Hemodynamic Disorders

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LEC 2

Hemostasis:

- **Normal hemostasis is a consequence of regulated processes that maintain blood in a fluid state in normal vessels.**
- **It also permit the rapid formation of a hemostatic clot at the site of a vascular injury.**
- **The pathologic counterpart of hemostasis is thrombosis which involves blood clot formation within intact vessels.**
- **Hemostasis involve three components:**

1- Normal endothelium
2- Normal platelets
3- Normal coagulation cascade

The endothelium has antithrombotic properties which are:
(a) Antiplatelets effect
(b) Anticoagulant properties
(c) Fibrinolytic properties
(d) Prothrombotic properties

NORMAL HEMOSTASIS

Sequences of events after vascular injury:

1- Transient arteriolar vasoconstriction due to reflex neurogenic mechanism & local secretion of endothelial derived vasoconstrictors.
2- Platelets adhere to the exposed sub endothelial extra cellular matrix (ECM) &activated leading to additional platelets aggregation forming primary hemostatic plug.
3- Tissue factors release at site of injury & with platelets factors, there will be activation of coagulation cascade leading to fibrin deposition .Thrombin activated in coagulation cascade causing further platelets recruitment &secondary hemostasis.
4- Polymerized fibrin & platelets aggregation form solid permanent plug to prevent any further hemorrhage.

THROMBOSIS: formation of solid or semisolid mass from blood constituents within the cardiovascular system during life.

Pathogenesis: (Virchow's triad):

1- Endothelial injury
2- Alteration of blood flow
3- Hypercoagulability

1- Endothelial injury:

a- Myocardial infarction.
b- over atherosclerotic plaque.
c- Trauma or inflammatory vascular injury (myocarditis and vasculitis)
d- Hypertension.
e- Sub acute bacterial endocarditis.

2- Alteration of blood flow: either

A- Turbulence: Important in arterial & cardiac thrombosis by causing endothelial injury & local pockets of stasis.
B- Stasis: Is major factors in venous thrombosis.

Both turbulence &stasis cause

1- Disruption of laminar blood flow & bring platelets in contact with endothelium.
2- Prevent dilution of clotting factors by fresh flowing blood.
3- Retard flow of clotting factor inhibitors & permit buildup of thrombus.
4- Promote endothelial activation leading to local thrombosis, adhesion of leukocytes.

Turbulence & stasis cause thrombosis in:

1- Ulcerated atherosclerotic plaques
2- Aneurysm
3- Myocardial infarction.
4- Mitral stenosis cause left atrial dilatation& atrial fibrillation leading to stasis & thrombosis
5- Hyperviscosity syndrome e.g polycythemia causing stasis in small vessels
6- Sickle cell anemia causing small vessels occlusion leading to stasis and thrombosis.

3- Hypercoagulability: Divided into primary & secondary disorders.

Primary disorders : as in **mutation in factor V and Inherited mutation of antithrombin III, protein C&S leading to venous thrombosis & recurrent thromboembolism in adolescent& early adult life.**

Secondary disorders:

1- Heart failure or trauma causing vascular endothelial injury or stasis.

2- Oral contraceptive pills because of increase hepatic synthesis of coagulation factors& decrease synthesis of antithrombin III.

3- Dissemenated tumors because of release of procoagulant tumor products.
4- Advancing age because of increase platelets aggregation & decrease PGI2 by endothelium.

5- Smoking.
6- Obesity
7- Lupus anticoagulants which are antibodies directed against anionic phospholipids & high frequency of venous & arterial thrombosis .Those patients may have SLE or thrombosis is the only clinical manifestation.

Morphology of thrombi:

- Thrombi can develop anywhere in the cardiovascular system (e.g., in cardiac chambers, on valves, or in arteries, veins, or capillaries).
- The size and shape of thrombi depend on the site of origin and the cause.
- Arterial or cardiac thrombi usually begin at sites of turbulence or endothelial injury; venous thrombi characteristically occur at sites of stasis.
- Thrombi are focally attached to the underlying vascular surface; arterial thrombi tend to grow retrograde from the point of attachment, while venous thrombi extend in the direction of blood flow (thus both propagate toward the heart).
- The propagating portion of a thrombus is often poorly attached and therefore prone to fragmentation and embolization.

Grossly and microscopically, thrombi often have laminated appearance called **lines of Zahn**; these represent pale platelet and fibrin deposits alternating with darker red cell–rich layers. Such laminations signify that a thrombus has formed in flowing blood; their presence can therefore distinguish antemortem thrombosis from the bland non laminated clots that occur postmortem.

- Thrombi occurring in heart chambers or in the aortic lumen are designated **mural thrombi**.
- Causes of mural cardiac thrombi: Abnormal myocardial contraction (arrhythmias, myocardial infarction) or endomyocardial injury (myocarditis or catheter trauma)
- Thrombi on heart valves are called **vegetations**. Blood-borne bacteria or fungi can adhere to previously damaged valves (e.g., due to rheumatic heart disease) or can directly cause valve damage; in both cases, endothelial injury and disturbed blood flow can induce the formation of large thrombotic masses (**infective endocarditis**).
- Sterile vegetations can also develop on no infected valves in persons with hypercoagulable states, so-called **nonbacterial thrombotic endocarditis**.

- Less commonly, sterile, verrucous endocarditis (**Libman-Sacks endocarditis**) can occur in the setting of systemic lupus erythematosus.

Arterial thrombi: (white thrombi)

- Are usually occlusive.
- Most common sites are coronary, cerebral &femoral arteries, superimposed on atherosclerotic plaques.
- Firmly adheres to arterial wall.
- Grayish white &composed of platelets, fibrin, RBCs &degenerated WBCs (lines of Zhan).
- These are usually superimposed on a ruptured atherosclerotic plaque.

Venous thrombi: (red thrombi)

- Almost invariably occlusive because they form in slowly moving blood.
- They contain more RBCs, known as red or stasis thrombi.
- Soft, gelatinous.
- 90% affect veins of lower limbs.

POST MORTEM THROMBUS:

- Confused with venous (red) thrombus.
- They are gelatinous with dark red dependent portion where RBCs settled by gravity with yellow fat “chicken fat” supernatant.
- Not attached to arterial wall.
- While red thrombi are: more firm, almost always have point of attachment & transaction reveals vague strands of pale gray fibrin.

Fate of thrombus:

1- Dissolution: Activation of fibrinolytic pathway will lead to shrinkage & total lysis of recent thrombus while older ones undergo fibrin polymerization & become more resistant to proteolysis.
2- Organization & recanalization: Ingrowth of endothelial cells, smooth muscle cells & fibroblasts into fibrin rich thrombus will create conduits from one end of thrombus to other & re-establish continuity of original lumen.
3- Propagation: Thrombus accumulates more platelets & fibrin &lead to obstruction.
4- Embolization: Thrombus dislodges & transported to other sites.