Revised & Reviewed by: Abdulaziz & Bahammam
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MED441
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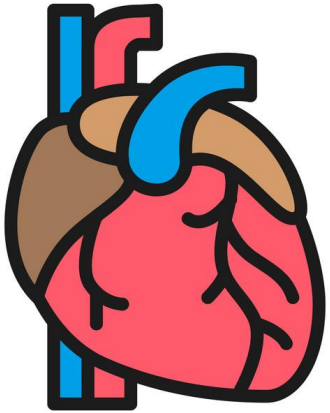

Pathophysiological changes in pulmonary embolism

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Editing File

Pulmonary Circulation

Click here
مفيد قبل مذاكرة الدرس

Pulmonary Circulation

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.

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

الثرمبوسز عبارة عن جلطه تتراكم بأي مكان وتبقى بنفس المكان ، مثلا تتكون بالرجل وبرضو موقع التجلط يكون بالرجل
بينما **الإمبولزم** تكون جلطة تتراكم باي مكان وبعدها تنتقل وتحدث الجلطة بالرئة ، مثلا تتكون بالفخذ وتنتقل إلى الرئة

اسامي الجلطات ومواقعها

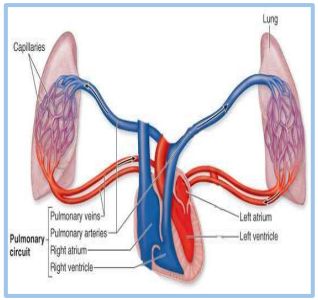
infraction = بالقلب
Embolism =بالرئة
Stroke =بالمخ
Clot=بالشريان
thrombosis =بالوريد

Deoxygenated blood

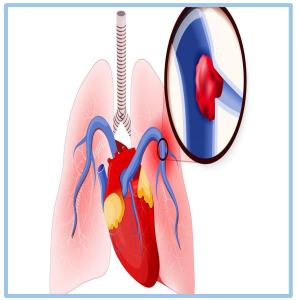
Is pumped through the semilunar pulmonary valve into the left & right main **pulmonary arteries** (one for each lung), which branch into smaller pulmonary arteries that spread throughout the lungs. *Exchange occurs here*

Oxygenated blood

Leaves the lungs through **pulmonary veins** to the left atrium completing the pulmonary cycle.



Pulmonary Circulation



Pulmonary Embolism

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**(تشريح بعد الوفاة)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 **CVS** (along with MI & stroke).

Can lead to immediate **death**, or serious **complications** among survivors.

Most episodes of pulmonary embolism carry a low mortality risk (about 1%) when properly diagnosed & treated (significance of early diagnosis).

The most common preventable cause of death among hospitalized patients in the USA.

High mortality rate (200,000 – 300.000) death annually in the USA.

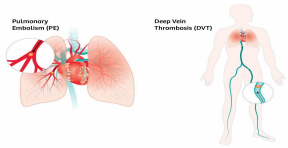
There is a lack of national data for incidence, prognosis, & rate of death of pulmonary embolism.

Pathogenesis & Source of Pulmonary Embolism

Pulmonary embolism can arise(تنشأ)from any clot anywhere in the body

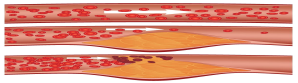
Pulmonary emboli often arise from thrombi originating in the deep venous system of the lower **extremities**(الأطراف)or pelvis.

Clot move mostly from a dislodge of in calf veins.

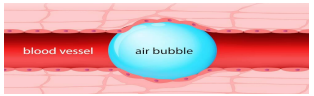


Minor sources:

- Fat embolism (droplet) (from atheroma).



- Air embolism (bubble) (from an unclear IV line)



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- Amniotic fluid embolism

تحدث عندما يُدخل السائل الأمنيوسي – وهو السائل الذي يحيط بالجنين داخل الرحم أثناء الحمل – أو سوائل الجنين، كالخلايا الجنينية، مجرى دم الأم. غالبًا ما يحدث انصمام السائل الأمنيوسي أثناء الولادة أو بعدها مباشرة.

- Septic embolism infection
- Tumor embolism

To reach the lungs, thromboemboli travel through the **right** side of the heart.

EXTRA SLIDE

PE is **FATAL:** PE caused by **F**at, **A**ir, **T**hrombus, **A**mniotic fluid, and **L**ess common, i.e., bacterial, tumor, and cement.

Special thanks to Yara Almufleh

Etiology & Risk Factors of Clot Formation

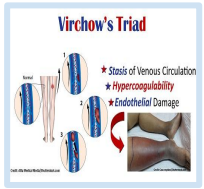
Virchow's Triad

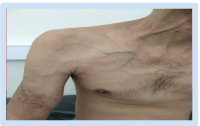
The function of Virchow's triad is to demonstrate the underlying physiology that drives the formation of venous thrombus. Formation of clots within the vasculature places th patient at risk for thromboembolic events such as CVA, pulmonary arterial embolus or organ infarction, ischemia, and cell death(439)

Click here

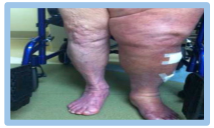
Hypercoagulability (Blood)
قابلية الدم للتجلط

- Major surgery/ trauma
- Malignancy
- Pregnancy (postpartum)
- Inherited thrombophilia
- Infection and sepsis
- Inflammation
- Dehydration
- Inflammatory bowel disease
- Autoimmune condition
- Estrogen therapy





Paget-Schroetter syndrome



May-Thurner

Vascular Damage (Vessel)

- Thrombophlebitis
  (major injury to blood vessels during IV infusion)
- Cellulitis
- Atherosclerosis
- Indwelling catheter/ heart valve
- Venipuncture عملية الحصول على منفذ وريدي لأجل إتمام عملية العلاج عن طريق الوريد أو الحصول على عينة من دم الوريد
- Physical trauma, stain or injury
- Microtrauma to vessel wall

Circulatory Stasis بُطئ الدورة الدموية (Flow)

- Immobility
- Venous obstruction (obesity, tumor, pregnancy)
- Varicose veins
- Atrial fibrillation or left ventricular dysfunction
- Congenital abnormalities affecting venous anatomy
  (**May-Thurner** & **Paget-Schroetter syndrome**)
- Low heart rate(bradycardia) & low blood pressure

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
• Asymptomatic • Shortness of breath • Chest discomfort	• Shortness of breath • Tachycardia • Tachypnea • Haemoptysis كحة الدم • Pleuritic chest pain • Pleural rub كل ما يتنفس راح يكون فيه الم	• Severe chest pain • Pallor • Sweating • Central cyanosis • Elevated JPV (jugular venous pulse) • loud P2, S2 split, gallop rhythm • Circulatory shock • Syncope • Death

Patient can also present with Deep vein thrombosis (DVT) as the origin of the clot.
Note: Deep vein thrombosis (DVT) occurs when a blood clot (thrombus) forms in one or more of the deep veins in your body, usually in your legs. Deep vein thrombosis can cause leg pain or swelling, but also can occur with no symptoms(439).

PE امراض تلخبطكم عن ال

Differential Diagnosis

Rib fracture	Myocardial infarction أكثر واحد فيهم يشبه PE	Pneumonia	Bronchitis	Pleurisy (Information of the plura)	Costochondritis (Inflammation of the cartilage in the rib cage)	Pneumothorax سكين / حادث

Hallmarks of Pathophysiological & Hemodynamic Events In PE

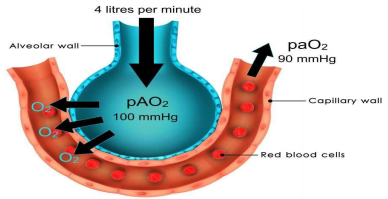
1. Ventilation perfusion **defects**
2. **Increased** pulmonary vascular resistance
3. **Decrease** pulmonary compliance
4. Development of **hypoxemia** بس الدكتوره قالت ذي اكبر مشكله وتودي الى الموت
5. **Right** ventricular failure الدكتور قال اكثر واحد مميت بيكون ذا

1. Ventilation perfusion defects

- The optimal V/Q ratio is (0.8)
- Pulmonary embolism leads to a **perfusion defect** (due to 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

- A (alveolar) – a (arterial 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).

Hallmarks of Pathophysiological & Hemodynamic Events In PE cont..

2. Increased Pulmonary Vascular Resistance

due to :

- Vascular obstruction.
- Release of vasoactive mediators from the platelets (neurohumoral reflex). **Neurohumoral** refers to increased activity of the sympathetic nervous system like renin-angiotensin system.

3. Decreased Pulmonary Compliance

due to :

- Local hypo-perfusion interfering with surfactant production by alveolar type II cells.

mnemonic
second = surfactant

- Surfactant is subsequently depleted, resulting in alveolar edema, alveolar collapse, & areas of atelectasis.

Atelectasis is the collapse or closure of a lung resulting in reduced or absent gas exchange. Remember surfactant function? is to increase compliance .

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.**

Hallmarks of Pathophysiological & Hemodynamic Events In PE cont..

4. Development of Hypoxemia

due to :

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

5. Right Ventricular Failure **Most fatal (MCQ)**

due to :

- Large emboli, particularly in patients with compromised cardiac function, may cause an acute **increase** in pulmonary vascular resistance.
  (large emboli→immediate failure of R ventricle, scattered big emboli occluding smaller arteries→pulmonary hypertension→back pressure on R ventricle→R ventricle failure).
- 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.

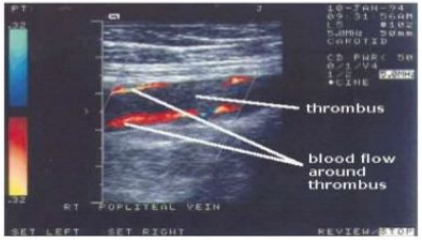
Diagnosis of Pulmonary Embolism

Pulmonary Embolism diagnosis is based on :

Signs & symptoms.

Investigations :

- Blood tests.
- Electrocardiogram (ECG).
- Chest x-ray.
- Computerized tomography pulmonary angiography (CTPA) & CT scan.
- Ventilation-perfusion scan.
- Echocardiography
- Lower limb venous system ultrasonography & Doppler.



Lower limb venous system ultrasonography & Doppler (detect for venous thrombosis)

Investigations

Both of them Not Gold Standard

1. Blood tests

CBC, Coagulation profile, ESR, LDH, ABG (Arterial blood gas)
Quantitative plasma D dimer ELIZA assay:

- D-Dimer is a small fibrin protein degradation fragment.
- Marker of coagulation.
- D-Dimer is a **very sensitive marker for clot formation but not specific** for PE= A rule out test.
- D-Dimer level increased in the blood of all DVT sufferers.
- D-Dimer level increased in various other conditions as myocardial infarction, pneumonia, sepsis, & some types of cancer.

Elevated cardiac biomarkers:

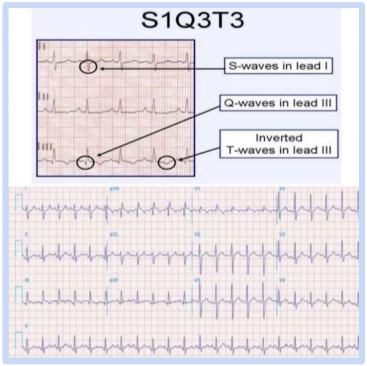
- Cardiac troponin.
- May indicate a concomitant myocardial injury (MI).

2. ECG

Usually done to exclude other conditions that may have similar symptoms

ECG:

- Sinus tachycardia.
- Non specific ST segment & T wave changes.
- Right ventricular strain pattern
- ECG changes are specific but not sensitive.
- Present in around 60% of cases only.

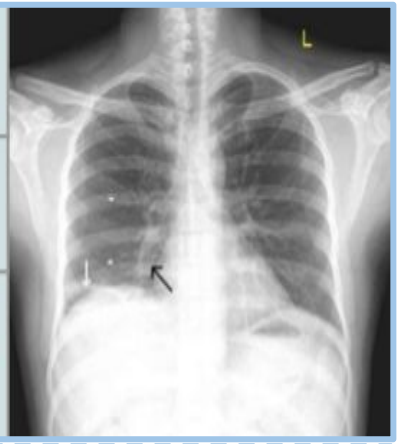


Investigations continue…

3. Chest X-ray

- Usually done to exclude other conditions that may have similar symptoms.
- Atelectasis.
- Parenchymal infiltration.
- **Elevated** diaphragm.
- **Enlarged** mediastinum.
- **Enlarged** hilum.
- Cardiomegaly.
- Pulmonary edema.
- Pleural effusion.
- Oligemia (Westermark's sign→ opacity of the lower margin of the lung) (a specific sign).
- Prominent central pulmonary artery (Fleischner sign) (a specific sign).
- Wedge-shaped pleural-based area of increased opacity (Hampton's hump) (a specific sign).

white arrow	lateral wedge-shaped opacity (Hampton's hump),
space between white arrowheads	focal area of oligemia (Westermark's sign)
black arrow	prominent right descending pulmonary artery (Palla's sign).



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 arrowheads) in the right lower zone (Westermark's sign) & a prominent right descending pulmonary artery (black arrow) (Palla's sign).

Investigations continue…

Chest Imaging Studies (*The Gold Standard*)

1
- CT Scans
  - CTPA
  - CT scan

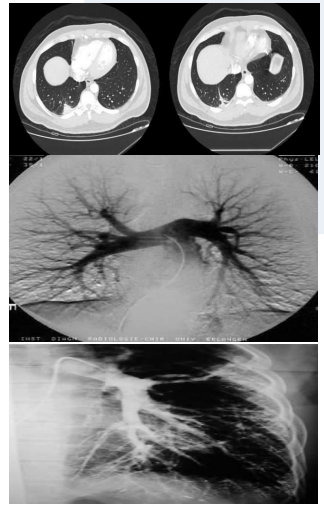
2
- Pulmonary V/Q Scanning Studies
  - Ventilation-perfusion scan

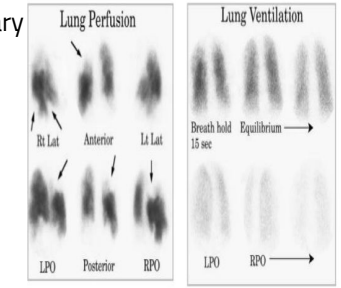
CT scans

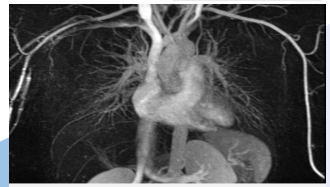
- Computerized tomography pulmonary angiography (CTPA) & CT scan.
- Invasive CT angiography, contrast enhanced or spiral chest CT scan.
- Done to visualize the pulmonary vessels & to scan the pulmonary emboli.

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). =dead space = PE







CT angiography

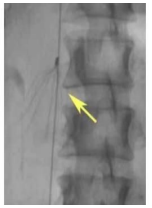
Management of Pulmonary Embolism

Emergency management

- **Oxygen therapy** to keep saturation > 90%
- Insert **Iv access** & send **baseline blood** for testing
- **Analgesia** (painkiller) (for chest pain)
- Perform **ECG**
- Management of cardiogenic shock (fluids & inotropes - Dobutamine)

Further management

- Immediate anticoagulation therapy **(is the foundation of treatment)**
  - anticoagulation Therapy
    - 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**
  - **Thrombolytic Therapy** to relieve pulmonary vascular obstruction, improve right ventricular efficacy, & correct hemodynamic instability.
- **Inferior vena cava filters** (to filter the clot)
  - **Inferior vena cava filters** may be used in selected cases, especially if the anticoagulation is contraindicated.
- Maintaining adequate circulatory support
- Surgical treatment لو ما ذابت الجلطة
  - **Pulmonary embolectomy** or **pulmonary thrombo-endarterectomy** (Catheter embolectomy) (use a catheter to remove the emboli) and it is applied in massive life threatening pulmonary embolism.



Assessment of Clinical Probability:

- Well's Score " or "Geneva rule"
- to follow up Improvements of signs, symptoms & risk factors from a baseline.
- 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

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

Team Leaders

Rand aldajani

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Team Members

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