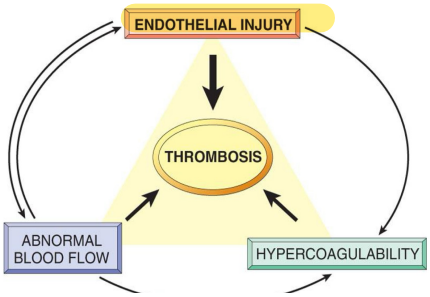
Hemodynamic Disorders III

Platelets, clotting factors and endothelium act together to maintain the balance which is the process of hemostasis.

Thrombosis



Called → "Virchow triad"

O Endothelial injury leading to platelet activation underlies thrombus formation in the heart & the arterial circulation,

O Cardiac and arterial clots are typically rich in platelets.

(1)Severe Endothelial injury triggers thrombosis by exposed vWF tissue factor (severe injury), or ..
(2) inflammation & other noxious stimuli endothelial activation or dysfunction

O An important role in triggering arterial thrombotic events.

1. Procoagulant changes:
+ Cytokines downregulate the expression of thrombomodulin →activation of thrombin → stimulate platelets and augment inflammation (PARs).
+ inflamed endothelium downregulates the expression anticoagulants (protein C & tissue factor protein inhibitor).
2. Anti-fibrinolytic effects: secrete Plasminogen activator inhibitors (PAI), which downregulate the expression of t-PA.

Abnormal Blood Flow
➢ Turbulence (chaotic blood flow) contributes to arterial and cardiac thrombosis, causing endothelial injury or dysfunction, also forming countercurrents and local pockets of stasis.
➢ Stasis is a major factor in the development of venous thrombi.

How stasis and turbulence cause thrombosis ?
Stasis Allows platelets & leukocytes to come into contact with the endothelium when the flow is sluggish (slow & irregular)
• Stasis slows the washout of activated clotting factors & impedes the inflow of clotting factor inhibitors.

• Clinical Examples:
✓ Ulcerated atherosclerosis expose subendothelial ECM & cause turbulence.
✓ Abnormal aortic and arterial dilations (called aneurysms) create local stasis → fertile sites for thrombosis.
✓ Acute myocardial infarction → focally noncontractile myocardium → local blood stasis →cardiac mural thrombi.
✓ Deformed red cells in sickle cell anemia cause vascular occlusions → resultant stasis → thrombosis

Hypercoagulability:
+ infrequently contributes to arterial or intracardiac thrombosis.
+ important risk factor for venous thrombosis.

Primary (inherited) hypercoagulability - factor V
factor V mutation (called the Leiden mutation)

A mutation that renders factor V resistant to proteolysis of by protein C → an important anti-thrombotic counter- regulatory mechanism is lost.

Heterozygotes → fivefold increased
homozygotes having a 50-fold increased

>>>Elevated levels of homocysteine contribute to arterial and venous thrombosis

Secondary (acquired) hypercoagulability
(1) Prolonged bed rest or immobilization
(2) Cancer
(3) Tissue damage
(4) Disseminated intravascular coagulation (DIC).
(5) Prosthetic cardiac valves .
(6) Heparin-induced thrombocytopenia
(7) Anti-phospholipid antibody syndrome

Morphology

+arterial thrombi grow in a retrograde direction from the point of attachment.
+venous thrombi extend in the direction of blood flow.

Thrombi have laminations called lines of Zahn; (grossly and microscopically)
Represent pale platelet and fibrin layers alternating with darker red cell–rich layers.

Fate of the Thrombus

1. Propagation: Thrombus enlarges, increasing the risk of occlusion or embolization.
2. Embolization: Thrombus dislodges and travels to another site.
3. Dissolution: New thrombi dissolve quickly with fibrinolysis; older thrombi resist lysis due to fibrin polymerization.
4. Organization and Recanalization: Older thrombi are replaced by connective tissue or develop capillaries to restore blood flow.

Type	Description	Key Features	Causes
Mural Thrombi	Thrombi occurring in heart chambers or in the aortic lumen.	- Located in heart chambers or the aortic lumen.- Associated with injuries or abnormal myocardial function.	- Abnormal myocardial contraction (e.g., arrhythmias, dilated cardiomyopathy, myocardial infarction).- Endomyocardial injury (e.g., myocarditis, catheter trauma).- Ulcerated atherosclerotic plaques in the aorta.- Aneurysmal dilation.
Arterial Thrombi	Thrombi that are often occlusive and rich in platelets, forming due to endothelial injury and platelet activation.	- Frequently occlusive.- Rich in platelets.- Often associated with ruptured atherosclerotic plaques.- Can result from vascular injuries.	- Endothelial injury leading to platelet activation.- Ruptured atherosclerotic plaques.- Vascular injuries (e.g., vasculitis, trauma).
Venous Thrombi	Also called phlebothrombosis; usually occlusive and rich in red cells, developing in sluggish venous circulation.	- Almost always occlusive.- Can propagate to the heart.- Forms long casts in the lumen.- Rich in red cells (red or stasis thrombi).	- Sluggish venous circulation.- Commonly occurs in 90% of veins in the lower extremities.
Postmortem Clots	Gelatinous clots mistaken for venous thrombi, formed after death.	- Gelatinous appearance.- Dark red lower portion and yellow “chicken fat” upper portion.- Not attached to the vessel wall.	- Postmortem phenomenon.
Red Thrombi	Venous thrombi that are firm, focally attached to the vessel, and show fibrin deposits (lines of Zahn).	- Firm and focally attached to the vessel wall.- Contain gray strands of fibrin (lines of Zahn).	- Slow blood flow in veins.