over production & COAD.
Secondary infection also contributes to discussion.

Phenotype: Sputum, ↑CO_2 ↓O_2 cyanosis.
Cor pulmonale + CHF

Reid index is ↑ (normal ~~0.4~~)
= thickness of wall b/w epithelium + cartilage.

ARDS

Pathogenesis: 1. Injury to alveolar capillary membrane (endothelium)
2. Acute inflammatory response
3. ↑ vascular permeability + alveolar flooding
4. Fibrin deposition, hyaline membranes & widespread surfactant abnormalities via damage to type II pneumocytes.
5. Scarring + fibrosis. (or death)

What conditions can lead to ARDS?
- Infection: sepsis, ~~trauma~~, diffuse pulmonary inf, aspiration
- Physical / Injury: (head trauma, pulmonary, #'s, near drowning, burns, radiation)
- Inhaled irritants (O_2 toxicity, smoke, irritant gas + chemicals)
- chemical injury (heroin, barbiturate, aspirin, paraquat
- haematological (multiple transfusions, DIC)
- other (pancreatitis, uraemia, bypass).

Bronchiectasis → permanent dilation of bronchus caused by destruction of muscle + elastic tissue

VIVA Q's:

TUBERCULOSIS

Pathogenesis

- Airborne spread
- Enters alveolar macrophages, they cant digest bacilli, bacilli replicate within macs + then spread.
- Delayed hypersensitivity reaction → T cells contribute to caseating granuloma formation
- Re-exposure causes heightened immune reaction & tissue destruction.
- Infection may be controlled & contained or may spread.

Natural History

1. primary infection
2. primary complex (Ghon focus) → calcified scar = Ghon complex. of local caseation
3. may heal vs become latent TB vs progressive primary TB
4. Latent period or progressive primary disease
5. Reactivation ⇒ secondary TB.
6. Localised caseating lesions or progressive 2° disease → miliary TB.

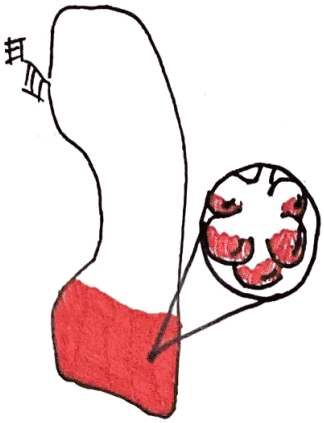
Diagnosis

- Clinical features plus CXR changes
- Sputum microscopy x 3
- PCR
- Mantoux test.

Stages of pneumonia

CONGESTION

- Vascular engorgement
- intra alveolar fluid
- Bacteria ++
- few Nϕ
- Boggy, heavy, red



RED HEPATISATION

- Massive confluent exudate
- Neutrophils ++
- RBCs ++
- Fibrin ++ fills alveoli
- Airless + red like liver

GREY HEPATISATION

- Progressive disintegration of RBCs
- Fibrinosuppurative exudate
- greyish brown lobe
- Dry surface

RESOLUTION

- Enzymatic digestion
- macrophages
- semifluid debris is reabsorbed.

* Wk 11 Pathology *

PNEUMONIA

Contributing factors:

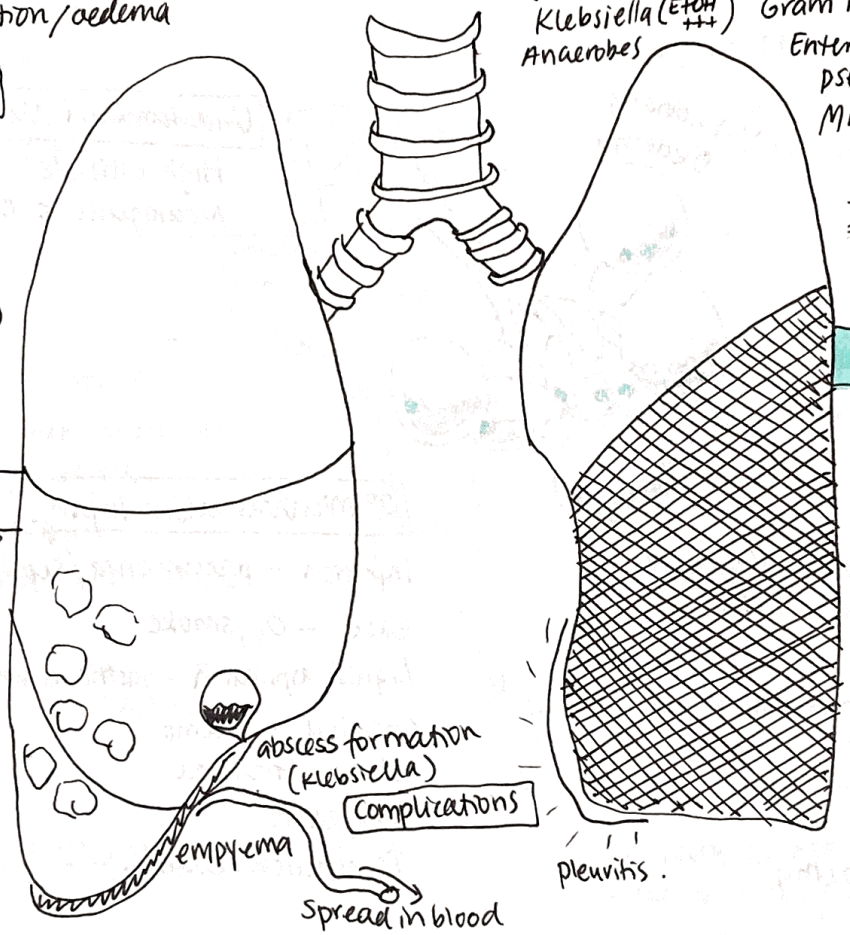
→ ↓cough reflex → aspiration
→ injury to mucociliary apparatus (smoking / viral URTI)
→ accumulation of secretions (CF / bronch)
→ ↓phagocyte action (EtOH / smoke / anoxia)
→ pulmonary congestion / oedema

Host baseline factors

- Extremes of age
- CCF / COPD / T2DM
- immunodeficiency
- No spleen or ↓ function (sickle cell)
- IVDU (endocarditis + pneumo)

Bronchopneumonia

→ patchy suppurative inflammation



Mycoplasma pneumonia

- droplet spread
- incubation 1–4 weeks
- spreads b/w housemates / schools / army barracks / nursing homes
- may not have productive cough (atypical)
- chest may be clear

CAP

COPD exac ← S. pneumo, H. influenz, Morax ella
post flu ← Staph aureus
Legionella → transplant pts. → water

Abscess or Necrotising

S. aureus
Klebsiella (EtOH +++)
Anaerobes

HAP

Gram negatives
Enterobacter
pseudomonas → (CF)
MRSA

"pneumonitis"

Atypicals (CAP)

Mycoplasma pneumo
Chlamydia spp.
Q fever (coxiella burnetti)
Viral

Aspiration.

Anaerobes from oral mucosa + aerobes → Spneumo
→ S. aureus
→ H. influenzae
→ pseudomona

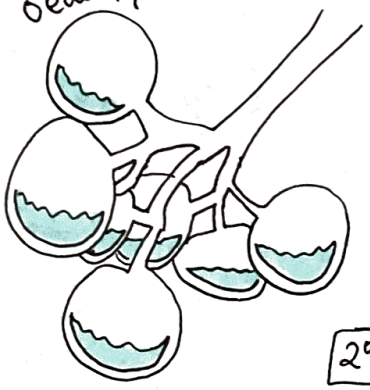
Immunocomp

CMV + PJP
Mycobact. avium.
Aspergillus
} also the typical stuff.

LOBAR PNEUMONIA

1. Congestion – engorgement.
2. Red hepatisation – nφ, RBCs, fibri
3. Gray hepatisation – fibrin + suppurative exudate ↓RBCs.
4. Resolution – enzyme digestion, ingested by macs,

Pulmonary oedema



Undetermined Mechanism

High altitude
Neurogenic i.e CNS trauma

Haemodynamic Causes

↑ hydrostatic pressure from ↓LV output
→ also pulmonary vein obstruction

↓ oncotic pressure (less common)
- low albumin
- Nephrotic sy
- Liver disease
- protein losing enteropathy

Morphology:

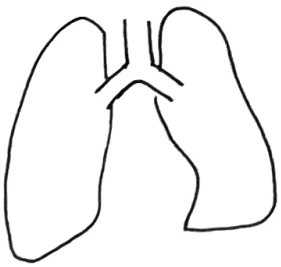
Heavy, wet lungs
Dependant oedema
Haemosiderin-laden macs "heart failure cells"
Long term → fibrosis + brown induration

2° Microvascular Injury

Infection – pneumonia / sepsis
Gases – O_2, smoke
Liquid aspiration – gastric contents, near drowning
Chemicals – chemo
shock / trauma
Radiation
Transfusion related.

Morphology:

Localised oedema
Overshadowed by the cause
Can cause ARDS if diffuse.



Pleural effusions

Bilateral exudative

→ SLE
→ Rheumatoid
(systemic inflammatory diseases)

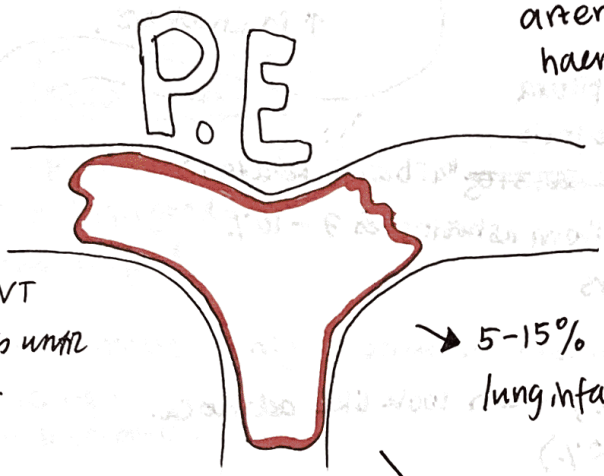
RISK FACTORS

1° Factor V Leiden, antiphospholipid syndrome, prothrombin mutations

2° Obesity, OCP, cancer, immobilisation, pregnancy, hip #, long flights.

95% from DVT

But DVTs occur twice as frequently as PE's.



Obstruction of medium sized arteries may result in pulmonary haemorrhage.

Pathogenesis

Fragmented thrombi from DVT carried through larger vessels until hitting pulmonary vessels.

Can be saddle or smaller.

Frequently multiple → risk of more

"paradoxical embolus" — crosses to arterial circulation via defect.

→ 5-15% of PEs progress to lung infarction

→ 60 - 80% are clinically silent.

→ sudden cardiovascular collapse occurs if 60%+ of pulmonary circulation is obstructed by emboli.

Symptoms + signs (60% - 80% silent)

- Chest pain
- Dyspnoea
- Collapse / syncope
- Hypoxia
- Tachypnoea
- Tachycardia
- Shock
- Sudden death
- RHF.
- Fever
- Haemoptysis
- Cough

Severity of patho physiological response determined by:

→ Extent of pulmonary arterial flow obstructed.

→ Size of occluded vessel

→ number of emboli

→ overall CVS status

→ Release of vasoactive factors i.e thromboxane A_2.

LUNG cancer – Pleural tumours

Primary or secondary (2° most common) → mets from lung + breast

Solitary fibrous tumour

- attached by a pedicle to pleural surface
- varying size
- confined to surface

NB No ↑ risk of mesothelioma in asbestos workers who smoke. But asbestos related lung carcinoma is ↑ in smokers.

Malignant Mesothelioma

- arise from visceral or parietal pleura
- ↑ incidence in people ẅ asbestosis
- up to 90% malignant meso. ~~2° asbestos~~ "asbestos related"
- lifetime risk of mesothelioma from asbestos is 7 – 10%
- latent period of 25 – 45 yrs
- Main types:
  - epithelioid (60%) – can look like adenoca.
  - sarcomatoid (20%)
  - mixed (20%)
- Clinical Presentation
  - cough, dyspnoea
  - recurrent pleural effusions
  - concurrent asbestosis 20% people.
  - 50% pts die within 12 months
  - ↑ #s of asbestos bodies found in meso pts.

± can have extrapulmonary disease i.e peritoneal in heavy exposure.

Bronchogenic cysts

Single or multiple.
Anywhere in lungs
Adjacent to bronchioles, can communicate ẅ tracheobronchial tree.
Lined by bronchiolar type epithelium + filled ẅ mucinous secretions.

Complications
- rupture + haemorrhage
- infection
- PTX
- interstitial oedema
- Small risk of malignant deterioration.

Malignant Epithelial Lung Tumours – 95% carcinoma, 5% carcinoid, 2-5% other

↳ usually arise in hilum 3/4 from bronchi.

Squamous Cell (SCC)

- Males 32%, females 25%
- preceeded by squamous metaplasia / dysplasia
- Associated w smoking

Path: SCC: keratin pearls
highest frequency of p53 mutations

Small Cell Ca (SCLC) Smokers cancer

- distinctive cell type: epithelial cells, small w scant cytoplasm, salt + pepper appearance.
- HIGHLY MALIGNANT & high grade
- cells round / oval / spindle shaped.
- Necrosis common
- strong relationship to smokers – only 1% occur in nonsmokers.
- paraneoplastic syndromes.
- surgical resection ineffective.

Adenocarcinoma (most common) @ the margins.

- Glandular differentiation or mucin production by tumor cells.
- Most common in women + nonsmokers.
- Lesions smaller + more peripheral than squamous cell ca. (presents as peripheral mass)
- slower growth than SCC but metastasise early + far.
- subtype → bronchioalveolar Ca.

Large cell Ca

- undifferentiated malignant epithelial tumour
- large nuclei, moderate cytoplasm
- can be neuroendocrine tumour

NB: lung cancer mets most likely to adrenals.

Horners Syndrome from pancoast tumour

Miosis, partial ptosis, anhydrosis & enophalmos.

Tumour in apex invades the wall
- invades lower brachial plexus causing ulnar distribution of pain

Sympathetic fibres from hypothalamus synapse in sup-erior cervical ganglion
sympathetic plexus (near ICA)

Sympathetic fibres to this ganglion go around subclavian artery where they can be invaded by tumour.