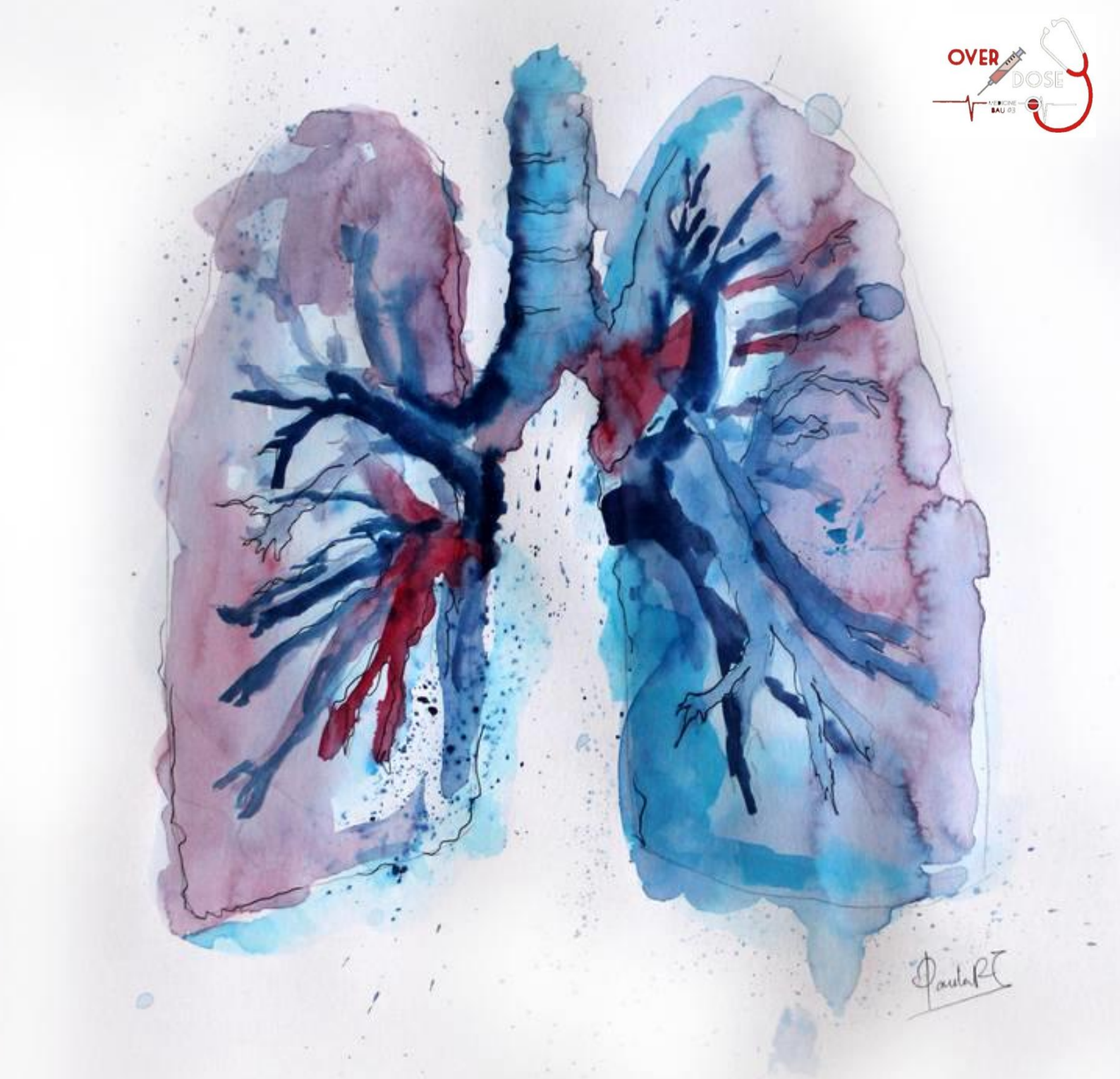

THE RESPIRATORY SYSTEM

Sub-system: Pathology

Lecture Title: Pulmonary diseases of vascular origin

Lecture Date: 14/11/2019

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Lecture outline

- Pulmonary thromboembolism and pulmonary infarction
  As you know there are many types of embolism: fat, air, thrombus. Here, we are talking about thromboembolism which is mainly DVT in deep veins of the lower limb that leads to embolism in pulmonary artery
- Pulmonary hypertension
  - Any lung disease (hypoxia, etc) will cause pulmonary hypertension.
  - Pulmonary hypertension causes a difficulty in right-side of heart to pump blood, and that will lead to cor pulmonare.
  - Left-sided heart failure is one of the causes of pulmonary hypertension.
  - Most common cause of right-sided heart failure is left-sided heart failure.
- Diffuse alveolar hemorrhage syndrome
  (Diffuse alveolar hemorrhage not Diffuse alveolar damage!!(which is microscopic feature of ARDS))

Pulmonary embolism

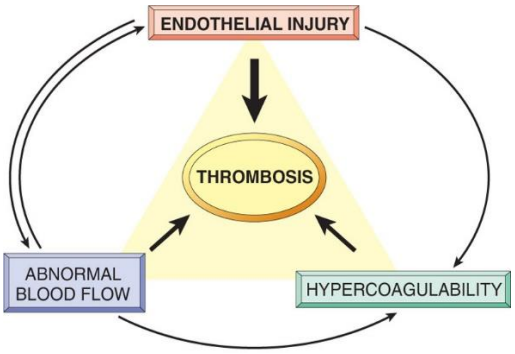
- Blood clots that occlude the large pulmonary arteries are almost always embolic in origin (not as systemic thrombus).
- More than 95% of all pulmonary emboli arise from thrombi within the large deep veins of the legs (most often those that have propagated to involve the popliteal vein and larger veins above it).

- Risk factors for DVT:
  (1) Prolonged bed rest (particularly with immobilization of the legs)
  (2) Surgery, especially orthopedic surgery on the knee or hip
  (3) Severe trauma (including burns or multiple fractures)
  (4) Congestive heart failure (stasis in veins of the lower limb which leads to edema).
  (5) In women, the period around parturition or the use of oral contraception pills with high estrogen content (therefore doctors advise her to move after days of delivery ~which is called ambulation)
  (6) Disseminated cancer (hypercoagulability state)
  (7) Primary disorders of hypercoagulability (e.g., factor V Leiden)

{factor C, factor S deficiency, factor V Leiden mutation (not deficiency)}

As the systemic thrombus, major risk factors are verchow triad:

1) Injury to endothelium.
2) Stasis of blood.
3) Hypercoagulability



Pulmonary embolism, clinical features

- Most (60% to 80%) are clinically silent because they are small
  …bronchial circulation compensates and fibrinolysis occurs
  (Because the lung has dual circulation: bronchial artery and pulmonary artery so small embolism in pulmonary artery don't affect too much)
- In 5% of cases, death, acute right-sided heart failure, or cardiovascular collapse (shock) occurs suddenly
  …when more than 60% of the total pulmonary vasculature is obstructed by a large embolus (for example: large embolus in the bifurcation of pulmonary trunk [saddle embolus]) or multiple simultaneous small emboli.
- Obstruction of small to medium pulmonary branches (10% to 15% of cases):
  pulmonary infarction (if some element of circulatory insufficiency also is present)…typically: dyspnea
  (red [hemorrhagic] infarction not white because of the dual circulation).
- <3%: recurrent "showers" of emboli lead to pulmonary hypertension, chronic right-sided heart failure…progressively worsening of dyspnea
- Patients who have experienced one pulmonary embolism have a 30% chance of developing a second

One of the most important risk factor of pulmonary embolism is previous pulmonary embolism.

- Prophylaxis:
  -anticoagulation
  -early ambulation after operations
  -elastic stockings {special type of socks that compresses the vascularity of lower limb to aid the flow of blood}.
  -intermittent pneumatic calf compression
  -isometric leg exercises for bedridden patients [physical therapy]

Pulmonary hypertension

- Pulmonary hypertension = pressures of 25 mm Hg or more at rest
- May be caused by a decrease in the cross-sectional area of the pulmonary vascular bed …or, less commonly, by increased pulmonary vascular blood flow

the World Health Organization has classified pulmonary hypertension into the following five groups:

- *Pulmonary arterial hypertension,* a diverse collection of disorders that includes heritable forms of pulmonary hypertension and diseases that cause pulmonary hypertension by affecting small pulmonary muscular arterioles; these include connective tissue diseases, human immunodeficiency virus, and congenital heart disease with left to right shunts
- *Pulmonary hypertension due to left-sided heart disease,* including systolic and diastolic dysfunction and valvular disease
- *Pulmonary hypertension due to lung diseases and/or hypoxia,* including COPD and interstitial lung disease
- *Chronic thromboembolic pulmonary hypertension*
- *Pulmonary hypertension with unclear or multifactorial mechanisms*

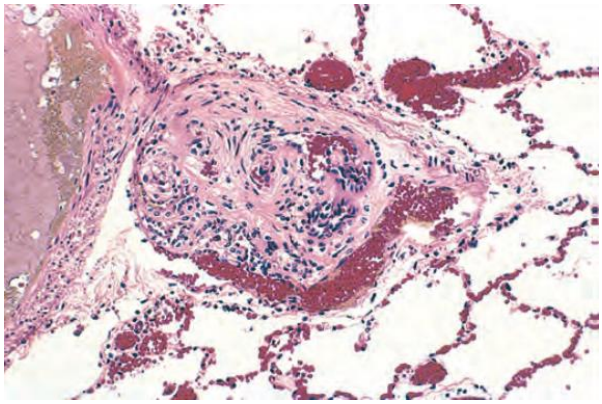
Idiopathic pulmonary hypertension

= Primary pulmonary hypertension …relatively much less common

- Genetic basis with familial predisposition
- Link to inactivating germ line mutations in the gene encoding bone morphogenetic protein receptor 2 (BMPR2) {important for development of bone and endothelial cells}.

Morphology

- Medial [tunica media] hypertrophy of the pulmonary muscular and elastic arteries.
- Pulmonary arterial atherosclerosis [because of the injury of endothelium].
- Right ventricular hypertrophy
- Plexiform lesions…characteristic but uncommon {small blood vessels proliferating inside a larger one}



Clinical features of Idiopathic pulmonary hypertension

- Idiopathic pulmonary hypertension is most common in women 20 to 40 years of age and occurs occasionally in young children.
- Dyspnea and fatigue, but some patients have anginal chest pain.
- Over time, respiratory distress, cyanosis, and right ventricular hypertrophy appear, and death within 2 to 5 years in 80% of patients.

Diffuse alveolar hemorrhage syndrome

{Anemia + Hemoptysis + Diffuse bilateral parenchymal infiltrates on x-rays}.

~~2 syndromes :

- Goodpasture syndrome

{antibodies against special type of collagen in basement membrane of Glomeruli of kidney and alveolar basement membrane}

…uncommon

…autoimmune

…involves the lungs and kidneys

...circulating autoantibodies against certain domains of type IV collagen that are intrinsic to the basement membranes of renal glomeruli and pulmonary alveoli
...necrotizing hemorrhagic interstitial pneumonitis and rapidly progressive glomerulonephritis
...most in teen and twenties
...males more
...the majority are smokers
...linear IgG deposition on immunofluorescence {in glomerulus or alveolar membrane}.

- Granulomatosis with polyangiitis
  - Previously called Wegener granulomatosis.

...>80%: The upper respiratory tract or lung or both are involved.

Necrotizing or granulomatous vasculitis (small-medium vessels)
+
Necrotizing granulomas in lungs
+
Crescentic glomerulonephritis

- Anti-neutrophil cytoplasmic antibodies (PR3-ANCAs) are present in close to 95% of cases [C-ANCA].