HEMODYNAMIC DISORDERS

THROMBOSIS

Hemostasis: Normally the blood is kept in a fluid state with rapid formation of a plug at the site of injury.

Thrombosis: is the formation of a blood clot inside the blood vessel.

Both hemostasis and thrombosis involve three components:

1-Vascular wall.

2-Platelets.

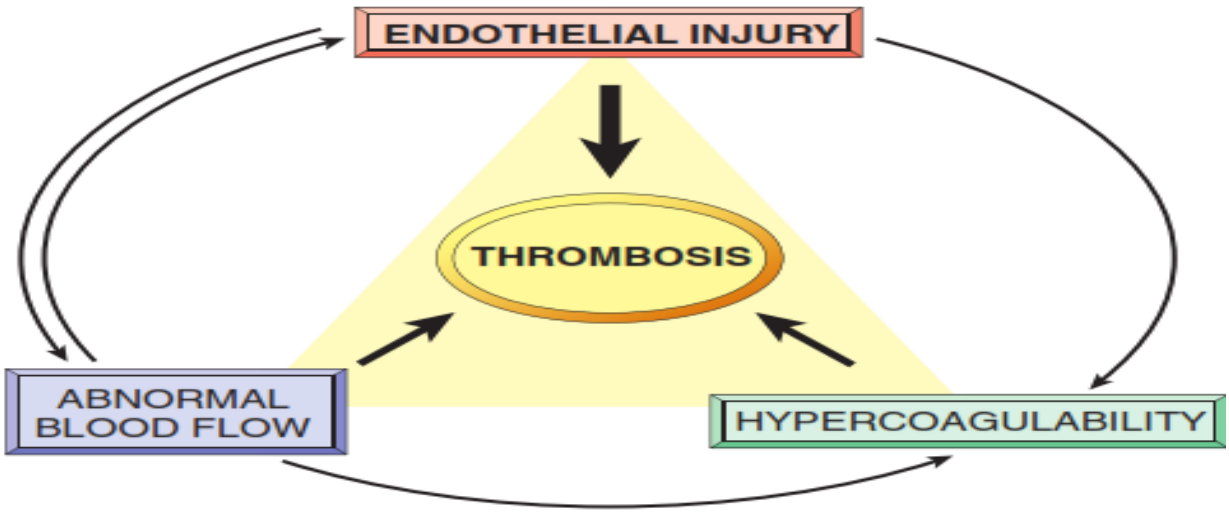
3-Coagulation cascade.

Pathogenesis of thrombus: There are three primary abnormalities that lead to thrombus formation called Virchow's triad:

(1) Endothelial injury.

(2) Stasis or turbulence of blood flow.

(3) Blood hypercoagulability.



1-Endothelial Injury: Is an important cause of thrombosis, particularly in the heart and the arteries. Normally high flow rates of blood in the heart or in the arterial circulation prevent clotting by preventing platelet adhesion and diluting coagulation factors. Physical loss of endothelium leads to exposure of subendothelial ECM, adhesion of platelets, release of coagulation factor that help in thrombus formation.

2-Alterations in Normal Blood Flow: Turbulence contributes to arterial and cardiac thrombosis by causing endothelial injury or dysfunction. Stasis is a major contributor to the development of venous thrombi**,** Normal blood flow is laminar, such that platelets flow centrally in the vessel lumen, separated from the endothelium by a slower moving clear zone of plasma.

Stasis and turbulence (disturbances in blood flow) will:

-Disrupt laminar flow and bring platelets into contact with the endothelium.

-Prevent dilution of activated clotting factors by fresh-flowing blood.

-Retard the inflow of clotting factor inhibitors.

-Promote endothelial cell injury, resulting in platelets adhesion.

Causes of turbulence and stasis:

1- Ulcerated atherosclerotic plaques: not only expose subendothelial ECM but also cause turbulence.

2- Abnormal aortic and arterial dilations, called aneurysms.

3- Acute myocardial infarction results in focally non contractile myocardium.

4- Mitral valve stenosis (e.g., after rheumatic heart disease) results in left atrial dilation which is a site of stasis.

5- Hyperviscosity syndromes (such as polycythemia) increase resistance to flow and cause small vessel stasis.

6- The deformed red cells in sickle cell anemia cause vascular occlusions, with the resultant stasis.

3- Hypercoagulability: It is any alteration of the coagulation pathways that predisposes to thrombosis. It contributes infrequently to arterial or intra cardiac thrombosis but important underlying risk factor for venous thrombosis and it can be divided into:

1- Primary (genetic) disorders like mutations in the factor V gene and the prothrombin gene.
2- Secondary (acquired) disorders, the pathogenesis of acquired thrombotic disorders are frequently multifactorial and more complicated and include- :

A- Cardiac failure or trauma: stasis or vascular injury may be most important causes.

B- Hypercoagulability is associated with oral contraceptive use and the hyperestrogenic state of pregnancy, probably related to increased hepatic synthesis of coagulation factors.

C- In disseminated cancers, release of procoagulant tumor products predisposes to thrombosis. (mucin from adenocarcinoma)

D- The hypercoagulability seen with advancing age has been attributed to increasing platelet aggregation.

E- Smoking and obesity promote hypercoagulability by unknown mechanisms.

Morphology of thrombus:

Thrombi can have grossly and microscopically apparent laminations called **lines of Zahn**; these represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers. These lines distinguish antemortem thrombosis from the bland nonlaminated clots that occur in the postmortem state. Although thrombi formed in the “low-flow” venous system superficially resemble postmortem clots, careful evaluation generally reveals ill-defined laminations.

Types of thrombus:

1-Mural thrombi: Thrombi occurring in heart chambers or in the aortic lumen.

Causes:

a- Abnormal myocardial contraction resulting from arrhythmias or myocardial infarction.

b- Endomyocardial injury.

2- Arterial thrombi: are frequently occlusive and are produced by platelet and coagulation activation; they are typically a friable meshwork of platelets, fibrin, erythrocytes, and degenerating leukocytes. Causes: Atherosclerotic plaque and vascular injury (vasculitis, trauma).

3- Venous thrombosis (phlebothrombosis): is almost occlusive, and it is the result of activation of the coagulation cascade, and platelets play a secondary role. Because these thrombi form in the sluggish venous circulation, they also tend to contain more enmeshed erythrocytes and are therefore called red, or stasis thrombi. The veins of the lower extremities are most commonly affected.

4- Vegetations: Thrombi on heart valves. Bacterial or fungal blood-born infections can cause valve damage, subsequently leading to large thrombotic masses (infective endocarditis).

Fate of the Thrombus:

If a patient survives the initial thrombosis, in the ensuing days or weeks thrombi undergo some combination of the following four events:

1- Propagation. Thrombi accumulate additional platelets and fibrin causing vessel obstruction.

2- Embolization. Thrombi dislodged or fragmented and are transported elsewhere in the vasculature.

3- Dissolution. Thrombi are removed by fibrinolytic activity which leads to rapid shrinkage and even total lysis of recent thrombi.

4- Organization and recanalization. Thrombi induce inflammation and fibrosis, recanalization (re-establishing some degree of flow).

Clinical significance:

Thrombi are significant because they:

1. Cause obstruction of arteries and veins

2. Are potential sources of emboli. Which effect is most important depends on the site of thrombosis.

Venous thrombi can cause congestion and edema in vascular beds distal to an obstruction, but they are most troublesome for their capacity to embolize to the lungs and cause death.

While arterial thrombi can embolize and even cause downstream tissue infarction, their role in vascular obstruction at critical sites (e.g., coronary and cerebral vessels) is much more significant clinically.

Venous Thrombosis (Phlebothrombosis):

Most venous thrombi occur in the superficial or deep veins of the leg. Superficial thrombi can cause local congestion, swelling, pain, and tenderness along the course of the involved vein, but they rarely embolize.

Deep thrombi in the larger leg veins at or above the knee joint are more serious because they may embolize. Although they may cause local pain and edema, deep venous thromboses are entirely asymptomatic in approximately 50% of patients.

The risk of deep venous thrombosis increased in:

1- Advanced age, bed rest, and immobilization, because reduced physical activity diminishes the milking action of muscles in the lower leg and so slows venous return.

2- Cardiac failure.

3- Trauma, surgery, and burns.

4- Peripartum and postpartum states; in addition to the potential for amniotic fluid infusion into the circulation during parturition, late pregnancy and the postpartum period are associated with hypercoagulability.

5- Hypercoagulable states.