Thromboembolism

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KSU, Riyadh
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Objectives

- Understand the basic pathology of thrombogenesis and the risk factors for development of venous and arterial thrombosis.
- Know the types of emboli and to able disrcibe the causes and pathology each one.

Thrombosis

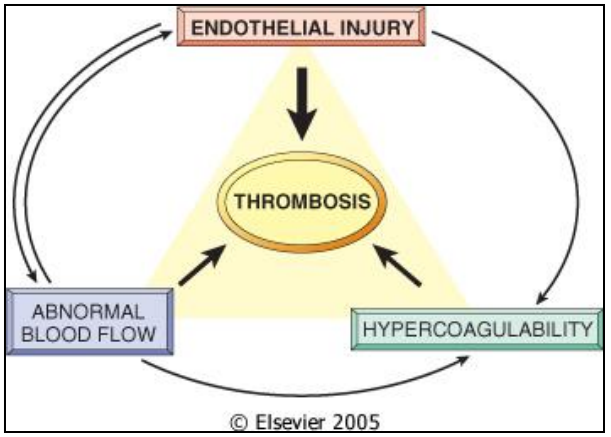
- A thrombus is a solid mass of blood constituents which developes in artery or vein.
- It is intravascular coagulation of blood and it often causes significant interruption to blood flow.

Pathogenesis

Three primary influences called as ***Virchow triad*** predispose to thrombus formation:

(1) endothelial injury
(2) stasis or turbulence of blood flow
(3) blood hypercoagulability

It results from interaction platelets, damaged endothelial cells and the coagulation cascade. All 3 are component of the hemostatic process.



Thrombotic

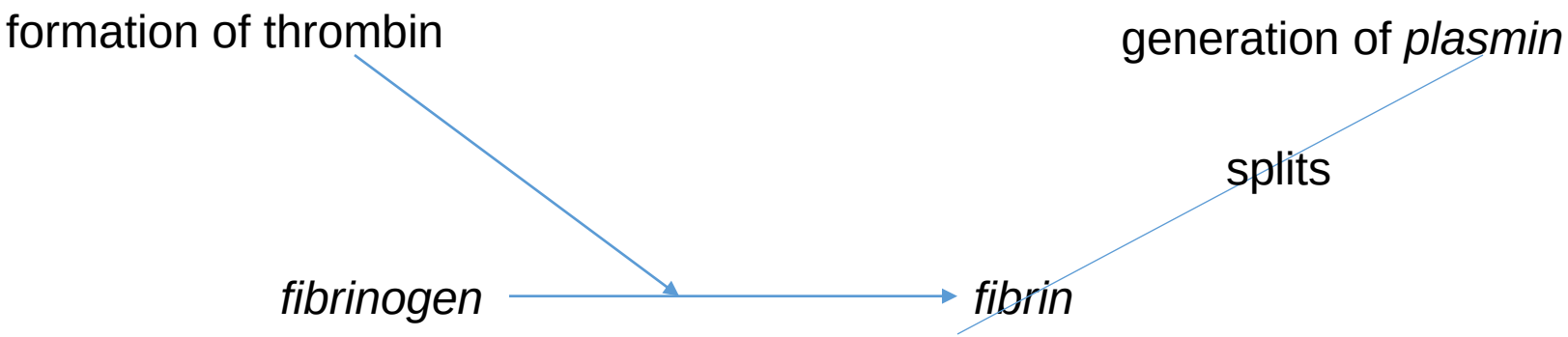
platelets

Anti-thrombotic

antithrombin 3,
protein C,
protien S

Coagulation Cascade

Fibrinolysis



Hypercoaguable States

Hypercoagulable states can be

1. **Primary/Genetic** (e.g. mutation in factor V gene or prothrombin gene, anti-thrombin III deficiency, protein C or S deficiencies, or fibrinolysis defects.
2. **Secondary/acquired states**: they can be high risk or low risk
    a) **High risk for thrombosis**
        - Prolonged bed rest or immobilization
        - Myocardial infarction, Atrial fibrillation
        - Tissue damage (surgery, fracture, burns)
        - Cancer=== release of procoagulant tumor products
        - Prosthetic cardiac valves
        - Disseminated intravascular coagulation=== Thrombin generation
        - Antiphospholipid antibody syndrome (lupus anticoagulant syndrome)=== Autoantibodies

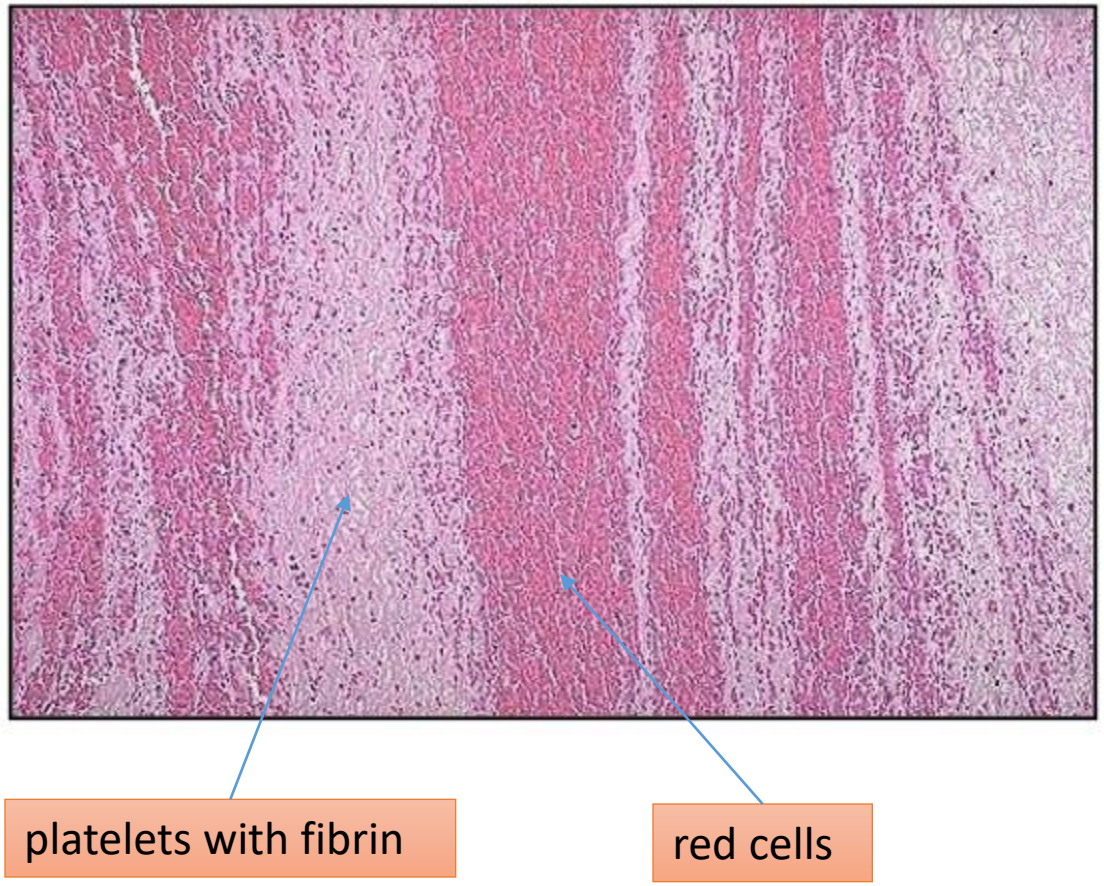
    b) **Lower risk for thrombosis**

    Cardiomyopathy, Nephrotic syndrome, Hyperestrogenic states (pregnancy), Oral contraceptive use, Sickle cell anemia, Smoking.

Morphology of thrombus

- Thrombi may develop anywhere in the cardiovascular system, the cardiac chambers, valve cusps, arteries, veins, or capillaries. They vary in size and shape, depending on the site of origin.
- Arterial or cardiac thrombi usually begin at a site of endothelial injury (e.g., atherosclerotic plaque) or turbulence (vessel bifurcation)
- Venous thrombi characteristically occur in sites of stasis.
- The propagating tail of either thrombi may not be well attached (particularly in veins) is prone to fragmentation, creating an **embolus**.

Lines of Zahn

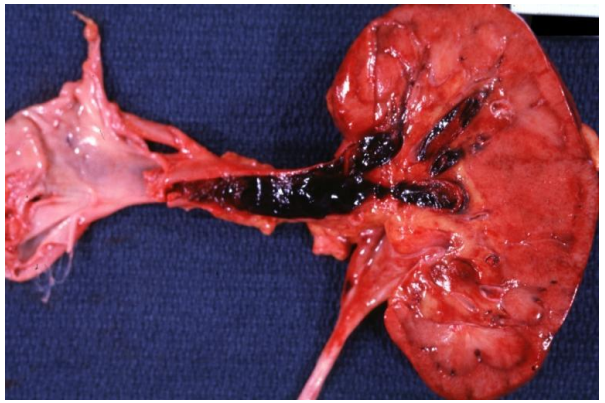


Arterial thrombi

- most common sites in descending order, are coronary, cerebral, and femoral arteries.
- It is usually superimposed on an atherosclerotic plaque and are firmly adherent to the injured arterial wall (mural).
- gray-white and friable.

Venous thrombosis

- Because these thrombi form in a relatively static environment, they contain more enmeshed erythrocytes and are therefore known as **red**, or **stasis thrombi**.
- Phlebothrombosis most commonly affects the veins of the lower extremities (90% of cases).

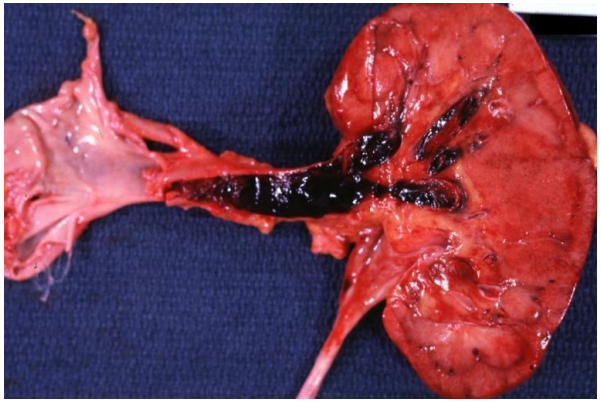


Postmortem clots

At autopsy, postmortem clots may be confused for venous thrombi.

Venous thrombus

- Firm
- rich admixture of RBCs and appear red
- Attached to the vessel wall



Postmortem clots

- rubbery and gelatinous
- dark red in one side and yellow in the other.
- Not attached to the vessel wall

Thrombi on Heart Valves

Thrombi on Heart Valves are called as vegetations.

Are infective or sterile:

1)Bacterial or fungal blood-borne infections may result in the development of large thrombotic masses on heart valves, called as **vegetations** (**infective endocarditis**).

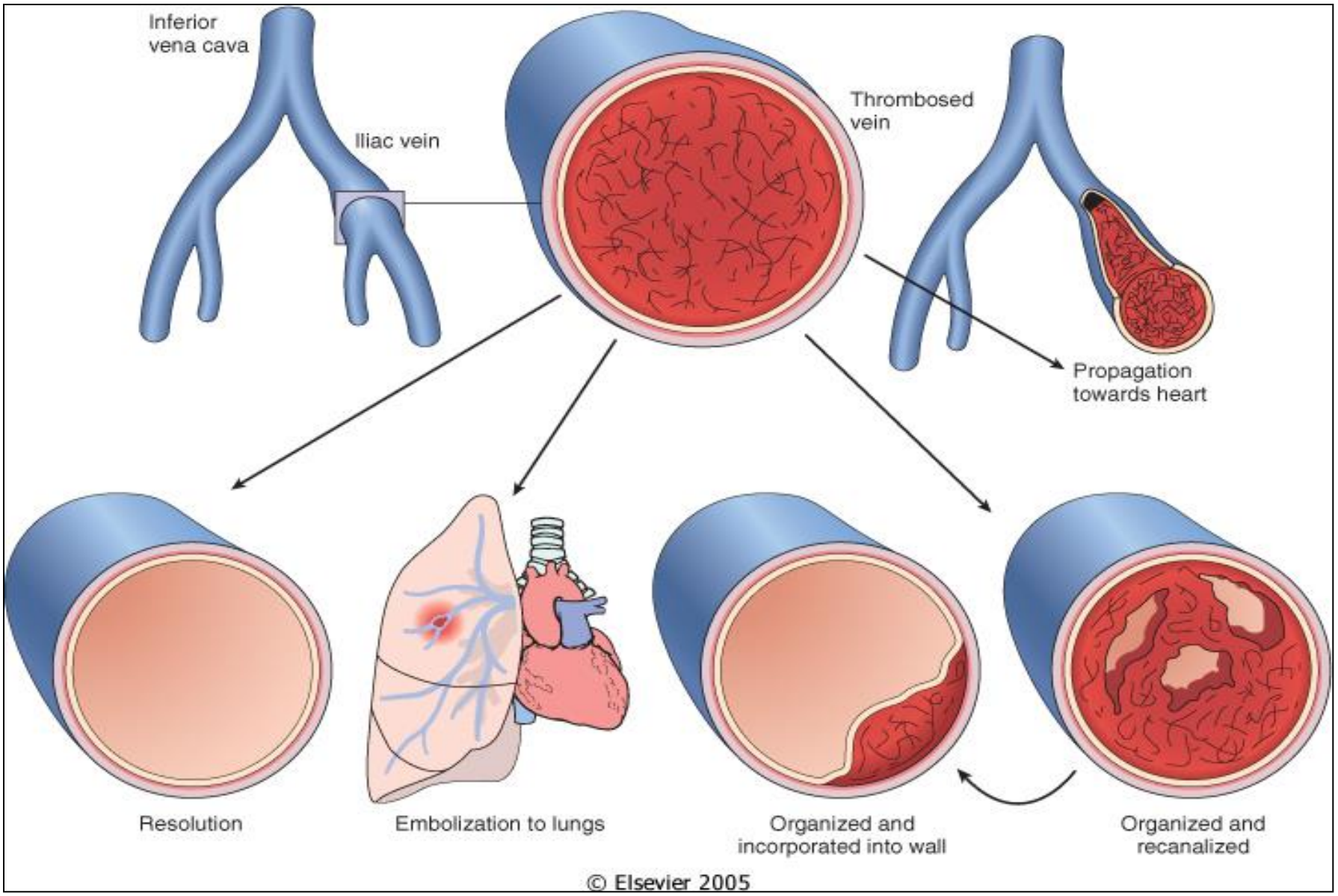
2)Sterile vegetations can also develop on noninfected valves in patients with hypercoagulable states, so-called **nonbacterial thrombotic endocarditis**.

Less commonly, noninfective, **verrucous (Libman-Sacks) endocarditis** attributable to elevated levels of circulating immune complexes may occur in patients with systemic lupus erythematosus

Fate of Thrombus

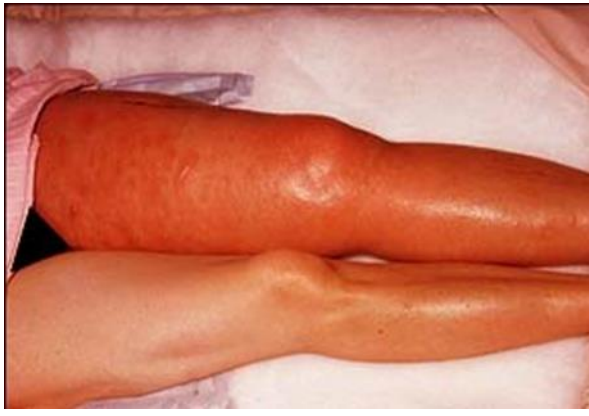
- Resolution
- Propagation
- Embolism
- Organization and recanalization
- Organization and incorporation into the wall.

Fate of thrombus



Deep vein thrombosis & Thrombophlebitis

- Venous thrombosis often arises in the deep veins of the legs and then it is called deep vein thrombosis (DVT).
- such thrombi more often embolize to the lungs and give rise to pulmonary infarction
- can cause local pain and edema.
- DVTs are asymptomatic in approximately 50% of affected individuals and are recognized only in retrospect after embolization



Deep vein thrombosis

Common predisposing factors for DVT (are included in the hypercoagulable status table):

1. **Bed rest and immobilization**
2. **Congestive heart failure** (a cause of impaired venous return)
3. **Trauma, surgery, and burns**
4. **Pregnancy**:
   - the potential for amniotic fluid infusion into the circulation at the time of delivery can cause thrombogenesis
   - late pregnancy and the postpartum period are also associated with systemic hypercoagulability
5. **Tumors**
6. **Advanced age**

EMBOLISM

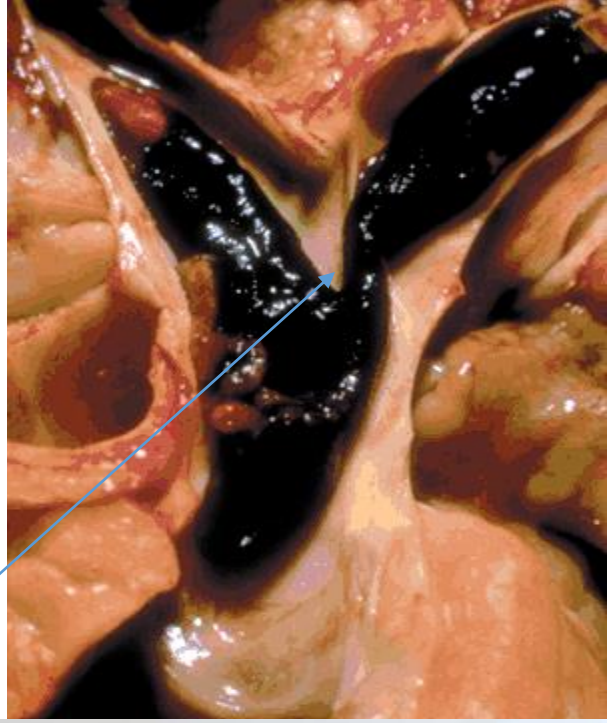
- *An embolus is a detached intravascular solid, liquid, or gaseous mass that is carried by the blood to a site distant from its point of origin.*
- Almost all emboli represent some part of a dislodged thrombus, hence the commonly used term *thromboembolism.*
- The emboli ultimately lodge in vessels too small to permit further passage, resulting in partial or complete vascular occlusion leading to ischemic necrosis of distal tissue (*infarction).*
- Depending on the site of origin, emboli may lodge in the pulmonary or systemic circulations.

Types of embolism

- Pulmonary thromboembolism
- Systemic thromboembolism
- Fat embolism
- Air embolism
- Amniotic fluid embolism

PULMONARY THROMBOEMBOLISM

- In more than 95% of cases, venous emboli originate from deep leg vein thrombi above the level of the knee
- Depending on size of embolus, it may occlude main pulmonary artery, or impact across the bifurcation *(saddle embolus)*, or pass out into the smaller, branching arterioles of the pulmonary circulation.
- Most pulmonary emboli (60% to 80%) are clinically silent because they are small. Sudden death, right heart failure *(cor pulmonale),* occurs when 60% or more of the pulmonary circulation is obstructed with emboli.



SYSTEMIC THROMBOEMBOLISM

- refers to emboli traveling within the arterial circulation.
- Most (80%) arise from intracardiac mural thrombi.
- The major sites for arteriolar embolization are the lower extremities (75%) and the brain (10%).

FAT EMBOLISM

- Microscopic fat globules may be found in the circulation after fractures of long bones (which have fatty marrow) or, rarely, in soft tissue trauma and burns.

- Fat is released by marrow or adipose tissue injury and enters the circulation through rupture of the blood vessels and act as an embolus.

- ***Fat embolism syndrome*** is characterized by pulmonary insufficiency, neurologic symptoms, anemia, and thrombocytopenia.

AIR EMBOLISM

- Gas bubbles within the circulation can obstruct vascular flow (and cause distal ischemic injury) acting as thrombotic masses. Bubbles may coalesce to form frothy masses sufficiently large to occlude major vessels.
- Air may enter the circulation during obstetric procedures or as a consequence of chest wall injury.
- An excess of 100 cc is required to have a clinical effect.

Decompression sickness

A particular form of gas embolism

- Occurs when individuals are exposed to sudden changes in atmospheric pressure.
- Scuba and deep sea divers, and individuals in unpressurized aircraft in rapid ascent are all at risk.
- When air is breathed at high pressure (e.g. during a deep sea dive), increased amounts of gas (particularly nitrogen) become dissolved in the blood and tissues. If the diver then ascends (depressurizes) too rapidly, the nitrogen expands in the tissues and bubbles out of solution in the blood to form gas emboli.
- '*Grecian Bend*' i.e. joint/muscle pain and 'chokes' i.e. respiratory distress.
- A more chronic form of decompression sickness is called *caisson disease* in which, persistence of gas emboli in the skeletal system leads to multiple foci of ischemic necrosis; the more common sites are the heads of the femurs, tibia, and humeri.

AMNIOTIC FLUID EMBOLISM

- A grave and uncommon complication of labor and the immediate postpartum period, caused by infusion of amniotic fluid or fetal tissue into the maternal circulation via a tear in the placental membranes or rupture of uterine veins.

- Characterized by sudden severe dyspnea, cyanosis, and hypotensive shock, followed by seizures and coma.

- If the patient survives the initial crisis, pulmonary edema develops, along with disseminated intravascular coagulation, owing to release of thrombogenic substances from amniotic.

- Microscopy: presence in the pulmonary microcirculation of squamous cells shed from fetal skin, lanugo hair, fat from vernix caseosa, and mucin derived from the fetal respiratory or gastrointestinal tract. Marked pulmonary edema and diffuse alveolar damage are also present. Systemic fibrin thrombi indicative of DIC can also be seen.

1) intracardiac mural thrombi
2) caisson disease
3) saddle embolus
4) fractures of long bones
5) obstetric procedures
6) Decompression sickness
7) Grecian Bend
8) Deep vein thrombosis
9) complication of labor and the immediate postpartum period
10) deep sea divers
11) Presence of squamous cells, lanugo hair, fat, and mucin in pulmonary circulation

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2. Systemic thromboembolism
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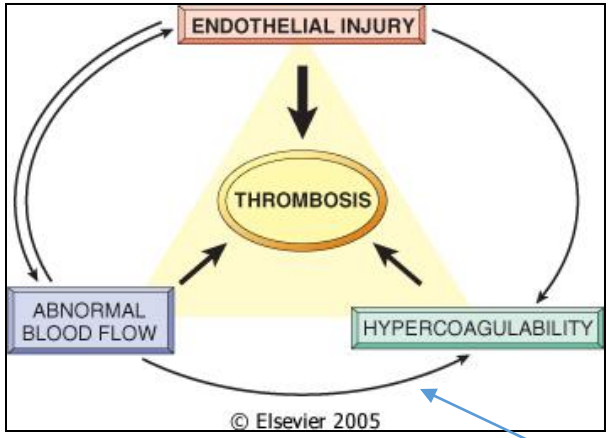

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