Cardiovascular Physiology

Pathophysiological Changes In Pulmonary Embolism

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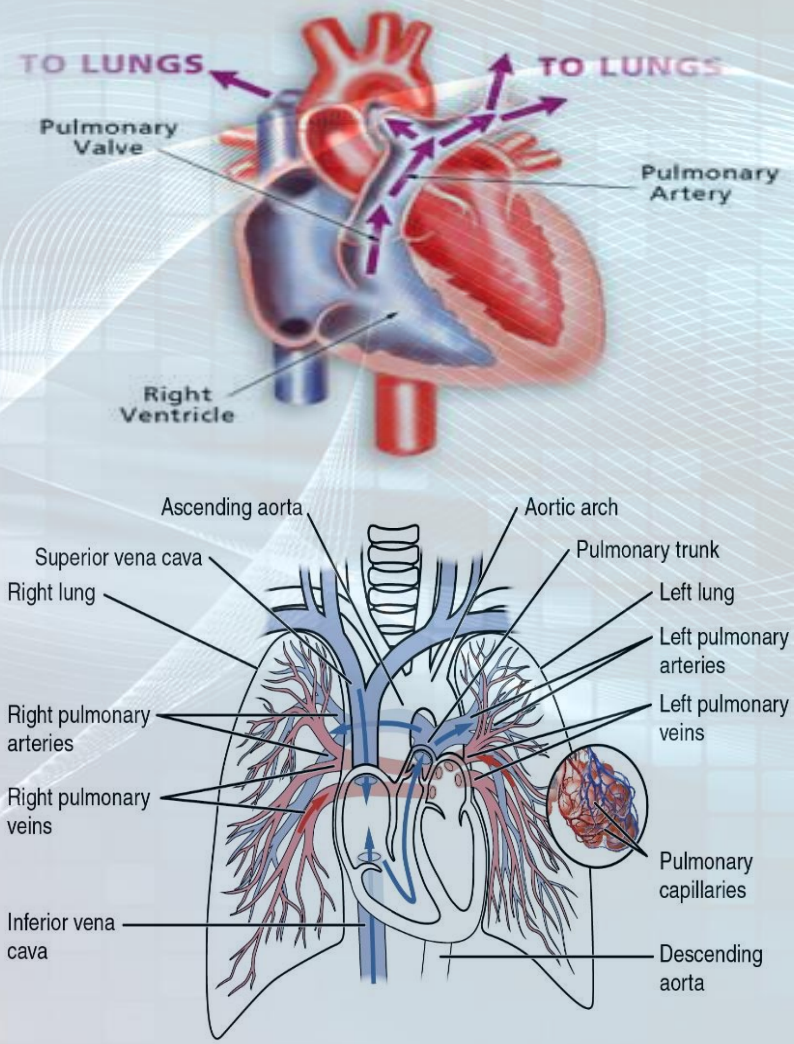
Lecture Outlines

- Pulmonary circulation.
- Definition of pulmonary embolism.
- Clinical significance of pulmonary embolism.
- Sources, etiology & risk factors of pulmonary embolism.
- Clinical presentation of pulmonary embolism.
- Differential diagnosis.
- Pathophysiological & hemodynamic changes of pulmonary embolism.

Pulmonary Circulation

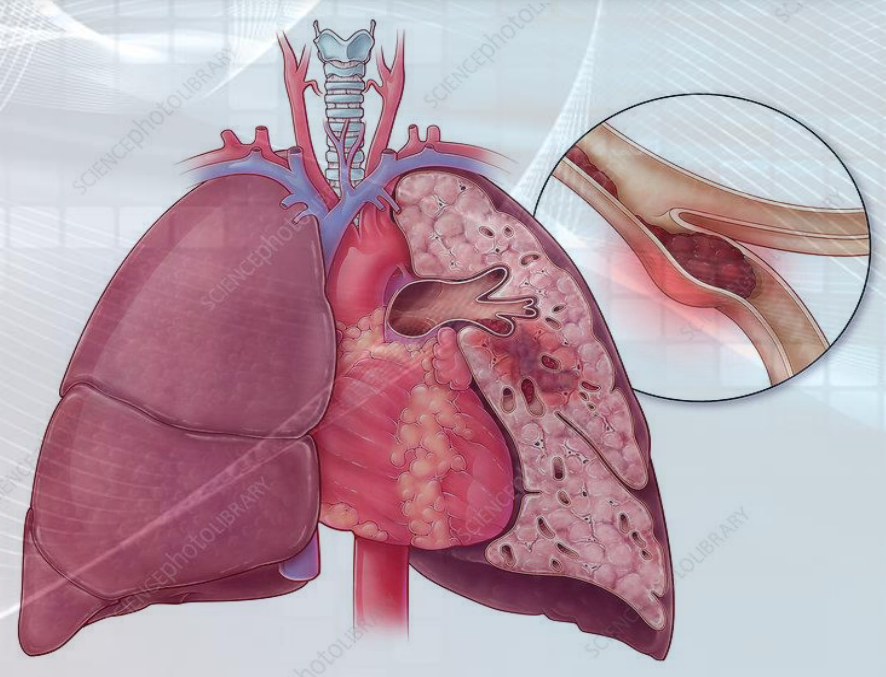
Pulmonary circulation is a part of the circulatory system that is pumped from the right ventricle to the lungs carrying deoxygenated blood, & returns oxygenated blood to the left atrium of the heart.



- **Deoxygenated blood** is pumped through the semilunar pulmonary valve into the left & right main **pulmonary arteries** (one for each lung), which branch into smaller pulmonary arteries that spread throughout the lungs.
- **Oxygenated blood** leaves the lungs through **pulmonary veins** to the left atrium completing the pulmonary cycle.

Pulmonary Embolism

Pulmonary embolism (PE) is a thrombotic disorder where an occlusion occurs in a pulmonary artery by a blood clot preventing blood flow to the lungs.



Clinical Significance

- The **incidence** of diagnosed pulmonary embolism (PE) increases with age.
- The **annual rate** is about 1 in 10 000 in individuals below 40 years of age & can reach 1 in 100 in patients over 80 years.
- According to autopsy studies, the disease is clinically suspected in less than half of fatal cases.
- PE is one of the 3 leading causes of death related to the cardiovascular system (CVS), along with myocardial infarction (MI) & stroke.
- Can lead to immediate death, or serious complications among survivors.

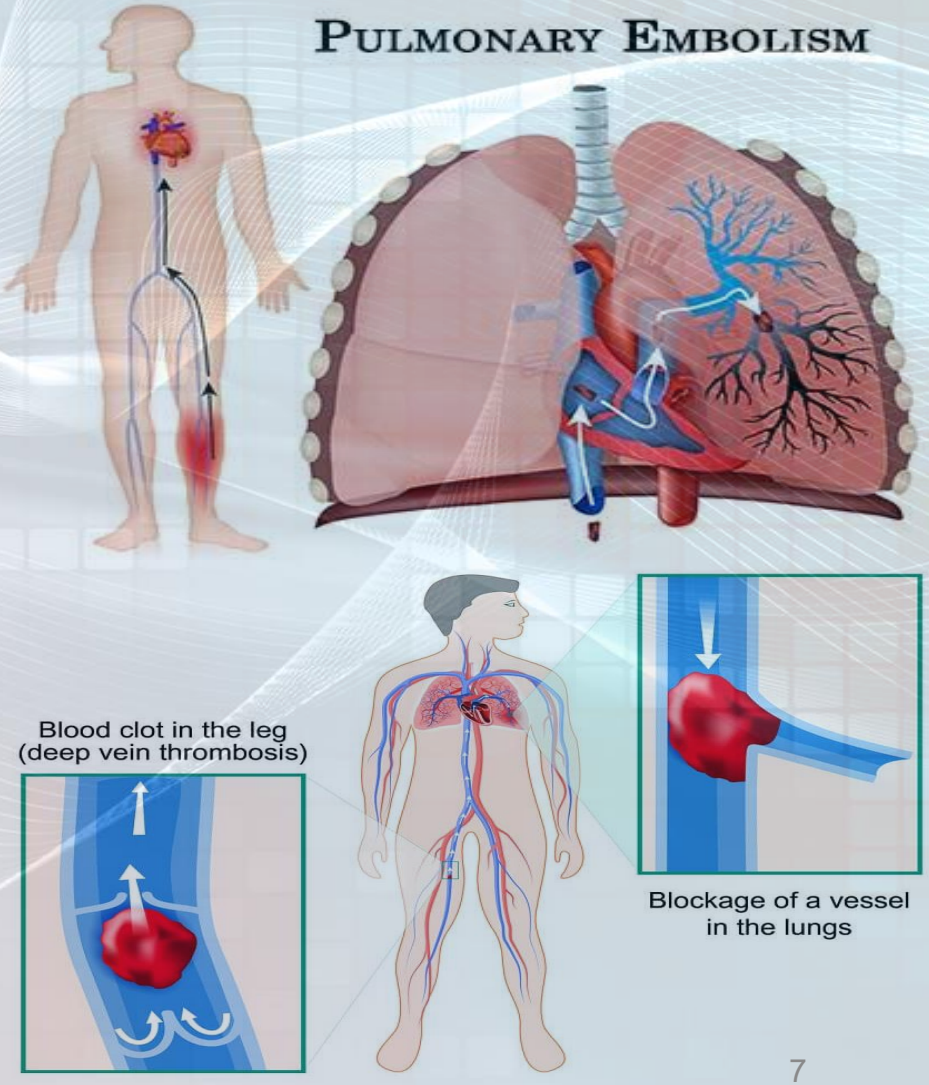
Guy Meyer et al., Pulmonary embolism, BMJ 2010

Clinical Significance

- Most episodes of pulmonary embolism carry a low mortality risk (about 1%) when properly diagnosed & treated.
- PE is the most common preventable cause of death among hospitalized patients in the USA.
- PE is of high mortality rate (200,000 – 300.000) death annually in the USA.
- There is a **lack of national data** for incidence, prognosis, & rate of death of pulmonary embolism.

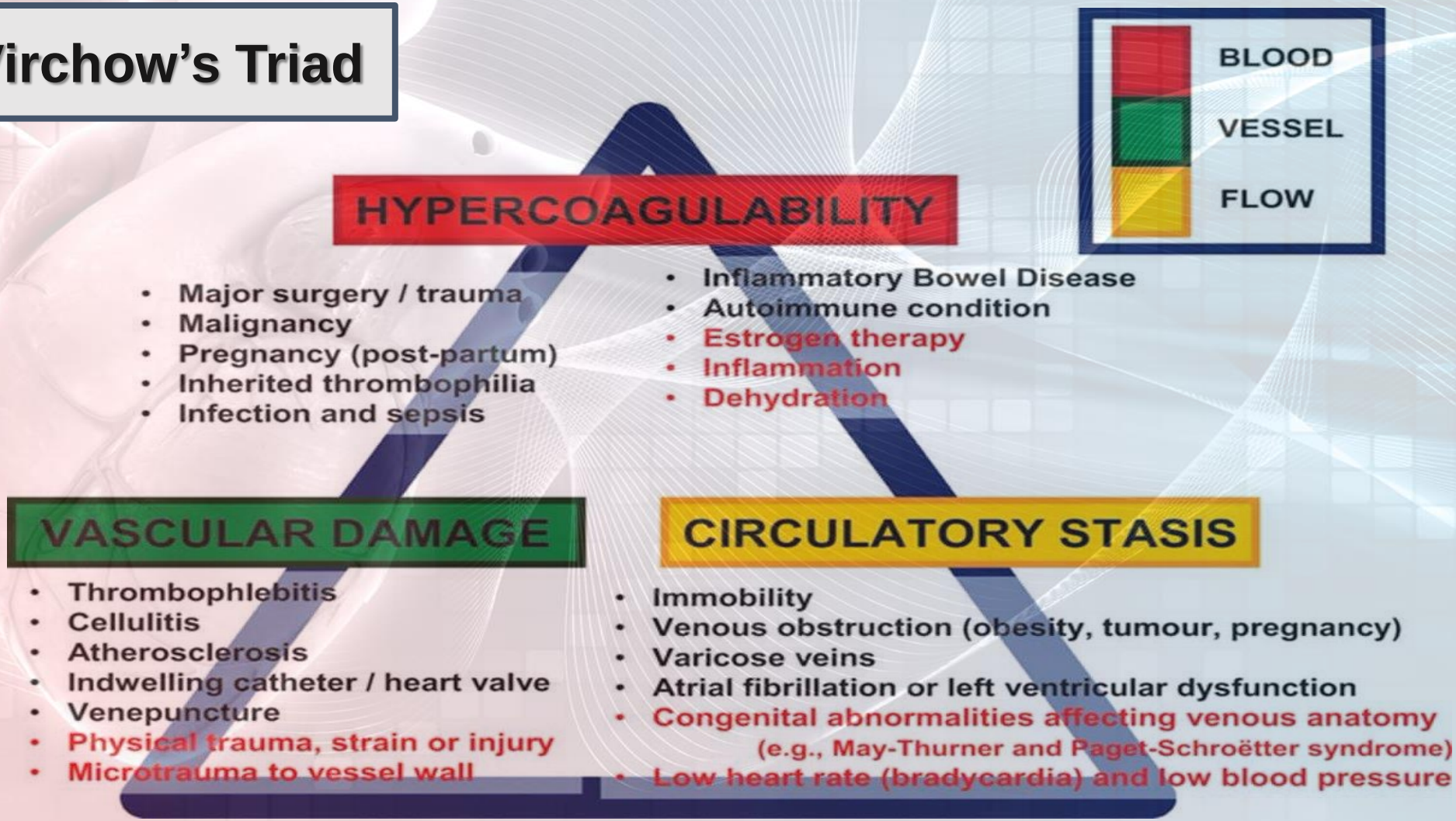
Pathogenesis & Source of Pulmonary Embolism

- **Pulmonary embolism** can **arise** from any clot anywhere in the body.
- Clot move mostly from a dislodge of deep vein thrombosis (**DVTs**) in calf veins.
- **Minor sources:** Fat embolism (droplet), air embolism (bubble), amniotic fluid embolism, septic embolism, & tumor embolism.
- To reach the lungs, thromboemboli travel through the right side of the heart.



Etiology & Risk Factors of Clot Formation

Virchow's Triad



Clinical Presentation

- The reduced blood flow to the lungs can cause debilitating symptoms including shortness of breath & can be life-threatening.

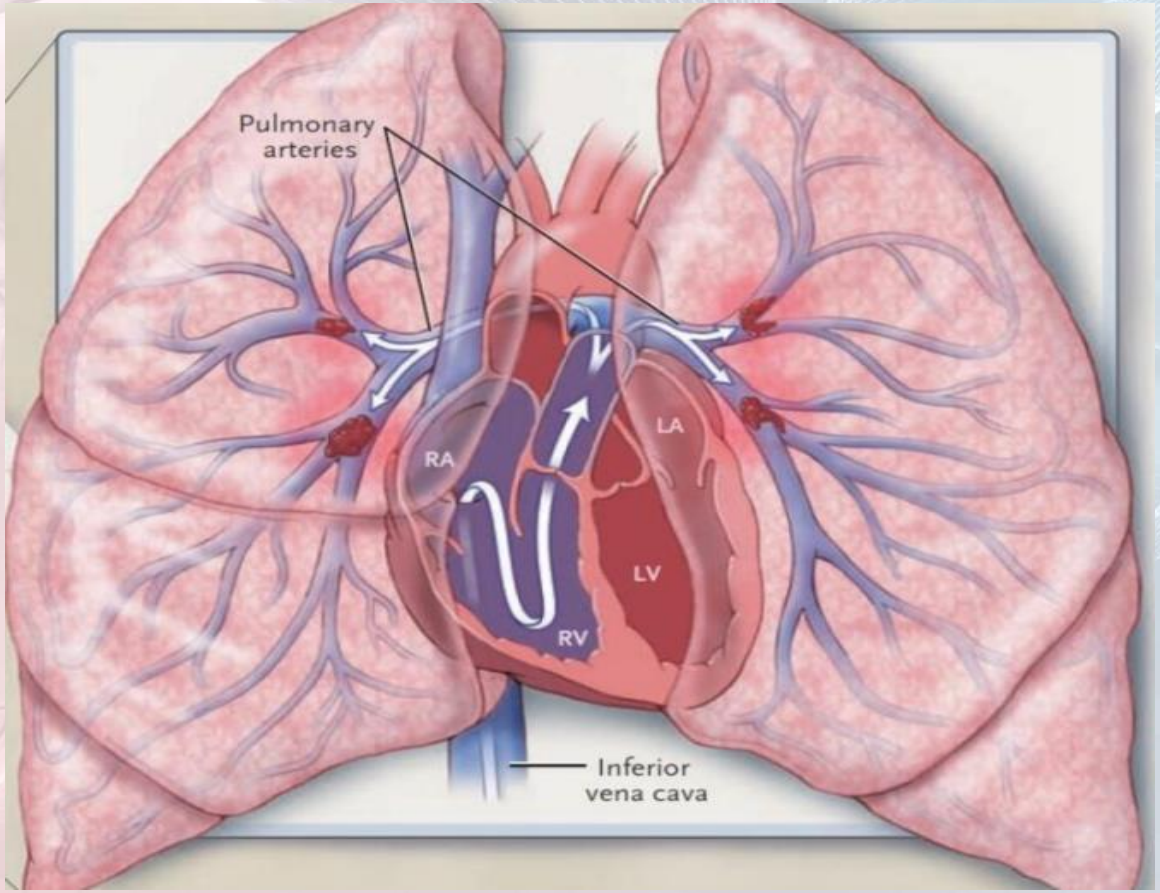
Small PE	Moderate PE	Massive PE
▪ Mostly asymptomatic ▪ Shortness of breath ▪ Chest discomfort	▪ Shortness of breath ▪ Tachycardia ▪ Tachypnea ▪ Haemoptysis ▪ Pleuritic chest pain ▪ Pleural rub	▪ Severe chest pain ▪ Pallor ▪ Sweating ▪ Central cyanosis ▪ Elevated JPV ▪ Loud P2, S2 split, gallop rhythm ▪ Circulatory shock ▪ Syncope ▪ Death

- Deep vein thrombosis (DVT).

Differential Diagnosis

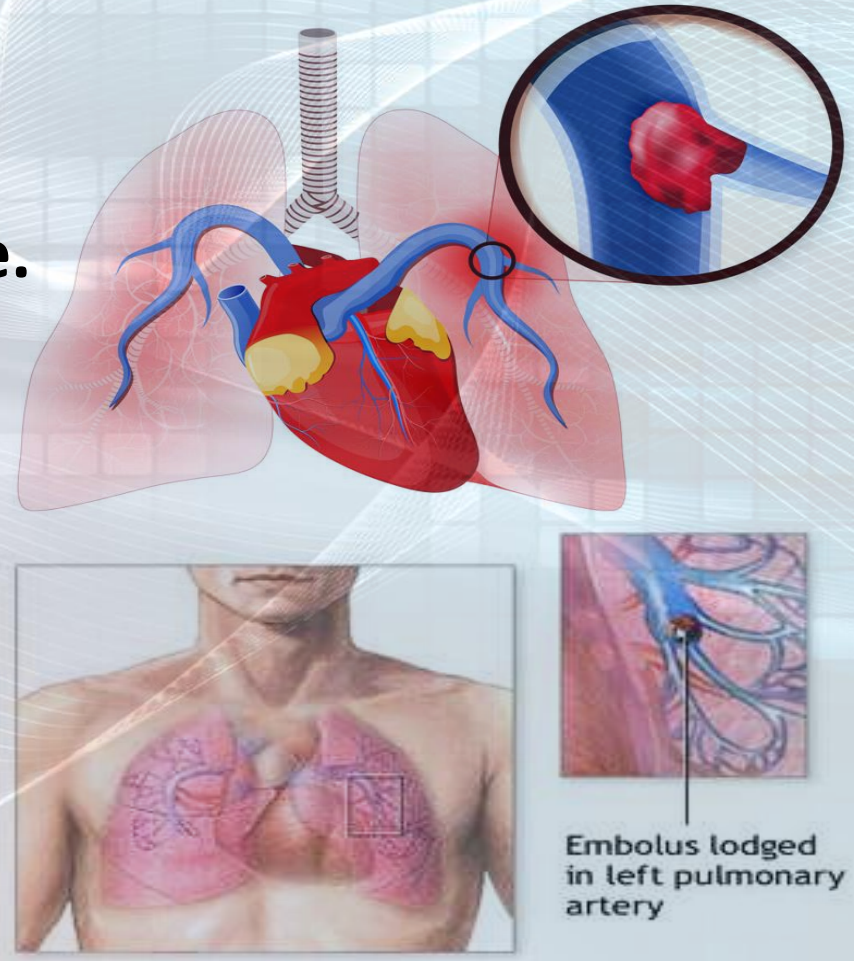
- Myocardial infarction (MI)
- Pneumonia
- Pneumothorax
- Bronchitis
- Pleurisy
- Costo-chondritis
- Rib fracture

Pathophysiological & Hemodynamic Changes In Pulmonary Embolism



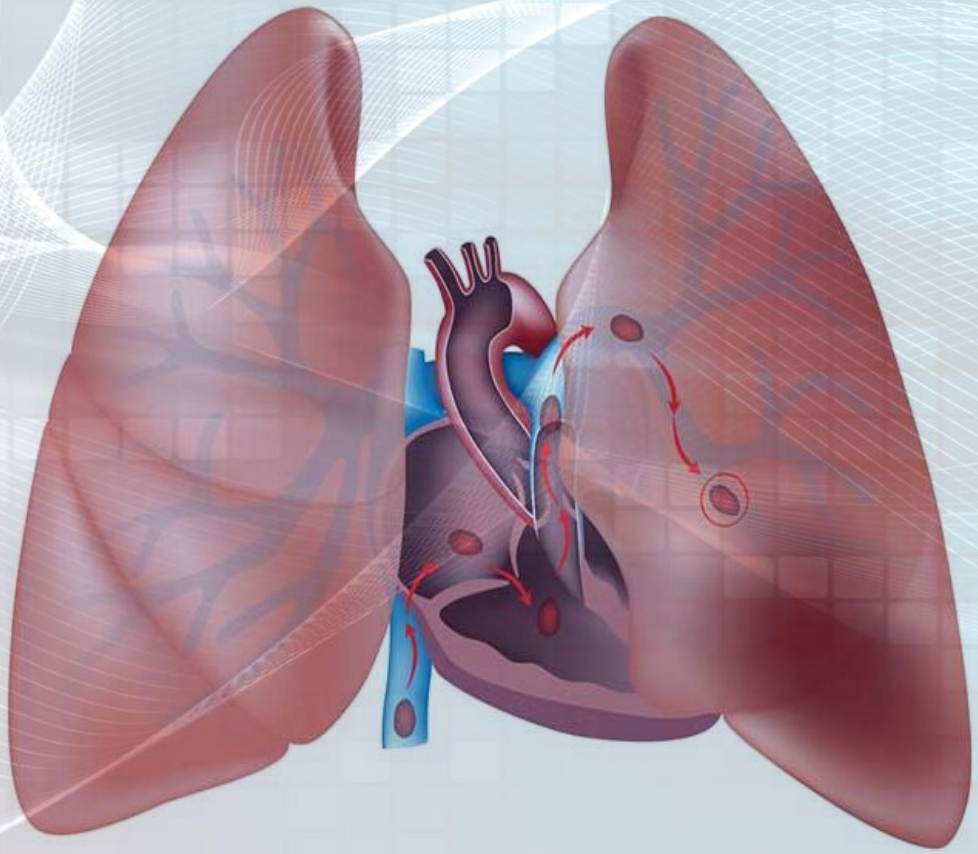
Hallmarks of Pathophysiological & Hemodynamic Events In Pulmonary Embolism

1. Ventilation perfusion defects.
2. Increased pulmonary vascular resistance.
3. Decreased pulmonary compliance.
4. Development of hypoxemia.
5. Right ventricular failure.



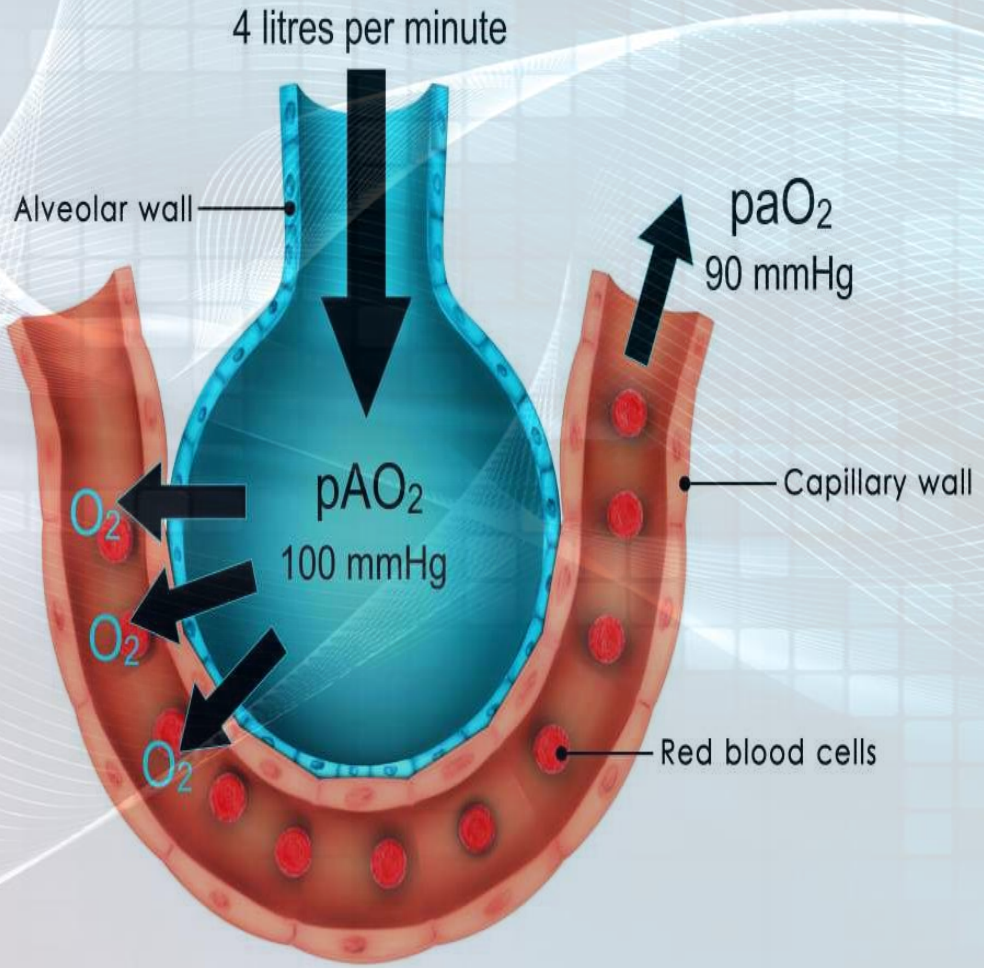
1. Ventilation Perfusion Defects V/Q Mismatch

- The optimal **V/Q ratio** is (**0.8**).
- **Pulmonary embolism** leads to a **perfusion defect** (wasted ventilation).
- Resulting in a segmental Dead space effect.
- Leading to pathological abnormalities of the **alveolar – arterial O2 gradient**.
- Eventually leading to the development of **hypoxemia**.



Alveolar – Arterial O2 Gradient

- **Alveolar – arterial O2 gradient** less than 10 mmHg is optimal. (up to 20 mmHg is considered normal).
- In **PE**, there is an abnormally **increased** value.
- This will lead to the development of **hypoxemia**.
- The severity of hypoxemia is related directly to the severity of mechanical obstruction (the clot burden).



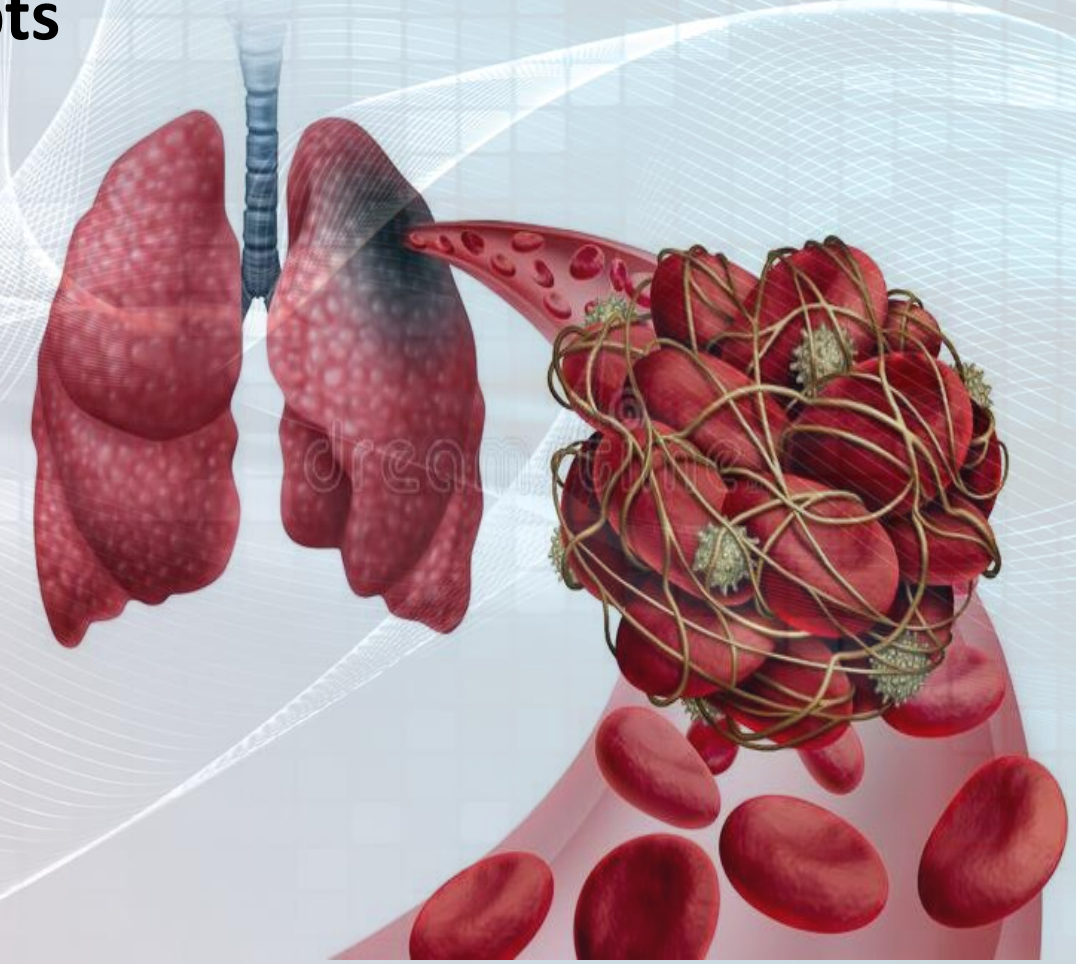
2. Increased Pulmonary Vascular Resistance

Due to,

- Vascular obstruction.
- Release of vasoactive mediators from the platelets (neurohumoral reflex).

Pulmonary Vascular Adaptation

- The normal **pulmonary circulation adapts** to the diverted blood flow through the recruitment & dilation of compliant pulmonary arterial vessels.
- These adaptive mechanisms **fail** when a greater proportion of the pulmonary circulation is compromised by larger emboli &/or by the elaboration of vasoconstricting mediators, at which point **pulmonary vascular resistance & pulmonary arterial pressure increase**.



3. Decreased Pulmonary Compliance

Due to:

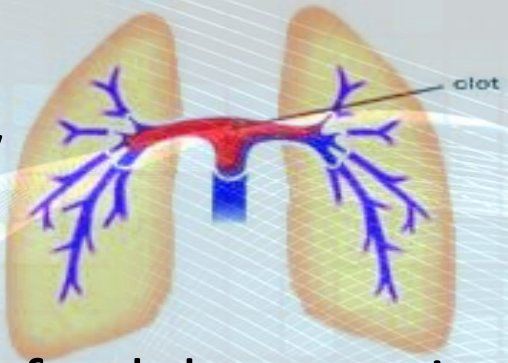
- Local **hypo-perfusion** interfering with surfactant production by alveolar type II cells.
- **Surfactant** is subsequently **depleted**, resulting in:
  - Alveolar edema,
  - Alveolar collapse, &
  - Areas of atelectasis.

4. Development of Hypoxemia

Due to:

1. Defective V/Q ratio.
2. Decreased pulmonary compliance.
3. Loss of surfactant with the subsequent development of pulmonary edema & areas of atelectasis.
4. Increased pulmonary vascular resistance leading to increased blood diversion through the physiological shunts.
5. Decreased pulmonary capillary surface area resulting in decreased lung diffusion capacity.
6. Reflex bronchoconstriction causes due to stimulation of irritant receptors, increasing the work of breathing in some patients.

5. Right Ventricular Failure



- **Large emboli,** particularly in patients with compromised cardiac function, **may cause** an **acute increase in pulmonary vascular resistance**.
- This leads to an **acute right ventricular strain** & can lead to a fatal decrease in cardiac output.
- This is the most devastating & feared complication of acute pulmonary thromboembolism.
- In complete obstruction (saddle embolus), cardiac output may be reduced to zero, causing immediate cardiovascular collapse & death.
- Such dramatic presentations occur in less than 5% of cases & are virtually untreatable. This highlights the importance of primary prevention of venous thrombosis.

Diagnosis of Pulmonary Embolism

Diagnosis of Pulmonary Embolism (PE) is based on:

- **Signs & symptoms.**
- **Investigations:**
  - Blood tests.
  - Electrocardiogram (ECG).
  - Chest X-ray.
  - Computerized tomography pulmonary angiography (CTPA). & CT scan.
  - Ventilation-perfusion scan.
  - Lower limb venous system ultrasonography & Doppler.
  - Echocardiography.

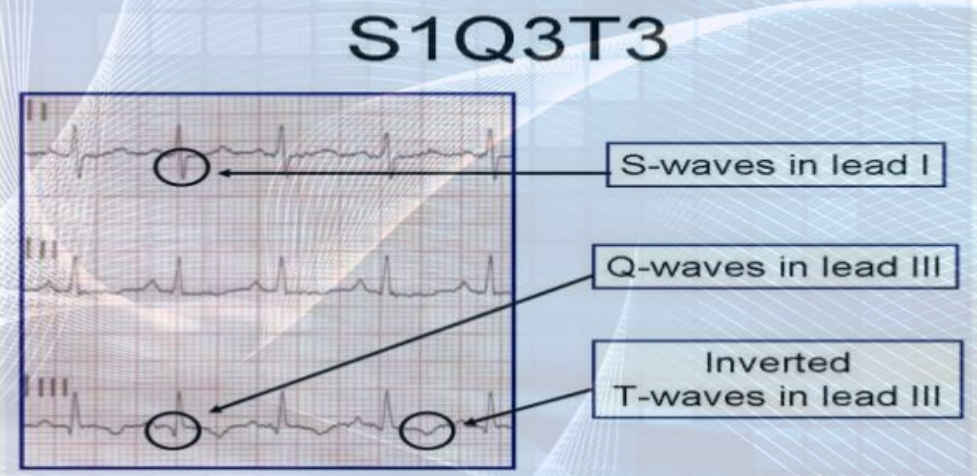
Investigations:
Blood Tests

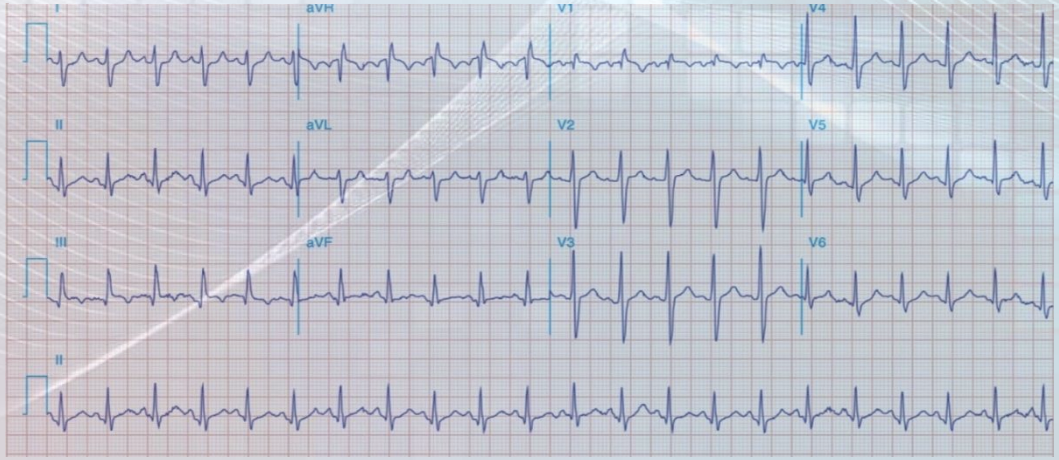
- Complete blood count **(CBC),** Coagulation profile**,** Erythrocytes sedimentation rate **(ESR), LDH,** Arterial blood gases **(ABG).**
- ***Quantitative plasma D- dimer ELIZA assay:***
  - D-Dimer is marker of coagulation.
  - D-Dimer is a small fibrin protein degradation fragment.
  - D-Dimer is a **very sensitive marker** for clot formation but **not specific** = A rule out test.
  - D- dimer level **increased** in the blood of all deep vein thrombosis (DVT) sufferers.
  - D- dimer level **increased** in various other conditions as myocardial infarction, pneumonia, sepsis, & some types of cancer.
- ***Elevated cardiac biomarkers*.**
  - Cardiac troponin.
  - May indicate a concomitant myocardial infarction (MI). or injury.

Investigations:
ECG

ECG is usually done to exclude other conditions that may have similar symptoms.

- ***ECG* findings:**
  - Sinus tachycardia.
  - Nonspecific ST segment & T wave changes (S1Q3T3).
  - Right ventricular strain pattern.
  - ECG changes are specific but not sensitive.
  - Present in around 60% of cases only.



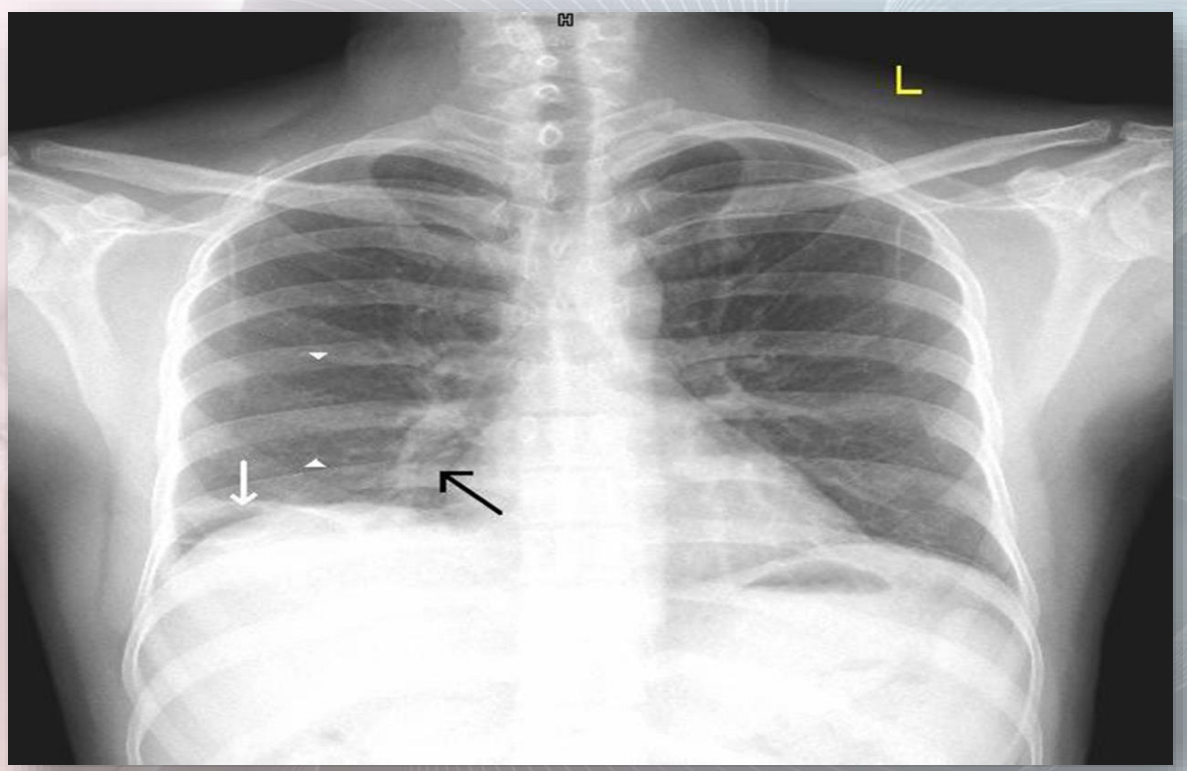


Investigations:
Chest X-Ray

CXR is usually done to exclude other conditions that may have similar symptoms.

- ***Chest X-Ray* findings*:***
  - Atelectasis.
  - Parenchymal infiltration.
  - Elevated diaphragm.
  - Enlarged mediastinum.
  - Enlarged hilum.
  - Cardiomegaly.
  - Pulmonary edema.
  - Pleural effusion.
  - Oligemia (**Westermark's sign**).
  - Prominent central pulmonary artery (**Fleischner sign**).
  - Wedge-shaped pleural-based area of increased opacity (**Hampton's hump**).

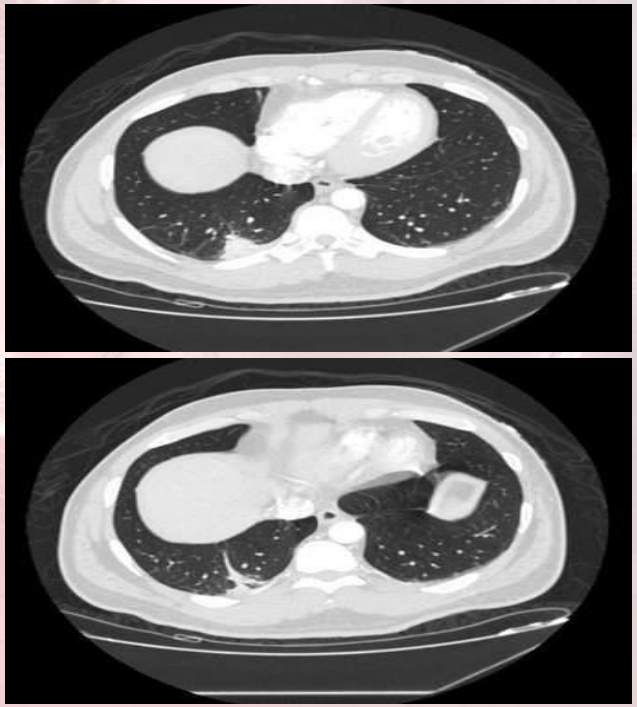
Investigations:
Chest X-Ray



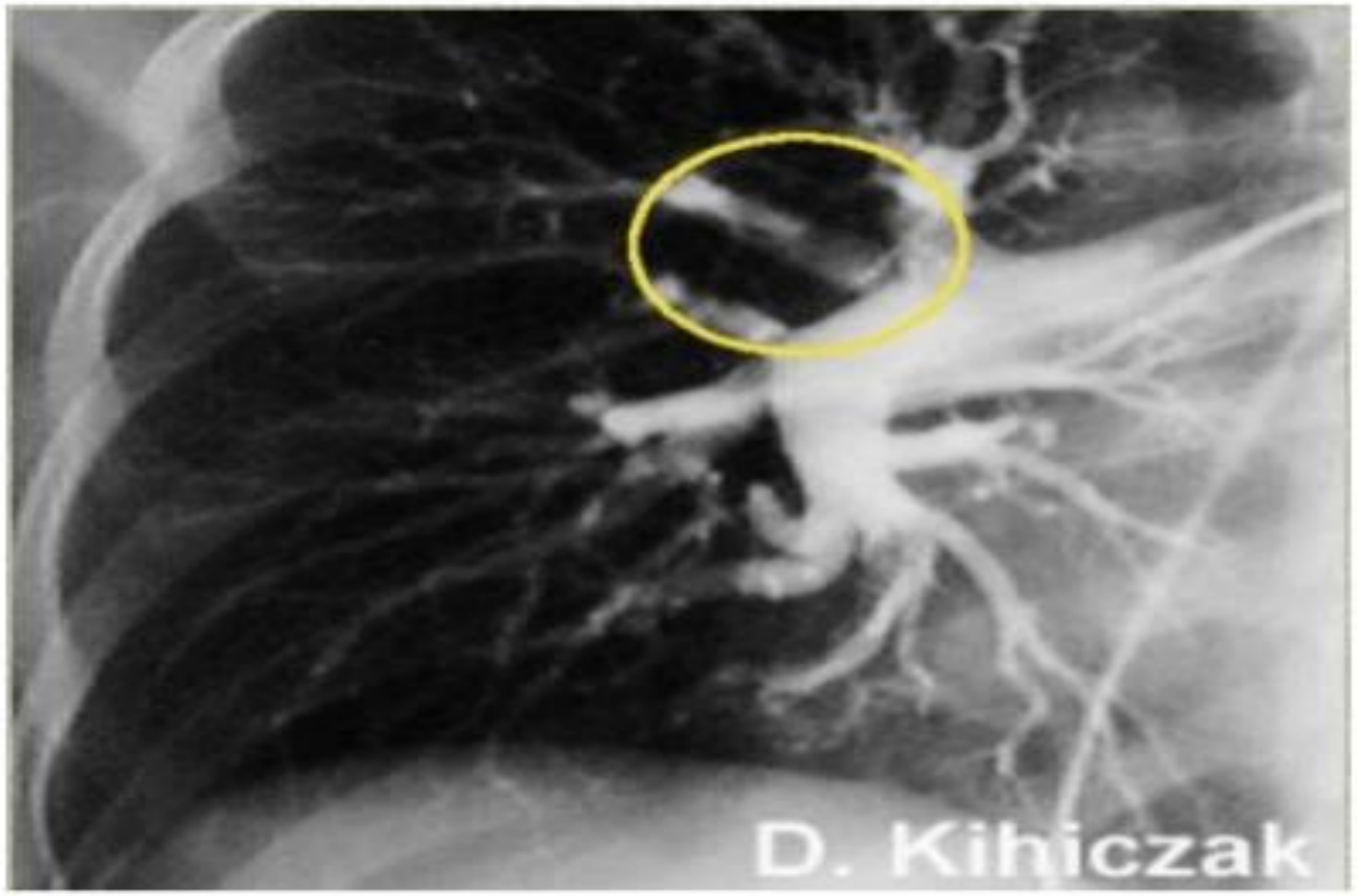
Chest radiograph (posterior–anterior view) showing, a lateral wedge-shaped opacity (white arrow) in the right lower zone (Hampton's hump), a focal area of oligemia (space between white arrow heads) in the right lower zone (Westermark's sign) & a prominent right descending pulmonary artery (black arrow) (Palla's sign).

Investigations:
Chest Imaging Studies (The Gold Standrd)

- ***CT Scans:***
  - Computerized tomography pulmonary angiography (CTPInvasive CT angiography, contrast enhanced or spiral chest CT scan).
  - Done to visualize the pulmonary vessels & to scan the pulmonary emboli.A) & CT scan.



Investigations:
Pulmonary Angiography

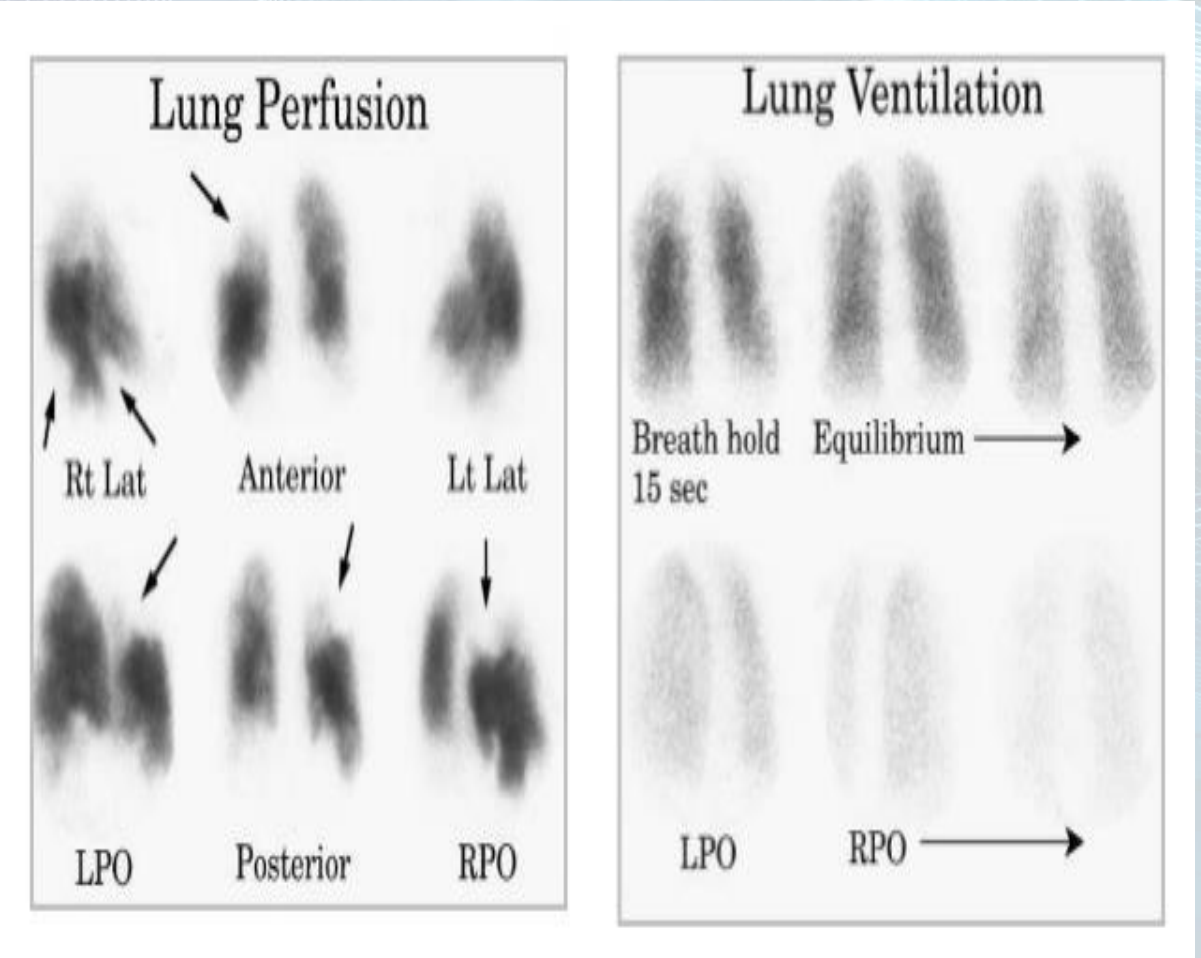


Investigations:
Chest Imaging Studies (The Gold Standrd)

- ***Pulmonary V/Q Scanning Studies:***

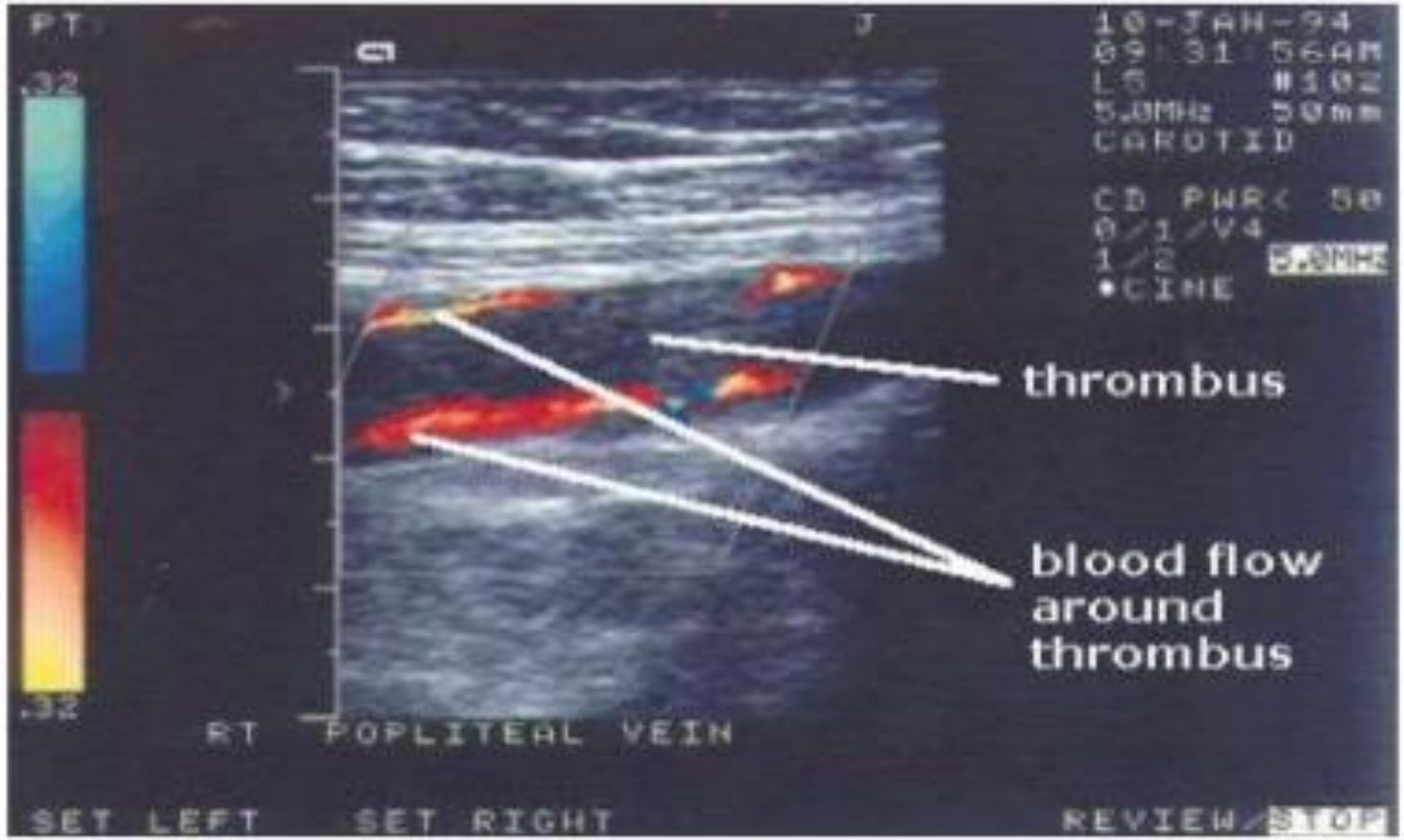
  Ventilation-perfusion scan.

  - Inhaling a slightly radioactive gas that is visible during this scan can show the parts of the lungs with no blood supply. This may be caused by a pulmonary embolism.
  - May be used in patients who cannot tolerate intravenous contrasts (segmental perfusion defect with normal ventilation).



Investigations:

Lower Limb Venous System Ultrasonography & Doppler



Management of Pulmonary Embolism

- Emergency management.
- Further management.

Emergency Management

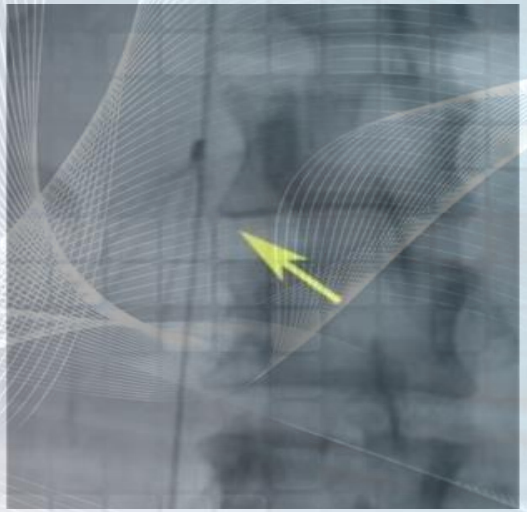
- Oxygen therapy to keep saturation > 90%.
- Insert intravenous (IV) access, & send base-line blood for testing.
- Analgesia.
- Perform ECG.
- Management of cardiogenic shock (fluids & inotropes- Dobutamine).
- Immediate anti-coagulation therapy.

Further Management of Pulmonary Embolism

- Immediate **anti-coagulation therapy** is the foundation of treatment:
  - Low molecular weight heparin (**LMWH**), Unfractionated heparin (**UFH**), or Fondaparinux, intravenously (**IV**).
  - Followed by, long term oral anticoagulation (**Warfarin**).
  - **Fibrinolysis**: Recombinant tissue plasminogen activator (tPA).
- **Thrombolytic therapy**: to relieve pulmonary vascular obstruction, improve right ventricular efficacy, & correct hemodynamic instability.

Further Management of Pulmonary Embolism

- **Inferior vena cava filters** may be used in selected cases, especially if the anticoagulation is contraindicated.



- Maintaining adequate circulatory support.
- **Surgical treatment:** Pulmonary embolectomy, or pulmonary thrombo-endarterectomy (Catheter embolectomy).
  - Is applied in massive life-threatening pulmonary embolism.

Assessment of Clinical Probability

- "Well's Score" or "Geneva rule"
- Improvements of signs, symptoms & risk factors.
- Improvements in diagnostic non-invasive & D-dimer tests.

Well's score[7] for DVT		Well's score[8] for PE		Revised Geneva score[9] for PE	
Items	**Points**	**Items**	**Points**	**Items**	**Points**
Cancer	+1	Previous PE or DVT	+1.5	Age >65 years	+1
Paralysis or recent plaster cast	+1	Heart rate >100 BPM	+1.5	Previous DVT or PE	+3
Bed rest >3 days or surgery <4 weeks	+1	Recent surgery or immobilization	+1.5	Surgery under general anesthesia or fracture of the lower limbs <1 month	+2
Pain on palpation of deep veins	+1	Clinical signs of DVT	+3	Active malignancy (solid or hematological malignancy, currently active or considered as cured for <1 year	+2
Swelling of entire leg	+1	Alternative diagnosis less likely than PE	+3	Unilateral lower limb pain	+3
Diameter difference on affected calf >3 cm	+1	Hemoptysis	+1	Hemoptysis	+2
Pitting edema (affected side only)	+1	Cancer	+1	Heart rate 75-94 BPM	+3
Dilated superficial veins (affected side)	+1			Heart rate >95 BPM	+5
Alternative diagnosis at least as possible as DVT	-2			Pain lower limb deep vein palpation and unilateral edema	+4
Clinical probability		**Clinical probability**		**Clinical probability**	
Low probability	0	Unlikely	<=4	Low	0-3
Intermediate	1-2	Likely	>4	Intermediate	4-10
High probability	>=3			High	>=11

BPM = Beats per minute, DVT = Deep venous thrombosis, PE = Pulmonary embolism

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Prognosis of Pulmonary Embolism

- **The prognosis of pulmonary embolism is greatly influenced by the premorbid vascular condition.**
- Patients ***without pre-existing cardiopulmonary disease*** **can accommodate** occlusion of **up to roughly one-third** of the **pulmonary circulation** with a negligible increase in pulmonary vascular resistance & pulmonary arterial pressure.
- normal **adaptive mechanisms** are **ineffective** in patients with ***pre-existing cardiovascular abnormalities*** (e.g., Atherosclerosis & pulmonary hypertension), making them susceptible to significant instability with any subsequent impairment of the pulmonary vasculature.

Prevention

- Compressive stockings.
- Aspirin.
- Anticoagulation.
- Management of risk factors.
- Follow up & assessment of clinical probability.


Thank You