Pulmonary vascular diseases

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Objectives

At the end of this lecture you should be able to

- List the causes, and describe the morphology of lung in pulmonary oedema
- List the causes and describe the morphology of lung in

  Acute respiratory distress syndrome (ARDS)
- List the causes and describe the morphology of lung in

  pulmonary embolism, haemorrhage and infarction
- List the causes and describe the morphology of lung in

  pulmonary hypertension

Pulmonary congestion and oedema

- Congestion is a passive process due to reduced outflow of blood from a tissue
- Red cell stasis and accumulation of deoxygenated hemoglobin gives a reddish-blue colour to the tissue
- Congestion usually leads to oedema

Chronic passive congestion - results in ischaemia and scarring of tissue

- Capillary rupture results in small haemorrhagic foci and later , haemosiderin laden macrophages

Pulmonary oedema - Causes

Oedema due to haemodynamic disturbances	Oedema due to microvascular injury
Increased hydrostatic pressure *(Read - Starling's law of capillary interstitial fluid exchange)*	Infectious agents - Viruses , mycoplasma etc.
Left side heart failure	Inhaled gases - oxygen , sulfur dioxide, cyanide , smoke
Mitral stenosis	Liquid aspiration - gastric contents, near drowning
Volume overload	Drugs and chemicals
Pulmonary vein obstruction	Shock, trauma, sepsis
Decreased oncotic pressure	Radiation
Hypoalbuminaemia	
Nephrotic syndrome	
Liver disease	
Protein loosing enteropathy	
Lymphatic obstruction	

Pulmonary oedema in heart failure

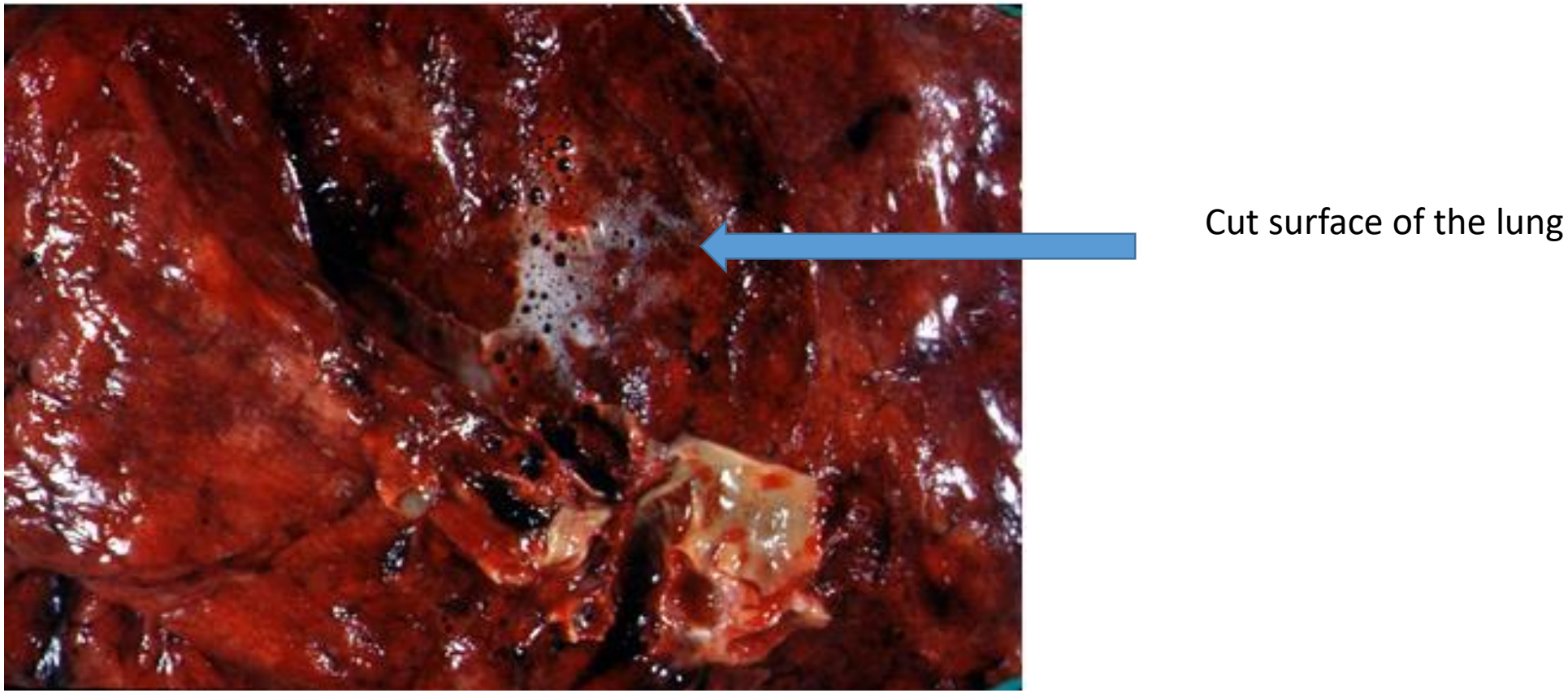
- Pressure in the pulmonary veins increase and transmitted to the capillaries and arteries
- Results in perivascular and interstitial transudate
  - Particularly in interlobular septae (*X-ray finding : Kerley B lines*)
  - Progressive oedema results in widening of the alveolar septae
  - Accumulation of oedema fluid in the alveolar spaces
  - Red cell extravasated in to the oedema fluid , engulfed by macrophages which later results in haemosiderin laden macrophages

Pulmonary oedema

- Macroscopy : Heavy and wet lungs: two to three times the normal weight

  Cut surface - frothy, blood stained fluid

  (a mixture of air, oedema fluid and extravasated RBC)



Pulmonary oedema

- Microscopy : **Acute pulmonary congestion**

  - Engorged alveolar capillaries, alveolar septal oedema

  - Focal intra-alveolar haemorrhage

  - Pink colour oedema fluid in the alveolar spaces

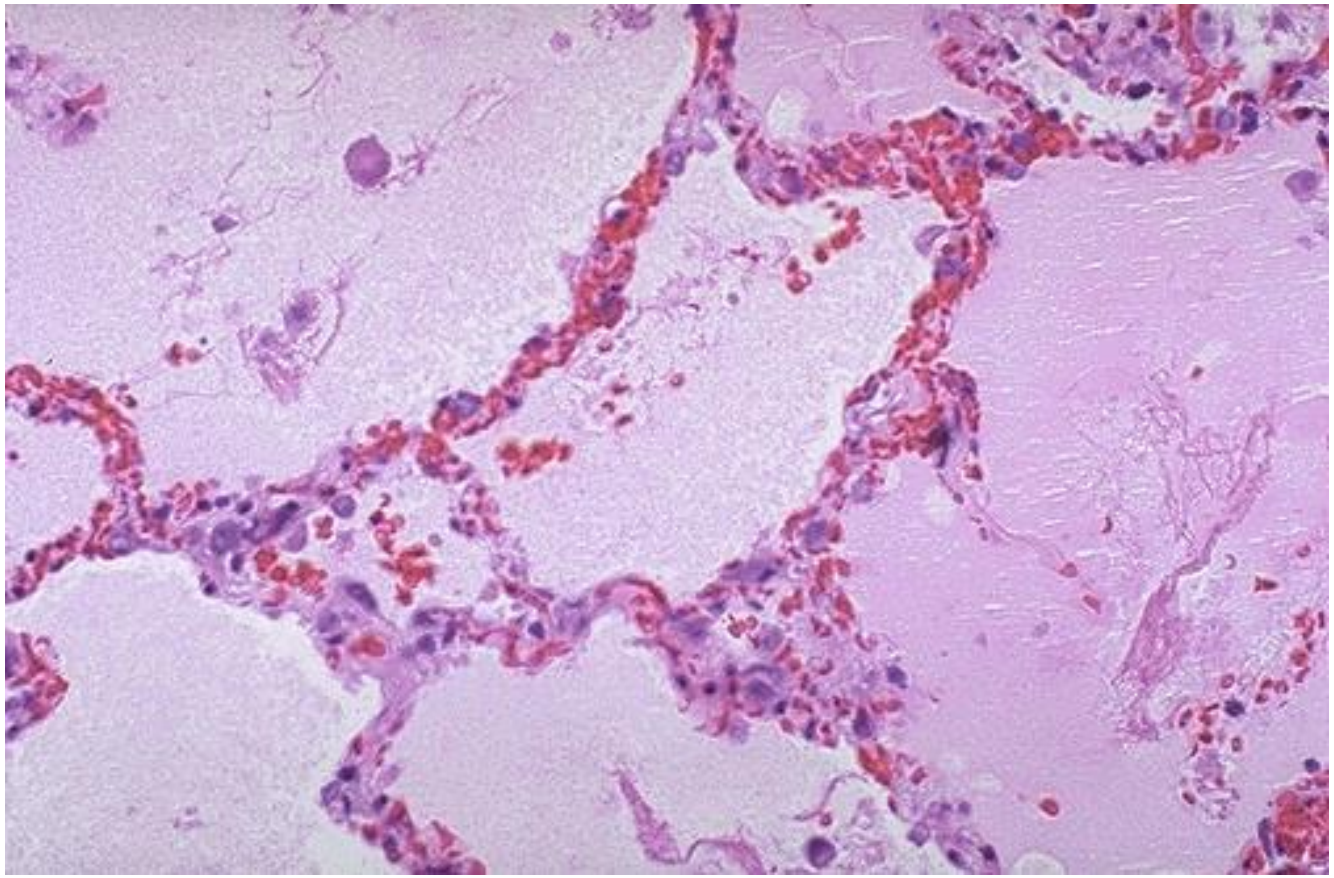
:**Chronic pulmonary congestion**

- Fibrosis and thickening of the alveolar walls

- Alveoli contain numerous haemosiderin laden macrophages

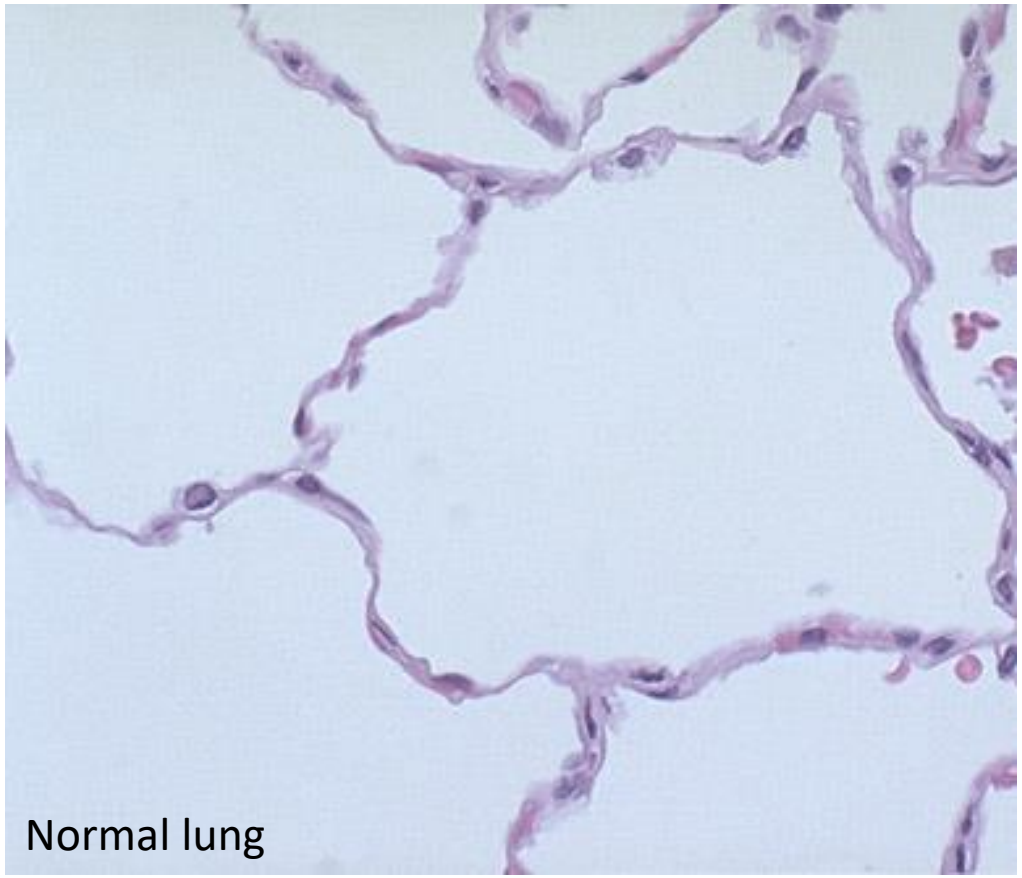
(also called siderophages / heart failure cells)

Pulmonary oedema



Note: Alveoli filled with a thin a pink colour material

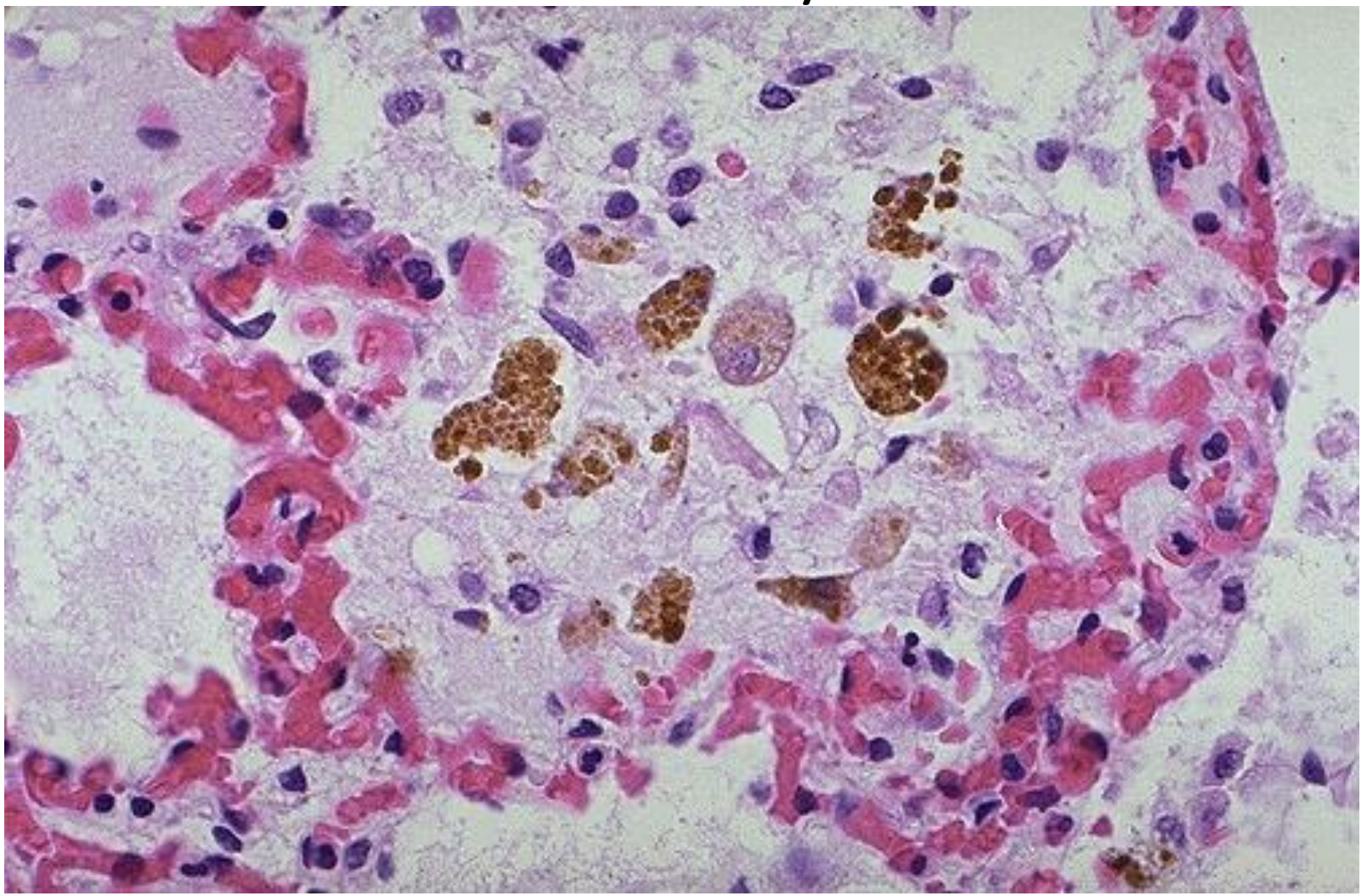
Congested capillaries in the alveolar walls



Normal lung

Note : Delicate alveolar walls of the lung

Pulmonary oedema



Note: - Dilated capillaries in the alveolar septae
- Alveoli are filled with a thin fluid
- Hemosiderin-laden macrophages in alveolar spaces

Acute lung injury (ALI) and ARDS (non-cardiogenic pulmonary oedema)

- Abrupt onset, significant hypoxaemia and diffuse pulmonary infiltrates in the absence of heart failure
- Acute respiratory distress syndrome (ARDS) – severe ALI
- Histological manifestation - Diffuse alveolar damage

Conditions associated with development of ARDS

Infection	Chemical injury
Sepsis	Heroin and methadone overdose
Diffuse pulmonary infections : Viral, mycoplasma, Pneumocystis pneumonia, miliary TB	Acetylsalicylic acid
Gastric aspiration	Barbiturate overdose
Physical injury	Paraquat
Mechanical trauma , including head injuries	Haematological conditions
Pulmonary contusions	Multiple transfusions
Near drowning	DIC
Fractures with fat embolism	Pancreatitis
Burns	Uraemia
Ionizing radiation	Cardiopulmonary bypass
Inhaled irritants	Hypersensitivity reactions
Oxygen toxicity	Organic solvents
Smoke	Drugs
Irritant gases and chemicals	

ARDS - Pathogenesis

- Evidence suggests lung injury is caused by an imbalance between **pro-inflammatory** and **anti-inflammatory mediators**
- Increased synthesis of IL-8, IL-1 a and TNF by macrophages results in

  - Endothelial activation

  - Sequestration and activation of **neutrophils** in pulmonary capillaries

  Neutrophils secrete - oxidants, proteases, platelet activating factor, leukotrienes

  Causing damage to alveolar epithelium and endothelium and

  trigger inflammation

ARDS - Pathogenesis

- Increased vascular permeability
- Reduction of surfactants
- Alveoli are unable to expand
- The destructive process is counteracted by endogenous antiproteases, antioxidants and anti inflammatory cytokines (eg. IL-10)

ARDS - Pathogenesis

Acute stage

- Damage to **alveolar capillary membrane**

  - capillary endothelium and alveolar epithelium

- Increased vascular permeability
- Alveolar flooding – rapidly fill with oedema fluid
- Loss of diffusion capacity
- Damage to type II pneumocytes - Surfactant deficiency
- Formation of microthrombi

ARDS - Macroscopy

- Heavy, dark, firm, airless lungs

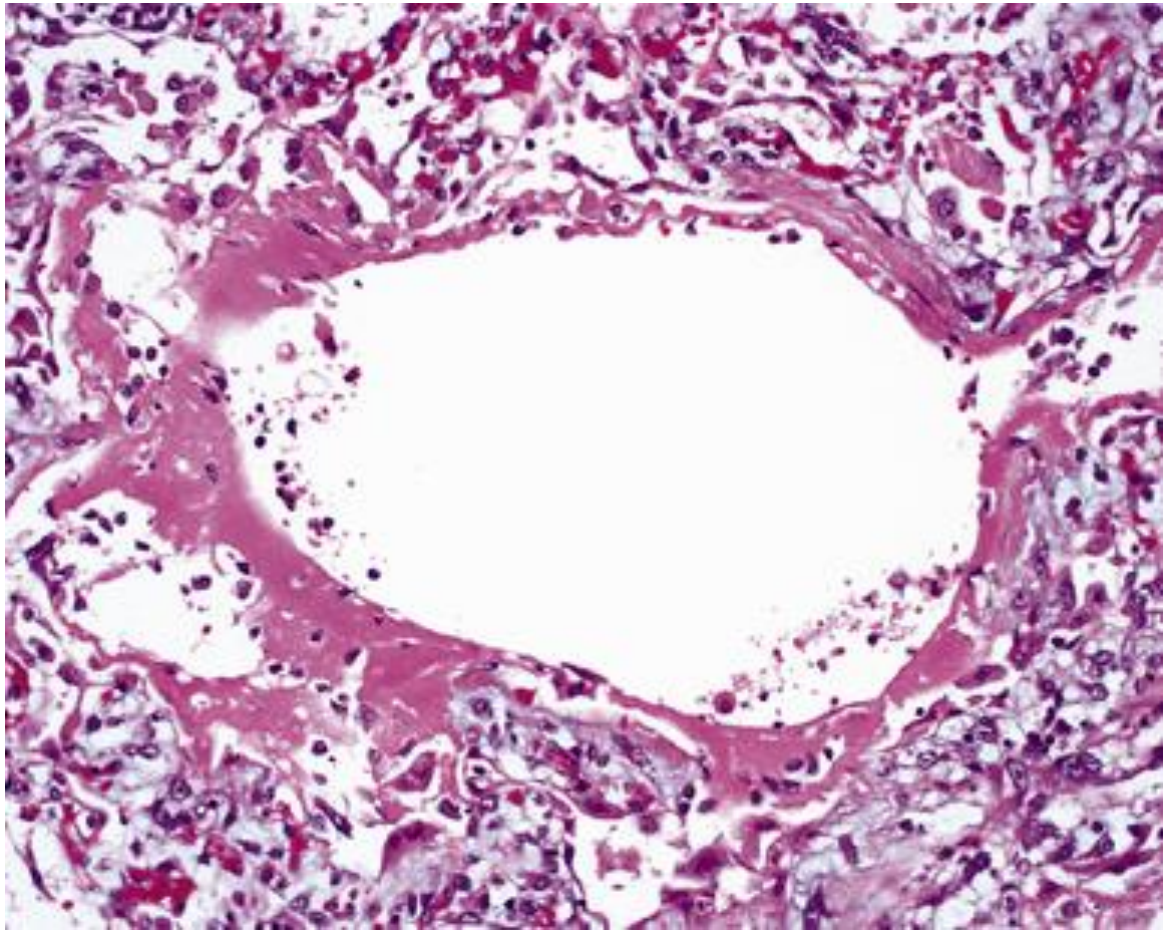
ARDS - Microscopy

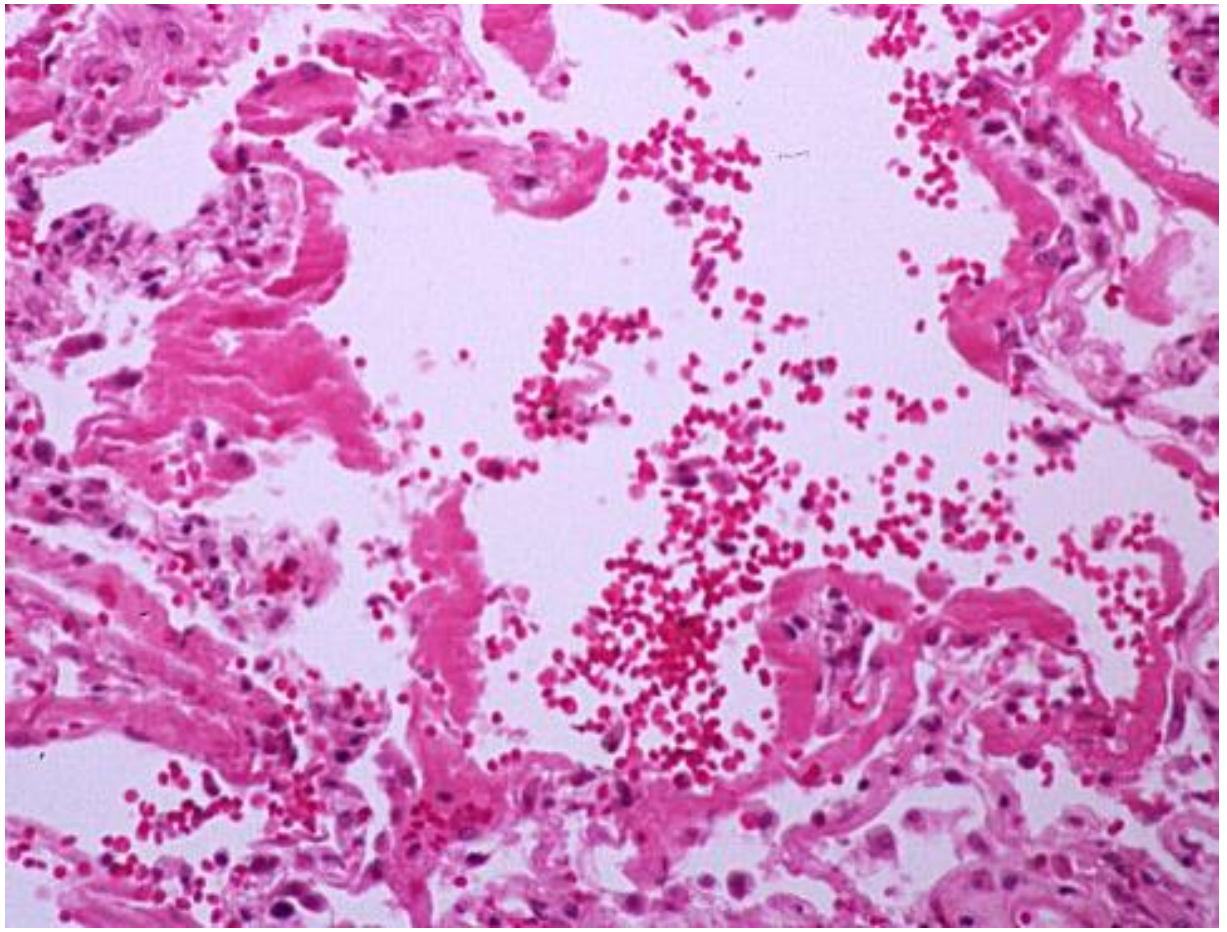
Acute stage: Congestion of the capillaries in the alveolar septae

- Interstitial and intra-alveolar oedema and focal haemorrhage
- Cell swelling, vacuolation, and necrosis of alveolar epithelial cells
- Collections of neutrophils in capillaries
- Characteristic histological feature : **Hyaline membrane formation**

  Thick, fibrin rich, eosinophilic oedema fluid admixed with necrotic cellular debris

ARDS - Hyaline membrane



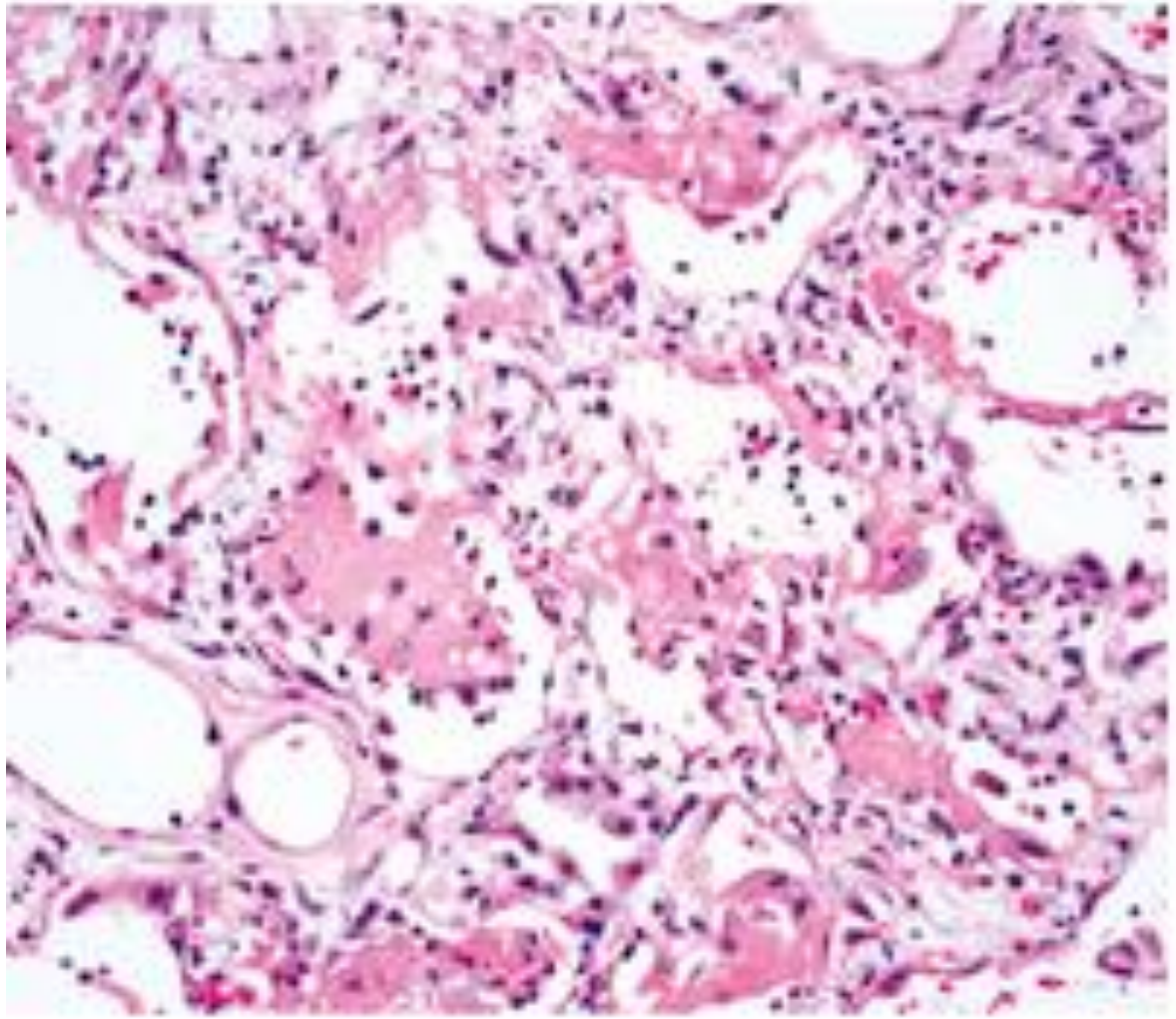


Proteinaceous alveolar exudates accumulate along the periphery of alveoli, closely adherent to alveolar wall–air space interface

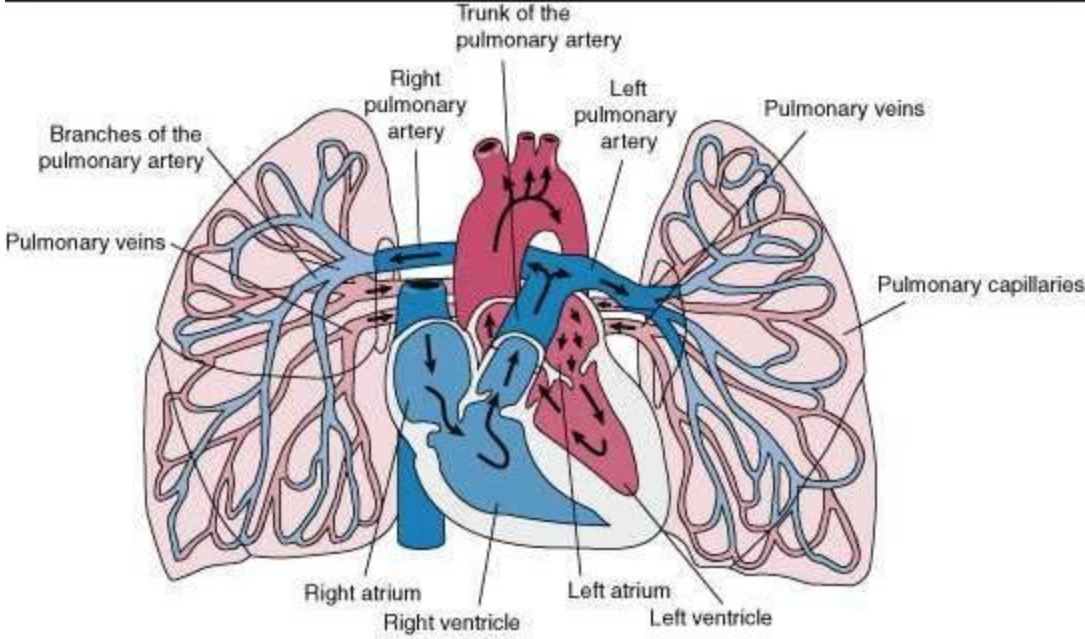
ARDS -Hyaline membrane

Organizing stage

- Proliferation of type II pneumocytes
- Granulation tissue in the alveolar walls and in alveolar spaces
- In some, proliferation of interstitial cells and collagen deposition causes thickening of the alveolar septae



Blood supply to the lungs



- Lungs are oxygenated by
  - pulmonary arteries
  - bronchial arteries
  - also, directly from air in alveoli
- Therefore ischaemia of the lungs is an exception
- Occurs only if
  - there is compromised cardiac function or bronchial circulation
  - the region of the lung is underventilated as result of underlying lung pathology

Pulmonary Embolism

- Occlusion of large pulmonary arteries is almost always due to embolism
- >95% arise from the deep vein thrombi in lower limb veins
  - thromboembolism (TE)
  - Arise from the popliteal vein and larger veins above it

Other causes of pulmonary embolism

- Air , fat and amniotic fluid embolism
- Foreign bodies - may cause granulomatous reaction

  within the pulmonary arteries – leads to pulmonary hypertension

  in the parenchyma – leads to fibrosis
- Bone marrow embolization

  - After massive trauma

  - Bone infarction secondary to sickle cell anaemia

Pathophysiologic consequences of TE in the lung

Depend on

- Size of the embolus which also decided the site of occlusion
- Cardiopulmonary status of the patient

Consequences of embolic pulmonary artery occlusion

- Increase in pulmonary artery pressure
- Vasospasm [neurologic mechanisms and / mediators (TXA2 and serotonin)]
- Ischaemia of the pulmonary parenchyma

Occlusion of major pulmonary artery

- Sudden increase in pulmonary artery pressure
- Diminished cardiac out put
- Right sided heart failure (acute cor pulmonale)
- Sometimes may result in sudden death
- Pulmonary ischaemia and infarction
- Reduced movements of the chest wall due to pain causes reduction in surfactant production results in collapse of alveoli

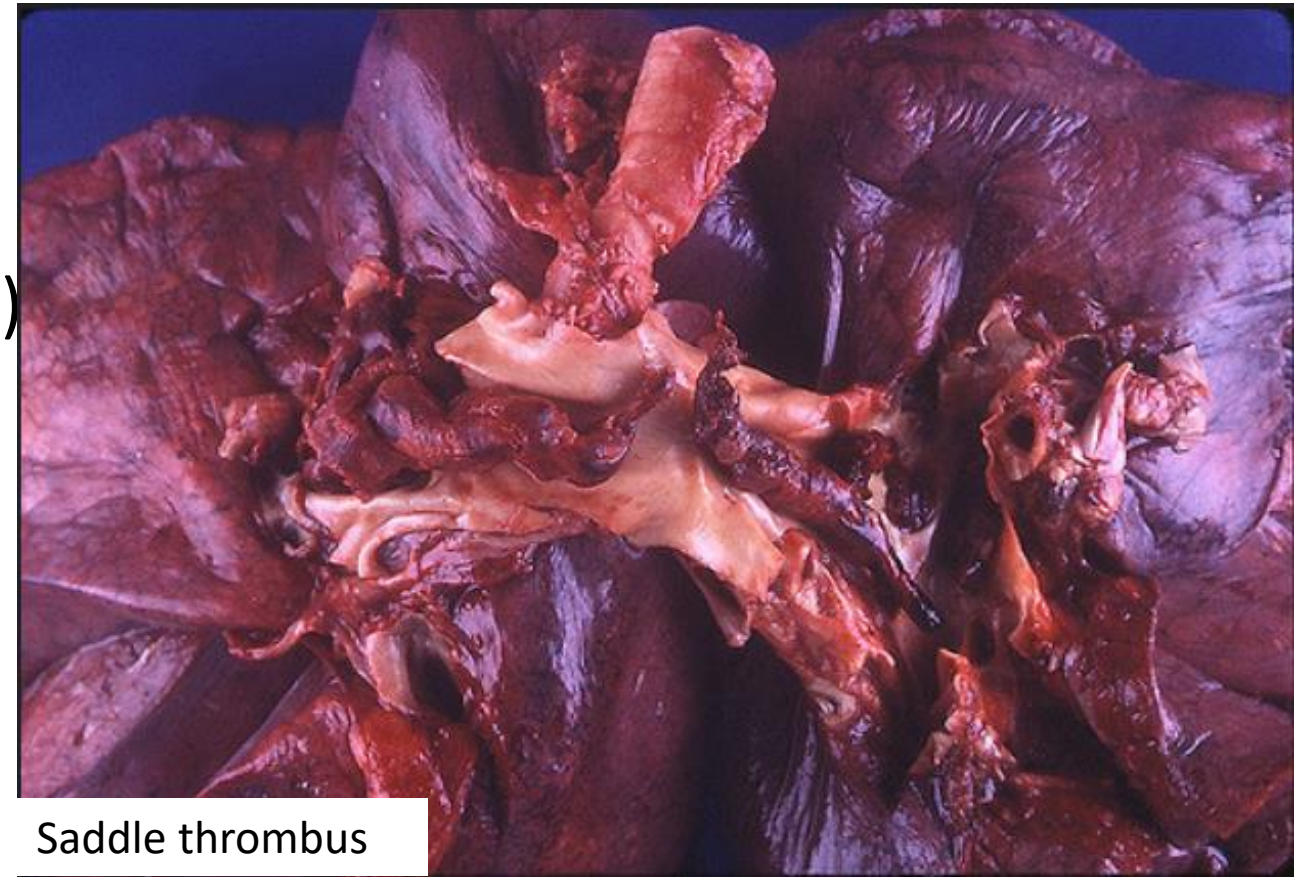
Macroscopy – Large embolus

- May embedded in the main pulmonary artery/ its major branches or at the bifurcation as a saddle embolus
- Usually – Sudden death

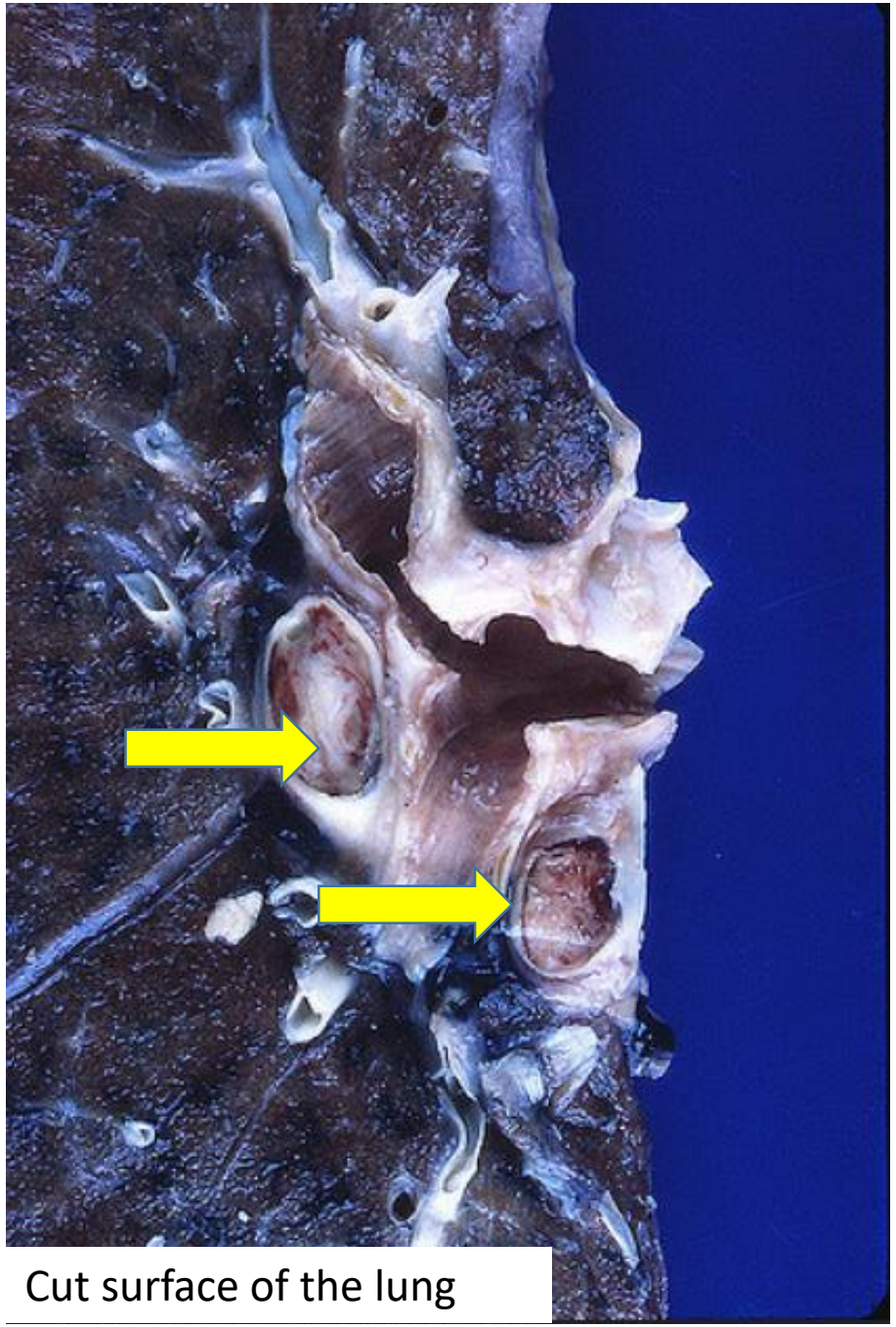
(acute cor pulmonale / cardiogenic shock)

- No time for tissue reaction

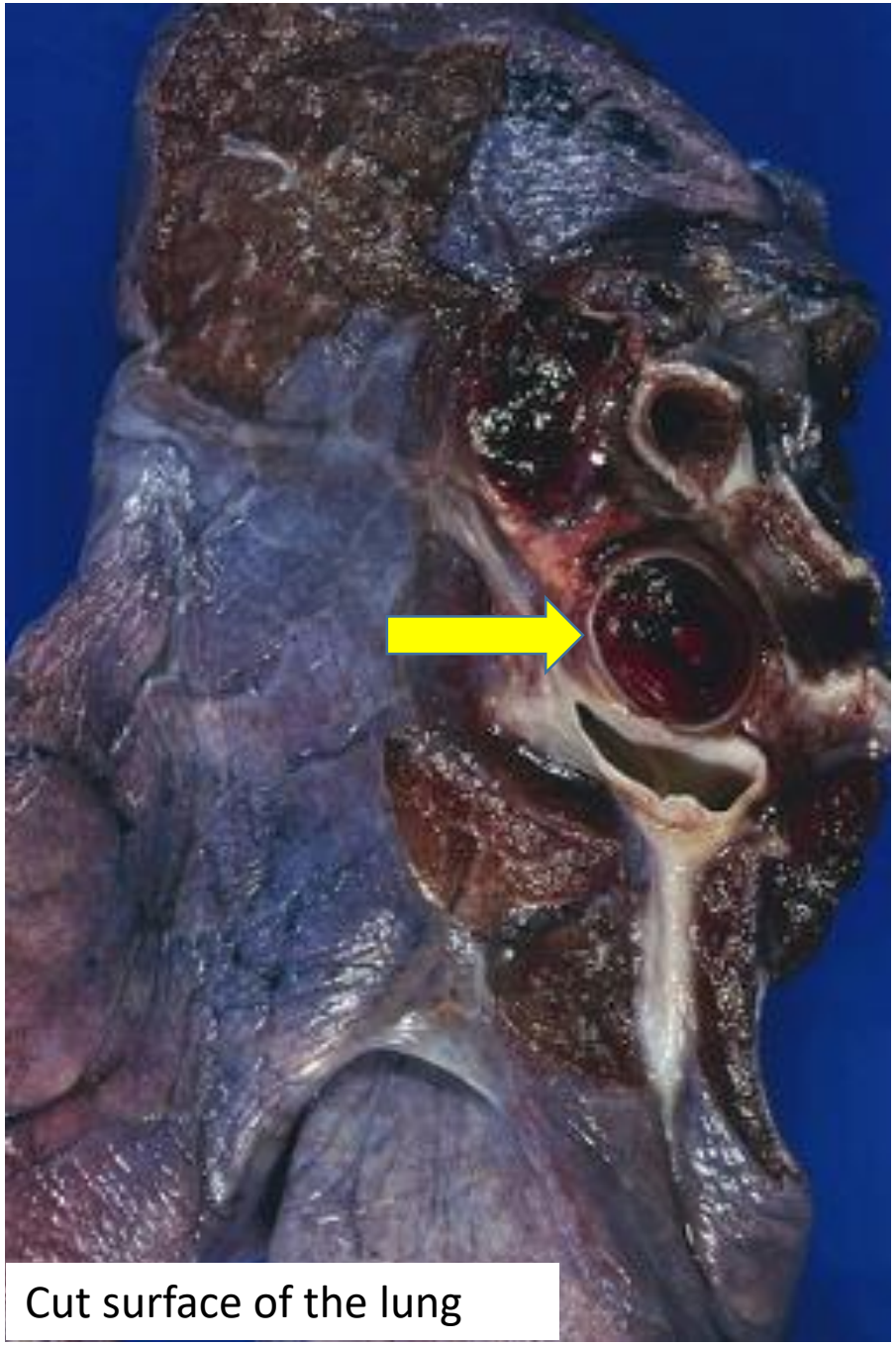
  - no morphological changes in the lung



Saddle thrombus



Cut surface of the lung



Cut surface of the lung

Macroscopy - Smaller emboli

- Occlude medium sized and small pulmonary arteries
- Ischaemic damage to the vascular endothelium – alveolar haemorrhage
- Usually there is no lung parenchymal damage

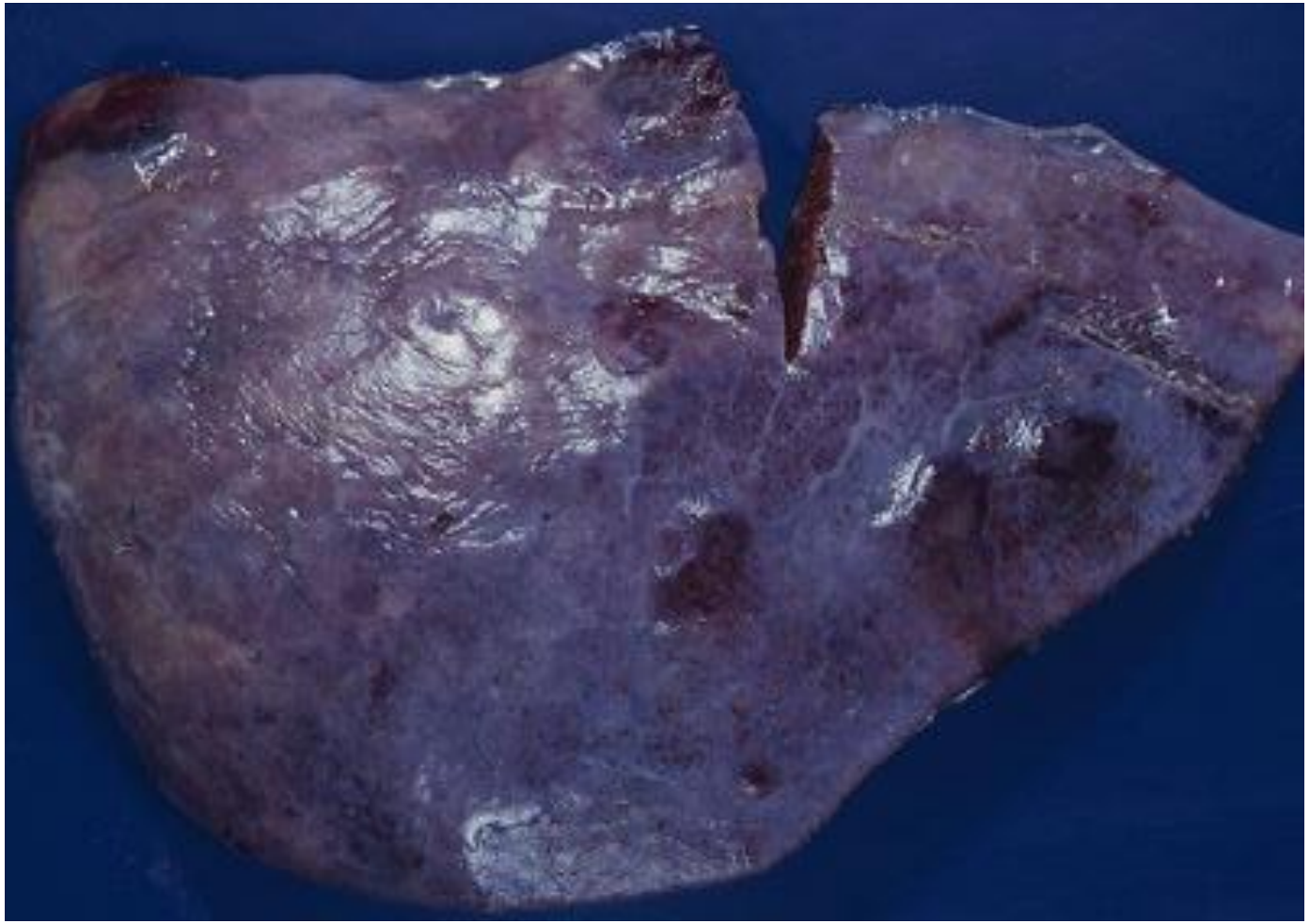
- If there is compromised cardiovascular status – Lung infarction
- The smaller the pulmonary artery, the higher the risk of infarction

- Usually – multiple infarcts
- Majority – lower lobes

Pulmonary infarcts

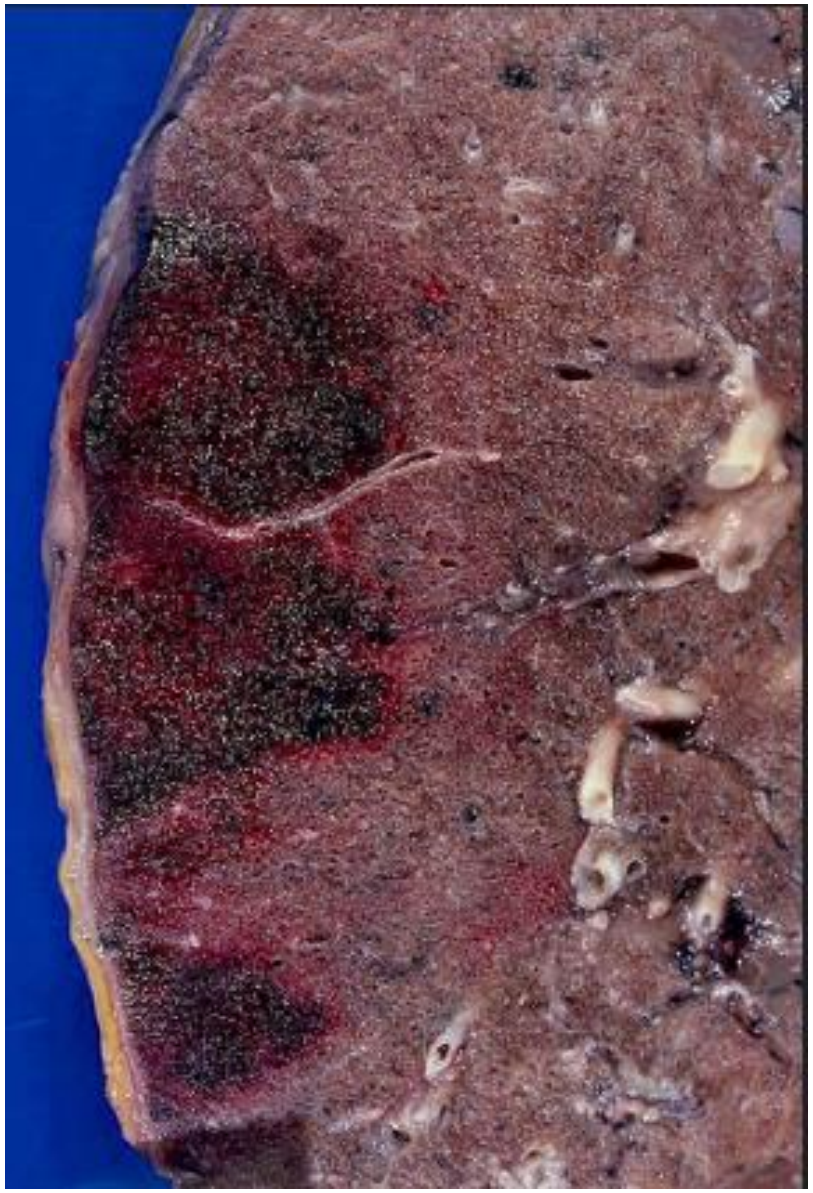
- Wedge shaped - base at the pleural surface
  - apex pointing towards the hilum of the lung
- Typically haemorrhagic infarcts – appear as red-blue raised areas
- Adjacent pleural surface - covered by fibrinous exudate
- Occlude vessel may be found near the apex of the infarcted area
- After about 48 hours – Red cells lyse and the infarct becomes paler, gradually becomes red-brown as haemosiderin is produced
- Fibrosis begins as a grey white peripheral zone and scar formation occurs

Pulmonary haemorrhage - Macroscopy



Note:
Multiple purple – blue lesions on the pleural surface

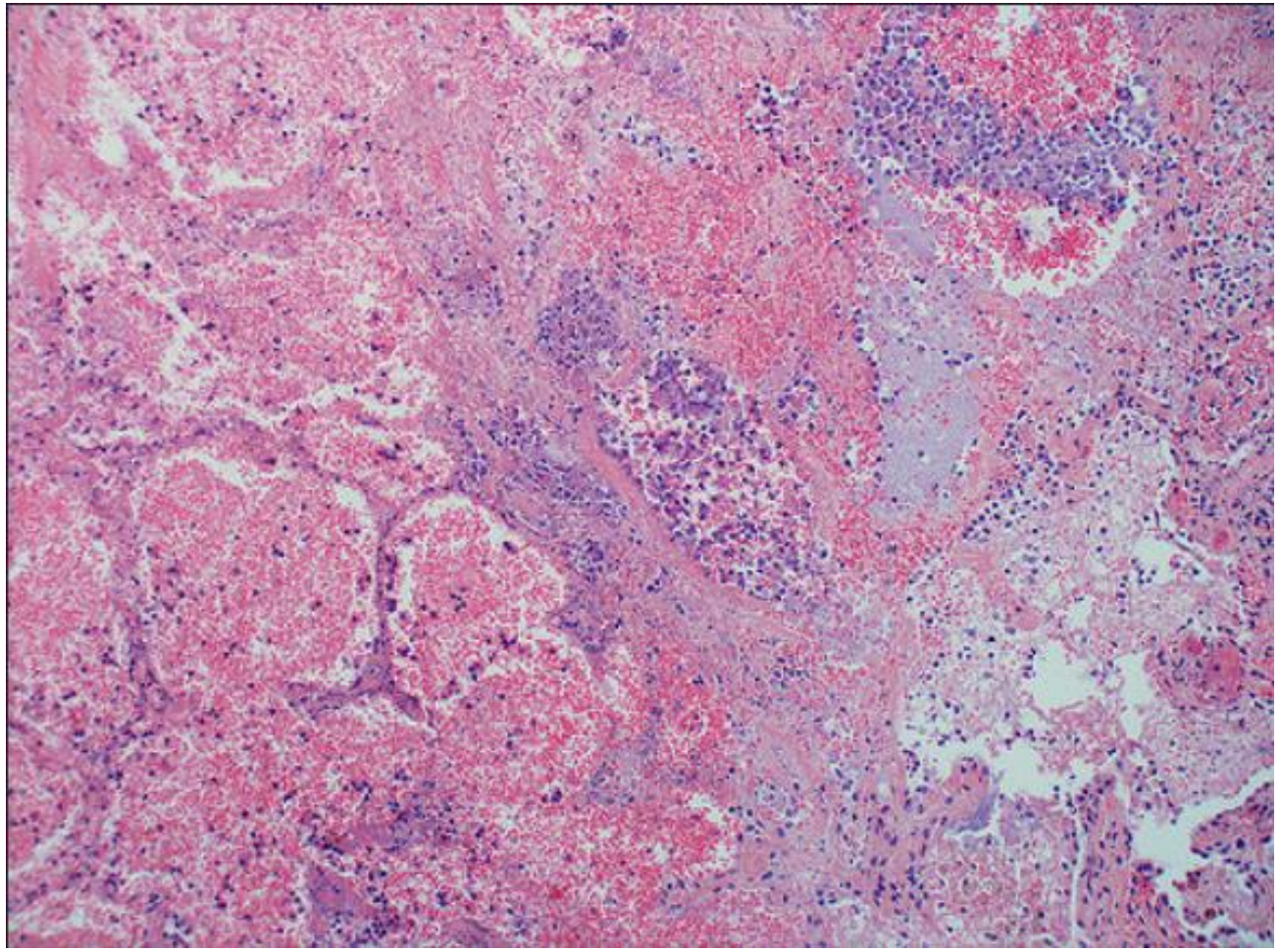
Pulmonary infarct



Recent haemorrhagic infarct of the lung

Pulmonary infarction - Microscopy

- Fresh infarcts - coagulative necrosis of the lung parenchyma
  - Haemorrhage



What happens to clinically silent small emboli?

- These emboli are removed from the occlusion site by fibrinolytic activity
- Until then the bronchial circulation maintains the blood supply to the lung parenchyma

What happens when there is recurrent multiple emboli ?

- Pulmonary hypertension
- Chronic cor pulmonale
- Pulmonary vascular sclerosis

Pulmonary hypertension

- Normally , pulmonary BP is about 1/8 of the systemic circulation

  When ¼ or more of the systemic BP circulation

  - pulmonary hypertension

- Usually due to

  - decrease in the cross-sectional area of the pulmonary vascular bed or

  - increased pulmonary vascular blood flow

- Secondary pulmonary hypertension – When there is an underlying cause

- Primary - Sporadic/ Familial

Secondary pulmonary hypertension – Causes

- **Chronic obstructive lung disease and chronic interstitial lung disease**

  - Destruction of the lung parenchyma and reduction in alveolar capillaries

  - Increased pulmonary arterial resistance and secondarily elevated

    arterial pressure

Secondary pulmonary hypertension – Causes

- **Recurrent pulmonary emboli**
  - Reduction in the functional cross sectional area of the pulmonary vascular bed
  - Increased vascular resistance
- **Mitral stenosis**
  - Increased left atrial pressure causing increased venous pressure
  - Then pulmonary arterial hypertension
- Congenital left - to - right shunts

Pulmonary hypertension - Pathogenesis

Increased blood flow

↓

Shear and mechanical injury to the endothelium

Recurrent thromboembolism

↓

Biochemical injury to the endothelium caused by fibrin

↘ ↙

Endothelial cell dysfunction

↓

Reduce production of vasodilatory substances - Nitric oxide , prostacyclin

Increase production of vasoconstrictive mediators - endothelin

Production of growth factors and cytokines - induce migration and replication of vascular smooth muscle cells

- increase production of ECM

Pulmonary hypertension - Morphology

Vascular alteration involve the entire arterial tree

- **Main elastic arteries**

  Atheroma formation

Pulmonary hypertension - Morphology

- **Medium-sized muscular arteries**

  Proliferation of myointimal cells and smooth muscle cells

  Thickening of the media and the intima of the vessel

  Narrowing of the lumina

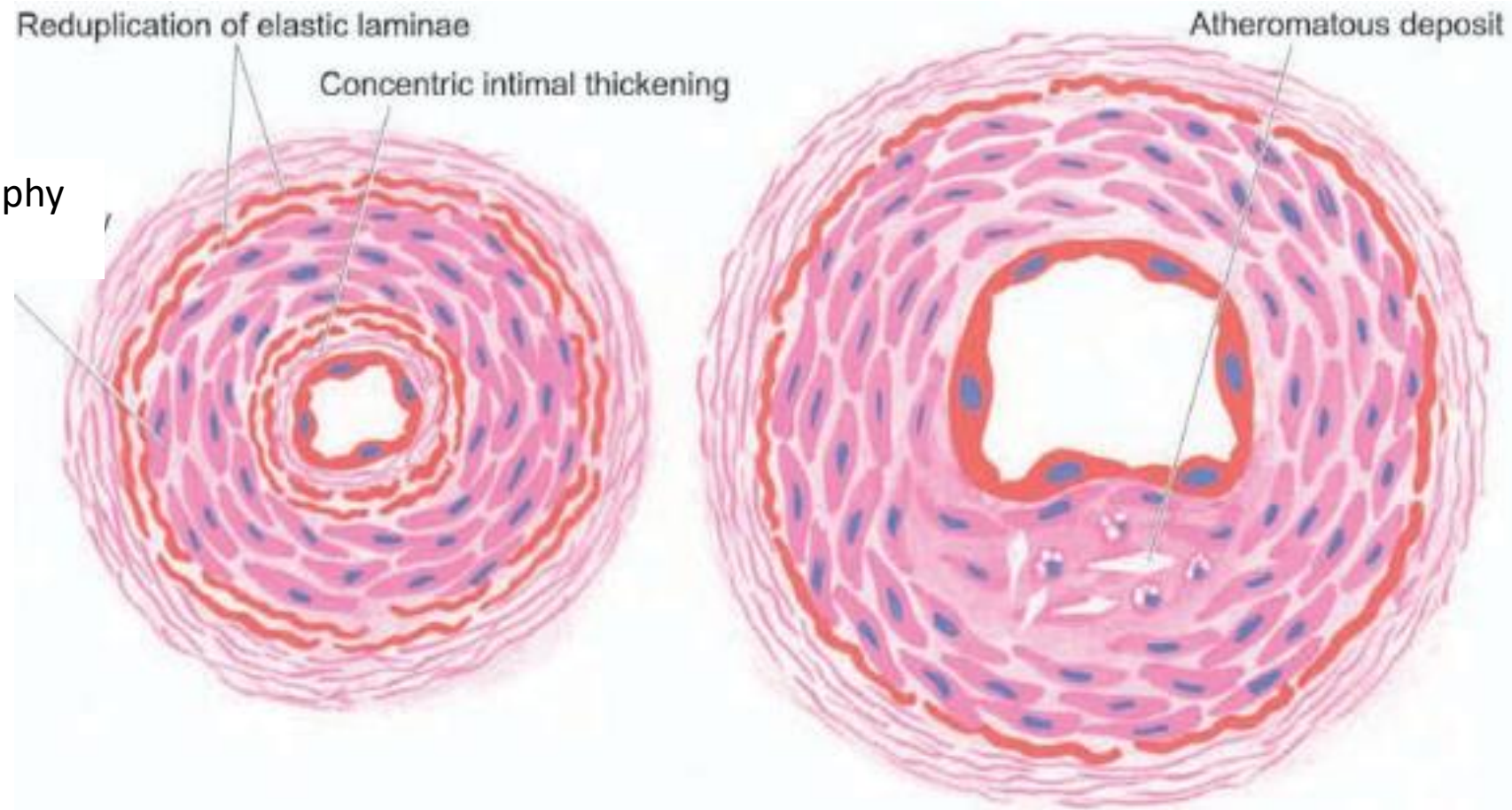
- **Smaller arteries and arterioles**

  Thickening, medial hypertrophy

  Reduplication of the internal and external elastic membranes

  Obliteration of the lumen

Medial hypertrophy

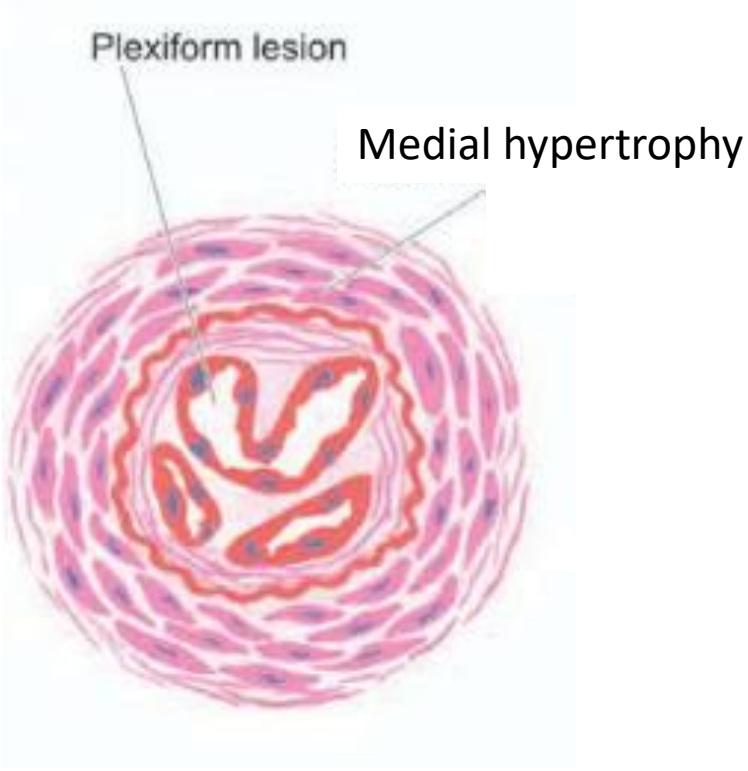


Idiopathic pulmonary hypertension

- Plexiform lesions

  -Endothelial proliferation forms multiple

  lumina within small arteries



Pulmonary hemorrhage – Causes

- Necrotizing bacterial pneumonia
- Passive venous congestion
- Bleeding diathesis
- Diffuse alveolar haemorrhage syndromes

  - Primary immune mediated diseases

  - Manifest as the triad of

    haemoptysis, anaemia, diffuse pulmonary infiltrates

Diffuse alveolar haemorrhage syndromes

- Goodpasture syndrome
- Idiopathic pulmonary haemosiderosis
- Pulmonary angitis and granulomatosis

Good pasture syndrome (GPS)

- Uncommon
- Characterized by rapidly progressive glomerulonephritis and haemorrhagic interstitial pneumonitis
- Underlying pathology

  - Antibodies targeted against the non-collagenous domain of α3 chain of type IV collagen

  - Antibody can be detected in more than 90 % of the patients

GPS - Morphology

- Macroscopy
  - Heavy lungs
  - Areas of red-brown consolidation due to diffuse alveolar haemorrhage

Microscopy
  - Focal necrosis of the alveolar walls
  - Intra-alveolar haemorrhage
  - fibrous thickening of the septae
  - Hypertrophic type II pneumocytes
  - Haemosiderin both within the macrophages and extracellular
- Immunofluorescence
  - Linear pattern of immunoglobulin deposition

Summary

Now you should be able to

- List the causes, and describe the morphology of lung in pulmonary oedema
- List the causes and describe the morphology of lung in

  Acute respiratory distress syndrome (ARDS)
- List the causes and describe the morphology of lung in

  pulmonary embolism, haemorrhage and infarction
- List the causes and describe the morphology of lung in

  pulmonary hypertension