THROMBOSIS AND EMBOLISM

THROMBOSIS

Thrombosis is characterized by the formation of semisolid masses, because of an abnormal blood clot formation without an injury of the vessel wall.
These thrombi consist of blood cells (different types, mainly platelets) and fibrin (important for the stabilization of the blood clot). As just said, these blood clots generally have the same composition of normal blood clots; however, in this case, they adhere to the vessel wall following an abnormal hemostatic process. For this reason, these blood clots (even if their composition is normal) are named "thrombi", since they imply a pathological process without an injury of the vessel wall (bleeding); on the contrary to normal blood clots that have the aim to block the bleeding.
This process is due to an inappropriate and pathological activation of the hemostatic processes occurring inside the vessels. This abnormality may be caused by:

- increased activity of coagulation factors: **hypercoagulability**;
- **reduction of hemostasis control**: reduction of the cascade inhibitors;
- **reduced fibrinolytic activity**;
- reduction of all the inhibitors that control the coagulation cascade.

Thrombosis can affect any point of the cardiovascular system. In fact the thrombi can develop in the cardiac cavities, especially at the sites of the valvular cusps, but also inside the arteries, veins and capillaries. So, any district of our cardiovascular system can be affected.

VIRCHOW TRIAD IN THROMBOSIS

In 1856, the scientist Virchow suggested possible causes of thrombosis proposing the so-called "triad in thrombosis" (*fig.1*).
This theory includes the three main important conditions that can lead to the development of thrombosis:

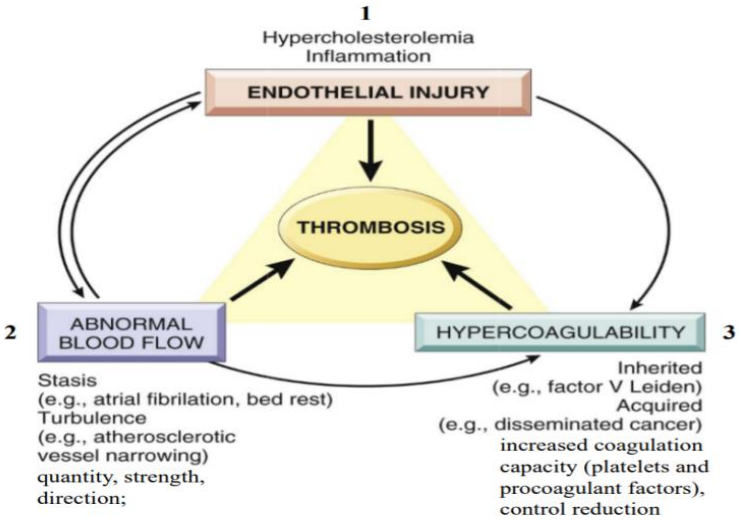


Fig.1

1. **Endothelial injury**: a dysfunction in the endothelium. It is mainly caused by hypercholesterolemia and atherosclerosis or in general any inflammation at the level of the vessel wall.
   Indeed, as said in the previous lecture, a well functioning endothelium has anti-thrombogenic properties inhibiting aggregation and adhesion of the platelets. This is possible through the secretion of some factors as: NO and prostaglandin E2 that inhibit platelet adhesion and aggregation, and other factors that can stimulate fibrinolytic activity as tissue plasminogen activators that will lead to the formation of plasminogen (main player in clot formation).
   In case of a damage, the endothelium is not able to contrast the platelets aggregation, losing its anti-aggregative properties. So, if the fibrinolytic system is not functioning, there will be problems in dissolving the abnormal blood clot. In this situation we can have formation of thrombi, especially in the heart and arteries.

The major causes for endothelial injury are:

a. **Infectious causes** (bacteria, virus, parasites),
b. **Mechanical causes** (trauma, iatrogenic maneuvers),
c. **Toxic and chemical causes** (drugs, radiation, hyperlipidemia; most frequently hypercholesterolemia in atherosclerosis, bile pigments, homocystinuria, cyanide and carbon monoxide anoxia, cigarette smoke, etc. - Note: all these factors are present also in atherosclerosis: indeed, the risk of thrombosis is directly associated with atherosclerosis. In fact, in advanced plaques, the rupture of a plaque is very easy to happen, resulting in the formation of a thrombus on the top of the plaque itself)
d. ***Immunological causes*** *(immunocomplex or anti-endothelial antibodies cytotoxic lymphocytes).*

2. **Abnormal blood flow**: especially in stasis conditions, in which blood flow is reduced, or in case of turbulence (so in changes in force, quantity and direction of the blood flow).
   a. One of the most common causes of thrombosis is the reduction of the blood flow: a condition of **stasis** (common especially in hospitalized patients in bed for long or that are immobilized for a long time).
   b. Another condition contributing to abnormal flow is blood stasis, when there is a marked reduction in the blood flow due to an irregularity in the vessel wall or an abrupt **change in flow direction**. This cas be seen in vascular bifurcations, arterial arches or when there is a narrowing of vessels.
   c. Another point that can favor the formation of thrombi is the **formation of vortices and turbulence**. This is typical in case of aneurysms, narrowing, ectasia (dilation)... In fact, these conditions alter the speed and regularity of the laminar blood flow resulting in:
      i. the promotion of platelet adhesion to the endothelium,
      ii. in reduced dilution of procoagulant factors,
      iii. in delayed flow of inhibitors of factors
      iv. in endothelial cell activation.

<u>Difference in probability of thrombosis in arteries and veins:</u>

We know that arterial blood flow is faster; hence, platelet adhesion and thrombus formation are limited. However, all these situations in which there is turbulence and/or a reduction in blood flow speed (like in aneurysms) can contribute to arterial and cardiac thrombi formation. Note: in case of arterial thrombi, usually you have only partial occlusion of the vessel, not a total one; this is due to the faster blood flow.

Venous flow is slower. So, the thrombus is more easily formed and grows more quickly, especially when there is a stasis of blood flow. Therefore, it is more common to have clots occluding totally the vessels. This condition is typical of veins of the lower extremities that, because of the numerous valves, allow venous thrombi to begin in their pockets.

3. The third point regards the **hypercoagulability**, meaning an increased coagulation that depends on:
   - abnormal trigger of the coagulation cascade,
   - increased production and secretion of factors that favor coagulation cascade
   - reduction or lack of one or more anticoagulative factors: factors negatively controlling the coagulation process.
   - alteration of the fibrinolytic system. This means that there is a predisposition to activate the coagulation cascade

CAUSES OF HYPERCOAGULABILITY

Hypercoagulability has many different causes:

Primitive forms (genetic):

- mutations of the factor V
- deficiency of antithrombin III that control the excessive coagulation
- defects of fibrinolysis

Secondary forms (acquired or associated to specific pathological conditions):

- prolonged bed rest or immobilization: these patients are more prone to develop thrombosis,
- myocardial infarction,
- atrial fibrillation,
- tissue injury (fracture, burn, surgery that imply an immobilization in bed for a long time).
- cancers,
- prosthetic cardiac valves: the thrombi can form more easily at the level of these artificial valves

DIFFERENT TYPES OF THROMBI:

The type of thrombus that will be formed depends on:

1. SPEED of the BLOOD FLOW
2. RAPIDITY of the COAGULATIVE PROCESS CASCADE.

From an anatomical point of view, in a thrombus we can observe:

- **head**: attachment point to the endothelium wall,
- **body**: variable size, composition, and mobility,
- **tail**: this is the part of the thrombus not attached to the vessel, often long. This is the portion that more easily detaches in the veins. This fragment, when detached, can travel in the circulation system, giving rise to the embolus. Hence, the difference between thrombus and embolus is:
  - A thrombus is attached to the wall
  - the embolus travels into the circulation

CLASSIFICATION BASED OF MORPHOLOGICAL CHARACTERISTICS:

There are different types of thrombi, which can be classified based on morphological characteristics.

- **White thrombi**: they have a grayish-white appearance and are the most friable and fragile, so they can be fragmented more easily causing an embolism. They are white in color because they consist mainly of platelets and fibrin. If there is inflammation, the white thrombus may contain leukocytes and erythocytes as well.
  - In arteries, the rapid blood flow makes it difficult for white thrombi to grow, resulting in normally small thrombi that do not occlude completely lumen of the vessels.
  - In case of a Slow-down current in veins (reduction of blood flow), these white thrombi can enlarge, become totally obstructive and contain increasing amounts of erythrocytes that are progressively entrapped in the thrombi and that substitute some of the platelets.
- **Red thrombi**: tenacious, elastic, firm, attached to the vessel wall with only a very small portion of the head (white thrombi are attached with the whole head). They are red in color because they consist of a few platelets, fibrin and a prevalence of red blood cells and some leukocytes.

- Typically formed in the venous district where the blood flow slows down (stasis), contributing to the quick growth of the thrombi, resulting in a very high risk of occlusion of veins. So, as venous flow is slower, these thrombi can become obstructive. They are typically found in the lower extremities due to immobilization.

- **Mixed or variegated thrombi** (*fig.2*): thrombi with grossly and microscopically apparent white laminations called lines of Zahn, which are pale platelet and fibrin deposits alternated with darker erythrocytes-rich layers. Mainly present in heart and less frequently in the legs.

  - In the white lines - lines of Zahn: prevalence of platelets
  - In the red lines: prevalence of erythrocytes

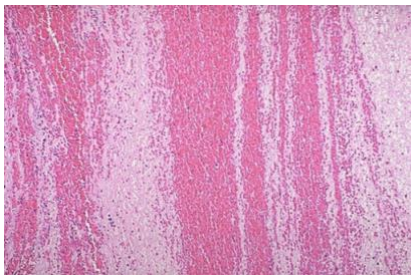


Fig.2

CLASSIFICATION ACCORDING TO THE EFFECTS ON THE VESSEL CANALIZATION:

- **Parietal or mural thrombi**: adherent to the wall, usually white, more frequent in arteries, especially in the the aortic lumen, and in heart chambers. Generally, they are not completely obstructive, just partially.
  - **Aortic thrombi**: mural or parietal, usually develop at the site of an aneurysm or on the top of an ulcerated atherosclerotic plaque (ruptured). Remember that one of the most severe risks of an advanced plaque is the rupture where, at the site of ulceration, there is the immediate activation of the platelet aggregation and activation of the coagulation cascade resulting in the formation of a thrombus that can compromise the already partially occluded artery.
  - **Cardiac mural thrombi**: develop in the heart chambers due to abnormal myocardial contraction. For example, in case of arrhythmias, dilated cardiomyopathy, myocardial infarction or endomyocardial injury.

    - In *fig.3* are represented thrombi in the left and right ventricular apices (arrows), overlying white fibrous scar.

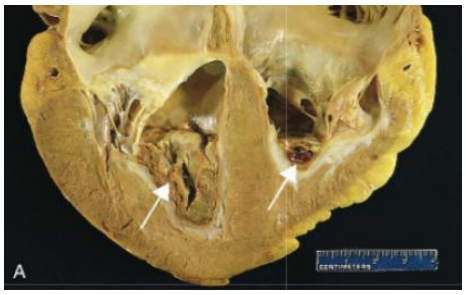


Fig.3

- **Obstructive thrombi**: they occupy all the vessel's lumen determining the obstruction and the block of the circulation. They can lead not only to ischemia but also to an infarction in case of a total obstruction (ischemic necrosis). *Usually they are mixed or mostly red thrombi because the red thrombi can develop in the venous system where the blood flow is slower in comparison to that of arterial blood flow, resulting in easier growth.*

CLASSIFICATION BASED ON THE VESSEL-FORMATION DISTRICT - LOCATION:

- **Cardiac thrombosis:**
  mural (or parietal) thrombi that don't occlude totally. They are formed in the cardiac cavities, quite often at the level of valve leaflets. Thrombi that develop at the sides of the heart valves are specifically called vegetations. They are generally favored by :
  - **arrhythmias**,

- **atrial dilatations or fibrillation**
- by bloodborne bacteria or fungi. These microorganisms can adhere and direcly damage the valves (e.g. rheumatic heart disease) leading also to **endocarditis**.

They are usually white or mixed (very fragile). Hence, they easily embolize and can go to:

- the lungs if they are in the right part of the heart → pulmonary embolism
- or to other areas such as the brain, kidneys and so on if they are in the left part.

- **Arterial thrombosis:**
  white thrombi present in the arteries and consisting mainly of platelets and fibrin. They are mural or parietal and usually not occlusive but, in conditions in which blood flow is slower, the thrombi can grow in size and become occlusive. They grow in a retrograde fashion (against blood flow) with respect to the point of attachment, meaning that they propagate towards the heart, and because of the blood flow that is opposite to their growth, it's more difficult for them to become bigger.
  - Causes: usually superimposed on a **ruptured atherosclerotic plaque** or other **inflammatory vascular injury** such as vasculitis, **traumas** or where there is a marked **turbulence**; at the level of aneurysms (aortic aneurysm) or in turbulent areas, like vessel bifurcation; **stasis** in the infarcted area due to non-contractile myocardium, *stasis due to dilation of the left atrium following atrial fibrillation or cardiac rheumatism which causes stenosis of the mitral valve, ischemic necrosis or cerebral infarction/stroke.*
  - Most common sites include **major arteries** like the coronary arteries, cerebral and femoral arteries, but also aorta.
  - **High risk of embolization**, like in cardiac thrombosis, which may target the brain, kidneys and spleen, as these thrombi are more fragile.

- **Venous thrombosis:**
  Characterized by red thrombi that consist mainly of red blood cells and only a few platelets and fibrin. They develop usually due to **stasis** (reduction in blood flow compared to arteries) where they can grow and easily become occlusive. In the veins, we can sometimes also find mixed thrombi. They can reach large dimensions and a morphological complexity. They grow in the direction of blood flow, meaning that they propagate towards the heart.

  We can distinguish two types of venous thrombosis, depending on the fact if they are associated with an inflammatory state or not:
  - **Thrombophlebitis**: condition in which these venous thrombi are implanted on endothelial lesions of inflammatory nature that cause the endothelial dysfunction. The symptomatology is similar to that of an inflammatory response: pain especially of legs, including redness, edema, pain, etc.
  - **Phlebothrombosis**: condition in which the venous thrombi are implanted on endothelial lesions in the absence of inflammation. As a result, this non-inflammatory condition presents no symptoms or a very limited edema because of obstaculation of blood flow. It is also typical of legs.

  90% of venous thrombosis affects the legs. In particular, we can also distinguish among deep and superficial thrombi:
  - **Superficial venous thrombosis**: affects the saphenous vein with the formation of varicose veins (varicosities) causing local pain, congestion, swelling and tenderness that then

degenerate towards varicose ulcers with rupture of the varices and sometimes rare embolization (they are the least severe type of thrombi).

- **Deep venous thrombosis**: most severe, affects the popliteal, femoral, iliac veins. It is asymptomatic in 50% of cases, but local pain and edema can be present in the remaining cases. This condition is more serious because these thrombi can easily embolize, resulting in pulmonary embolism. In fact, we can also talk about pulmonary thromboembolism because it is caused by fragments of venous thrombi that have ruptured/detached from the main thrombus in the legs and traveled via the circulation to the lungs.

Venous thrombosis is one of the most frequent thrombosis because it is associated with all the cases of hypercoagulation and of stasis such as:

- surgery,
- traumas and burns
- cancer,
- long immobilization, advanced age and reduced physical activity
- after childbirth
- oral contraceptive (which can induce hypercoagulation of blood)

A particularly serious form of venous thrombosis is the one occurring at the level of the **sine of dura madre**. This is an life-threatening condition, as it is often connected to septic processes and infections of mastoid, auricular or sinus cavities (sinusitis) that activate hypercoagulation. The result is a neurological problem.

THROMBUS EVOLUTION

A thrombus can totally or partially occlude the blood flow of a vessel (more often totally in veins), causing:

- ischemia if it is partial
- or ischemic necrosis or infarction when total.

After being formed, the thrombus can also be **digested** by the fibrinolytic system and monocytes and macrophages, resulting in its resolution/digestion.
However, in this case the thrombus becomes more fragile and can easily be fragmented. The risk is that these fragments can travel in the circulatory system causing embolism where they meet a narrow vessel and block it.
Another evolution is the **reorganization of the thrombus**, in which new vessels develop within the thrombus. Therefore, we have vascularization, causing the thrombus to grow faster and quickly. As a result, this now bulkier thrombus, which previously only partially occluded the lumen of the vessel, can now completely occlude the vessel causing infarction.

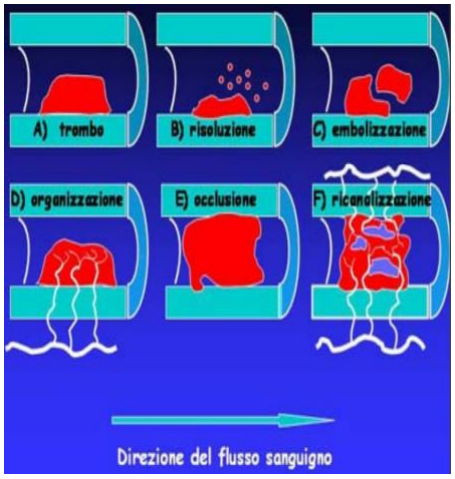


Fig.4

Another possibility is that there is a **recanalization** within the thrombus, meaning that there is a continuity of the circulation (with new vessels formed) through the thrombus thanks to the interaction between the thrombus vessels and other vessels nearby it. In this way, as this process develops, there will be an **integration of the thrombus** in the vessel wall after a 'reorganization' of the thrombus, and a resulting thickening of the wall in the point where the thrombus was.

Reported below is the mechanism of thrombus evolution taken from the slides:

1) *After 1 day from aggregation there is the autolysis of platelets and their replacement by erythrocytes and fibrin (initially all the thrombi are white and subsequently become red or variegated)*
2) *Thrombus is then invaded by monocytes/macrophages. The macrophage activity and fibrinolysis cause lysis or dissolution or softening of the thrombus, which all result in the resolution or dissolution: reduce the blood flow obstruction.*
3) *This process is a risk factor for embolization: where part of thrombus dislodges and travels to other sites in the vasculature. The total digestion of the thrombus and repair of the vessel (recent thrombi) can be achieved.*
4) *ECs, SMCs, and fibroblast can invade the thrombus forming solid cords and then capillary channels can organize to favor the growth of the thrombus and lead to occlusion.*
5) *Subsequently, possible recanalization of the vessel: event that restores the continuity of the blood flow, takes place. In the end the thrombus is a vascularized mass of connective/fibrous tissue embedded in the wall (intimate thickening or scar repair) (older thrombus)*
6) *Further evolution of the thrombus may consist in the precipitation of calcium salts resulting in calcification.*

CLINICAL FEATURES OF THROMBOSIS

The presence of a thrombus in the vessels' lumen is a highly dangerous condition *characterized by symptoms that are mainly due to the alteration of the blood circulation following the obstruction or occlusion (partial or total) of arteries or veins, or the rise of emboli.* Therefore, thrombosis complications present different degrees of severity:

1. In the absence of collateral circulation, the **total occlusion** evolves in serious damage and eventually an infarction characterized by ischemic necrosis.
   (Sometimes, also in the case of a complete occlusion, some collateral vessels may be formed perfusing the obstructed area. Hence, This way, we won't have an infarction but only ischemia).
2. **Partial occlusion** or **possibility of collateral circulation** results in more or less serious damage leading to hypoxia, swelling, hypotrophy or atrophy, fibrosis over time.
3. Complete or partial detachment of the thrombus causes **embolism**, a very high-risk condition. As previously stated, we can distinguish three different types of thrombosis:
   - cardiac thrombosis: detachment of part of the thrombus can easily happen resulting in the high risk of pulmonary embolism, especially when the thrombus is present in the right side of the heart. Similarly, if the thrombus originates from the left side of the heart, its partial or complete detachment can cause embolism in other target organs.
   - arterial thrombosis: fragmentation of these thrombi can cause embolism in various organs.
   - venous thrombosis: fragments of these thrombi, which are mainly located in the lower extremities, are also responsible for mainly pulmonary embolism.

PREVENTION OR THERAPIES

Treatment for thrombosis is focused on reducing the possibility of the formation of these abnormal clots, by administering:

- **Main antithrombotic therapies**:
  - Antiplatelet drugs to prevent arterial thrombosis.
  - Anticoagulants, like heparin, dicumarolic or activators of the fibrinolytic system (plasminogen activators), to dissolve the clots and prevent venous thrombosis.

- **Thrombus removal**:
    - Angioplasty and subsequent placement of a medicated STENT (treated with antiproliferative and antithrombotic factors). *(Addition from the web) A stent is a tiny tube that is inserted into a blocked passageway to keep it open. The stent restores the flow of blood or other fluids, depending on where it's placed.*
- **Thrombotic disease prevention**:
    - Risk factor control focused on the lifestyle: diet (i.e. The Mediterranean diet to prevent hypercholesterolemia and the rupture/ulceration of atherosclerotic plaques), physical activity, smoking, oral contraceptives (in particular when reaching a certain age).

EMBOLISM

Embolism is the presence in the blood of material, including even components of the blood, that cannot be mixed with the blood itself. Emboli travel through the blood until they encounter vessels that are too small to permit further passage. Therefore, when the size of the vessel is smaller than that of the embolus, it causes a partial or complete vascular occlusion that results in the alteration of the circulation leading to local ischemia and, in worst cases, in tissue infarction in case of total occlusion. In fact, emboli can lodge anywhere in the vascular tree and their clinical consequences depend on:

- position and size of the lodged embolus
- which vessels is occluded,
- occluded vessel caliber,
- *vulnerability of the tissue to ischemia,*
- *degree and duration of the occlusion and of ischemia,*
- *existence or not of collateral blood supply, etc.*
- organ that is not perfused

Embolism, as well as thrombosis, is a frequent cardiovascular problem, commonly leading to death.

CLASSIFICATION ACCORDING TO THEIR NATURE/STATE:

We can distinguish three different types of emboli depending on their physical states:

A. solid,
B. fluid,
C. gaseous (air).
   The fluid and gaseous emboli can cause permanent obstruction of small vessels.

A. SOLID EMBOLISM, Different types:

1. **Thrombotic masses detached from the sites of fragmentation**. They are solid masses detached from a thrombus, following fragmentations. We refer to it as "**thromboembolism**". As This makes up the 99% of cases, this is the most common type of solid thrombus.
   Most common systemic emboli (80%) arise from intracardiac mural thrombi, which are present in the chambers of the heart:
    a. 2/3 are present in the left ventricular wall and are associated with left ventricular wall infarction,
    b. 1/3 are associated with left atrial dilatation and fibrillation,
    c. The remaining emboli originates from aortic aneurysms, atherosclerotic plaques *(atherosclerotic debris or cholesterol emboli),* valvular vegetations, or venous thrombi.

2. **Fragments of pathological tissues** (detaching from neoplasms that have permeated the vessels, from endocarditic or atherosclerotic ulcers → the emboli will be composed of some of the necrotic material detached from the plaque), or even from normal tissues (liver cells, marrow cells, etc.).
3. **Microscopic and macroscopic parasites and fungi** that utilize the circulation to spread: echinococcus, schistosome filarias, ascarids, hookworms, plasmodia, leishmanias, trypanosomes, or from fungi, etc.
4. **Foreign bodies** of various kinds (needles, bullets, spines, etc.) which have occasionally or accidentally penetrated into the cardiocirculatory system.

One of the main risks associated with solid embolism is pulmonary embolism:

Pulmonary thromboembolism

Pulmonary emboli (PE) mainly originate from deep venous thrombosis of lower extremities (95% of cases), but also from thrombi originating in the right side of the heart, and it is the most common form of thromboembolic disease. It has a high incidence in hospitalized patients that are immobilized in bed, which allows the emboli to be carried through progressively larger veins, reaching the right part of the heart through the vena cava before slamming into the pulmonary arterial vasculature. From a clinical point of view depending on the size and on the artery occluded, the embolus can:

- occlude the main pulmonary artery leading to very severe consequences,
- stop in the pulmonary artery bifurcation, in this case we are talking about a saddle embolus,
- pass out into the smaller branching arteries, if smaller in size.

Quite frequently, there are often multiple emboli, from one or more thrombi, occurring sequentially or simultaneously as a "shower of smaller emboli" from a single large mass. This shower of smaller emboli can occlude smaller branches of the arteries. In this case for a patient who had one, they are at high risk for more over time.

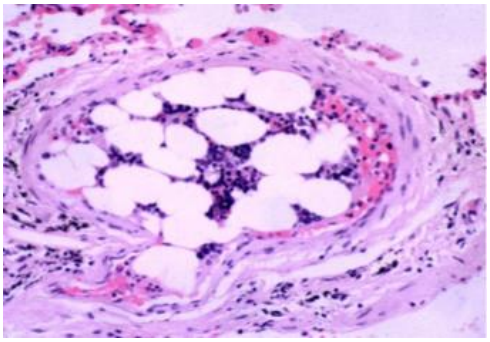
Clinical consequences of pulmonary embolism

- In 60-80% of PE cases the emboli are small, making them "clinically silent" as they cannot trigger any clinical manifestations. Later on, small emboli can become organized and be incorporated into the vascular wall that will show fibrosis.
- In other cases (5% of cases), bulky emboli can obstruct more than 60% of vessels and alter the pulmonary circulation causing sudden death, right heart failure, or cardiovascular collapse, due to the fact that the area is not perfused anymore.
- Sometimes, the embolic obstruction of medium-sized arteries can cause the vascular rupture and subsequent pulmonary hemorrhage. Normally, we do not talk about pulmonary infarction because the bronchial arteries are sufficient to perfuse the affected area even if the pulmonary arteries are occluded. In other words, the bronchial arterial flow acts as a collateral blood supply that is sufficient at maintaining a basal circulation.
  If there is a left-sided cardiac failure, the bronchial arterial flow is compromised and leads to a lung infarction. This can also be seen in the occlusion of small end-branches of pulmonary arteries, as they can also result in pulmonary hemorrhages or infarction.
- Lastly, multiple emboli, over time, can progress towards chronic pulmonary hypertension with right ventricular hypertrophy because of the difficulty for the blood to reach lungs from the heart and therefore there will be an increased workload for the heart → right ventricular failure.

B. FLUID EMBOLISM: consists of

1. **lipids and oil material** not miscible with blood. In fact, these fats or oil can accidentally penetrate the veins and cause FAT EMBOLISM because of:
    a. Erroneous intravenous injections of drugs dissolved in oil that should for example go intramuscularly
    b. Microscopic fat globules, sometimes with associated hematopoietic bone marrow, that have escaped from the adipose tissue after long bone fractures or tissue trauma and burns. This is the most common cause of fat embolism, especially in the elderly population and especially following femoral fractures. As known, elderly long bones contain yellow bone marrow, which contains high amounts of adipose tissue, instead of brown bone marrow. Therefore, after a fracture the risk is the release of yellow marrow into the circulation, which can then occlude the pulmonary and cerebral microvasculature resulting in pulmonary insufficiency, neurological symptoms, etc.

    Fig.5

    Fat embolism occurs in 90% of individuals with severe skeletal injuries but less than 10% of them have clinical findings. Still, the fatality is 5%-15% of cases and fat embolism is considered one of the main causes of death in elderly patients that have fractured their femur.
    Fig.5 represent an image of fat embolism
2. **amniotic fluid embolism** with introduction of amniotic fluid into maternal venous and pulmonary systems at the time of labor.

A: How are these fat emboli resolved physiologically?
Q: there are some compensatory mechanism of the body, but these emboli are difficult to be solved by ourselves. In general, it is always better to directly act on it and remove them with therapy treatment (dissolving fats) or surgically (as typically occurs in the lungs). The Professor does not know precisely, however most probably the aim is to dissolve or remove the embolus.

C. AIR EMBOLISM:

Gas bubbles within the circulation that can obstruct vascular flow and cause distal ischemic injury. *A large volume of air, more than 100 cc, in the blood is necessary to produce clinical effects and occlude the vessel.* A typical form of gas embolism is the "decompression sickness", typical condition associated to hyperbaropathy and present especially in scuba and deep-sea divers, underwater construction workers, etc.
Two forms of decompression sickness:
a. acute // b. chronic

a. Focusing more specifically on deep sea and scuba divers, they can develop **acute decompression sickness** due to the tank full of gases they use. Increased amounts of gas (nitrogen) is dissolved in the blood and tissue when they go deep down underwater. The problem concerns nitrogen, which normally is removed easily via respiration, as the nitrogen changes form from liquid to gas, but in a controlled way and by providing enough time.
    When divers ascend (depressurize) too quickly without compensation stages, the liquid nitrogen changes its status again via dissolution in the tissue and in the blood and forms gas bubbles and even aggregate together forming bigger bubbles. Different consequences:

- These big gas bubbles spread to skeletal muscles and skeletal tissues, especially accumulating around joints, causing severe pain and necrosis. This occurs especially in the legs.
- Then, they can reach and stop in the lung vasculature causing edema, hemorrhage, focal emphysema, resulting in severe respiratory distress.
- *In cases in which the gas embolism reaches the heart or brain, patients can die.*

b. There is also a **chronic form**, known as **Caisson disease**, that mainly affects underwater construction workers (i.e. who may be involved in the construction of tunnels under the sea) and is caused by the persistence of gas emboli in the skeletal system which then generates multiple foci of ischemic necrosis in the femoral heads, tibia, and/or homerus.

The treatment consists of placing affected individuals in a hyperbaric chamber (chamber under high pressure) to force gas bubbles back into solution (so to simulate again the change of status of nitrogen from gaseous to liquid). Thanks to a slow decompression, gradual resorption and exhalation of nitrogen can take place to avoid intoxication.

CLASSIFICATION ACCORDING TO THEIR LOCATION:

Emboli can never exceed the capillary filter, because of their mass, so they remain located in the left or right circulation section in which they were originated. So if they are in arteries they will stay in arteries and same for veins. In general, an arterial embolus cannot pass into the venous system, and vice versa → so we can distinguish between venous embolism and arterial embolism. On the contrary, very rarely a venous embolism can pass into the arterial circulation due to the presence of a cardiac defect, an interatrial or interventricular defect, that allows its translocation. This is commonly seen in conditions of Patent foramen ovale (PFO). In this consition, the foramen ovale did not close properly at birth. Therefore, in these patients, venous emboli can go into arterial circulation by passing through the foramen.

We can have:

- **Arterial embolisms**: most severe, it is responsible for ischemic necrosis or infarction of various organs whose arteries are occluded, such as heart or brain. It is one of the most common causes of death, especially when the embolus occludes major arteries.
- **Venous embolisms**: even if they are not as severe as the previous ones, they usually reach the lungs, which is the most affected organ, causing pulmonary embolism (main cause of death in hospitalized patients). They origin from deep venous thrombosis of the lower extremities and then travel to the lungs where they lodge. This is different from arterial emboli, which instead travel to a wide variety of different sites.

Venous embolism mainly affects the lungs. While the arterial ones can reach any organ in our body.

Following the effects of gravity in arterial embolism:

- Arterial emboli in 60-70% of the cases will stop in the legs (of course less dangerous than in other cases);
- 10-20% in the brain;
- the remaining in the intestine, kidneys, spleen and upper extremities.

The Professor advised us to watch the following videos:
Platelet activation: https://www.youtube.com/watch?v=R8JMfbYW2p4
Thrombosis: https://www.youtube.com/watch?v=aW6WscFqli8
https://www.youtube.com/watch?v=2vVqBjk-oqQ