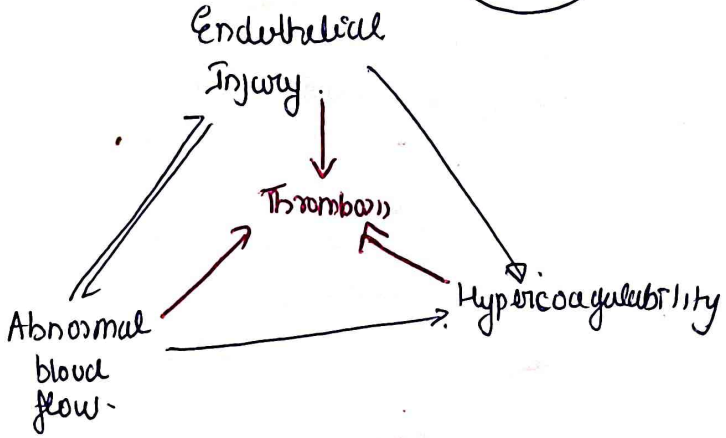
Hemodynamics.

Q) Thrombosis - definition.
pathophysiology, morphology.
fate of thrombus.
pathology of arterial & venous thrombosis.
↳ future in Robbins ✓ As Vs Vena
. Virchow's triad.
. types.

Definition. — from Robbins ✓

Thrombosis is the formation of a ✗ blood clot inside a blood vessel, obstructing the flow of blood.
{Tikran notes... super Robbins too.. study in Robbins}

The primary abnormalities that lead to thrombosis : Virchow's Triad



. these factors can promote thrombosis individually, or in combination.

Figure from Robbins. ★

Endothelial Activation.

Mechanism

- Turbulent blood flow
- Hypertension.
- cytokines.
- complement proteins
- Bacterial products.
- viruses.
- inflammatory mediators
- hypercholesterolemia
- hyperhomocysteinemia.
- advanced glycation end products
- oxidocs
- hypoxia.
- toxins from cigarette smoke.

can cause ⟹ Endothelial Injury.

↓

Endothelial activation

↓

disturb balance between prothrombotic & anti thrombotic activities of endothelium By

- producing more procoagulant factors.
- synthesizing less anticoagulant effectors.

↓

prothrombotic state

How Endothelial Activation/ dysfunction creates a prothrombotic state.

- procoagulant changes. ✓
- platelet effect ✓
- antifibrinolytic effect ✓

Endothelial dysfunction: defined as an altered state, which includes endothelial surface that is thrombogenic or abnormally adhesive to platelet & inf. cells.

① procoagulant changes.

↓

down regulation of Expression of thrombomodulin ; Protein C.

. PGI_2 , t-PA.

&

· tissue factor pathway Inhibitor.

↑ in platelet adhesion molecules, tissue factor.

② Anti-fibrinolytic effect

↓

· Secretion of plasminogen activator inhibitor that ⊖ tPA

③ E - damage expose sub endothelium.

↓

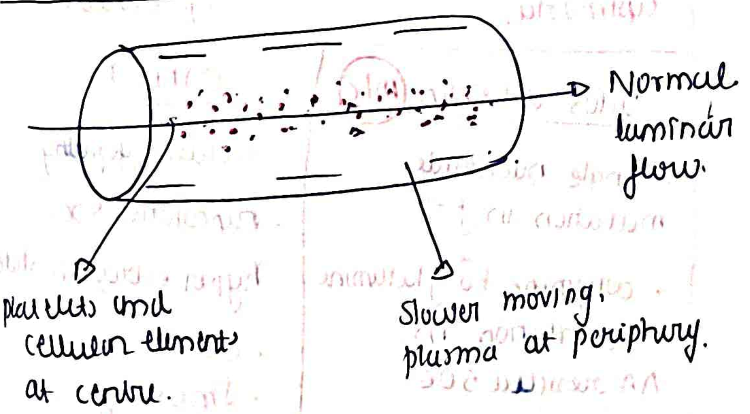
↑ adhesion.

Thrombosis.

Draw figure - RN

Abnormal blood flow.

Normal flow: Laminar.



Alterations in flow.

- turbulence → arterial & Cardiac thrombi.
- Stasis. → venous thrombi.

mechanism

Turbulence & stasis

① disrupt laminar flow.

↓

which brings platelets in contact with Endothelium.

② prevents dilution and wash out of activated clotting factors

③ prevents flowing in of clotting factor Inhibitors.

④ ~~Turbulence~~ promote endothelial activation and enhances procoagulant activity and leucocyte adhesion, partly through flow induced ↑ in adhesion molecules. & partly through pro-inflammatory factors.

Examples of Abnormal flow of blood.

① Atherosclerotic plaque once ulcerated.
↓
- Exposes Subendothelial collagen & VWF
+
turbulence.
→ thrombosis

② aortic & arterial dilatations. (aneurysms)
↓
local stasis.
↓
thrombosis.

③ acute MI.
↓
Stasis
↓
thrombosis.

④ sickle cell anemia.
↓
deformed RBC impede blood flow
↓
Stasis → thrombosis.

⑤ Hyperviscosity.
↓
resistance to flow & causes.
Small vessel stasis.
↓
thrombosis.

Hypercoagulability (thrombophilia)

Hypercoagulability refers to an abnormally high tendency to clot, and is typically caused by alterations in coagulation factor.

- primary (genetic)
- Secondary (Acquired)

Common:
- Factor V mutation } m/c.
- Prothrombin mutation.
- ↑ FVIII, IX, XI, fibrinogen

Rare:
- Anti-thrombin } deficiency.
- protein C/S

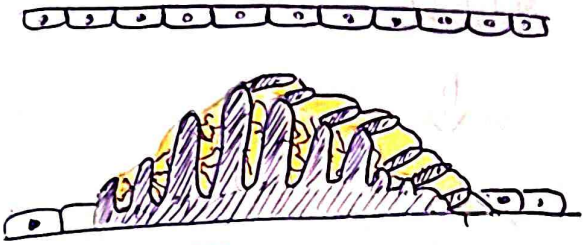
Very rare:
- fibrinolysis defects.
- Homozygous homocystinuria.

Factor V Leiden (m/c)
- Single nucleotide mutation in f-V.
- arginine to glutamine substitution in AA residue 506.
- C/F - recurrent thrombosis.

Strong Risk factor
- prolonged bed rest
- Immobilization.
- MI, AF, DIC
- cancer.
- surgery, burns, fracture.
- HIT ★
- APLA ★
- prosthetic valves

Other RF
- cardiomyopathy
- nephrotic Sx.
- hyperestrogenic state
- OCP.
- Smoking.

MORPHOLOGY



GROSS

Layers in thrombus

- first layer of thrombus on endocardium is platelet layer.
- on top of platelet layer, fibrin is precipitated to form upstanding laminae ~~white~~ + anastomosing fibrin meshwork.— resembles coral. - coralline thrombus).
- RBC get trapped in the upstanding laminae of fibrin meshwork.

Q/ pathogenesis & pathology of arterial & venous thrombi.

GROSS & MICROSCOPY

Lines of Zahn.

- alternating light (pale/white) area of platelets held together by fibrin
  &
  dark - ruptured area of fibrin meshwork with trapped RBC's

↓↓

alternating laminations of light & dark are called

↓

Lines of Zahn.

↓

Helps to distinguish antemortem vs postmortem clots.

Fate of Thrombus

degen

Randes

① propogation.

- thrombi accumulates additional platelets, fibrin and increase in size.
- mural thrombus $\xrightarrow{\text{can become}}$ occlusive.
- propogating portion is poorly attached to wall, so
  ↓
  prone to fragmentation & embolism.

→ arterial thrombi → grow retrograde to blood flow

→ venous thrombi grows anterograde to blood flow. (both towards heart)

② Embolisation.

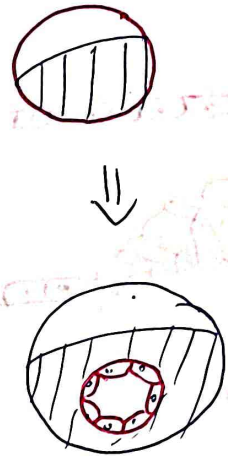
- thrombi dislodge and travel to other sites in vasculature.

③ Dissolution

→ Rapid shrinkage and total disappearance of Recent thrombi due to fibrinolysis

→ Older thrombi are resistant to fibrinolysis.

④ Organization & Recanalization.



Organization.

If thrombi are not dissolved, these older thrombi become organised by ingrowth of endothelial cells, smooth muscle cells & fibroblasts.

Recanalization

- new channels lined by endothelial cells form in an organised thrombus

⑤ mycotic aneurysm

Rarely, thrombi may undergo enzymatic digestion by WBC & platelet lysosomal enzymes.

↓

If bacteremia occurs, thrombus can get infected.

↓

Inflammation, vessel wall weakening.

↓

leading to mycotic aneurysm