THROMBOSIS

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CARDIOVASCULAR SYSTEM

Venous circulation

Arterial circulation
NORMAL BLOOD VESSEL HISTOLOGY
**ARTERY (A) VS VEIN (V)**

Diagram showing the differences between an artery and a vein. The artery (A) has thicker walls and a smaller lumen compared to the vein (V).
PHYSIOLOGY OF THROMBOSIS

HEMOSTASIS

1. Vessel injury
   - Red blood cells

2. Vascular spasm
   - Platelets

3. Formation of the platelet plug
   - Fibrin

4. The coagulation
   - Fibrin filaments, red blood cells and white blood cells the blood clot is formed
THROMBOSIS- PATHOLOGICAL ASPECTS

- Blood coagulation is a very important physiological event to protect our hemostasis, and life
- However, at certain points, this process can be pathological that may endorse injury and cause harm to our body
- This happens whenever unnecessary blood clotting is activated
- The “pathological” thrombosis is caused by the presence of at least one of 3 factors (together called Virchow’s triad):
Virchow’s triad

ENDOTHELIAL INJURY

THROMBOSIS

ABNORMAL BLOOD FLOW

HYPERCOAGULABILITY
**THROMBOSIS- PATHOLOGICAL ASPECTS**

- **Pathogenesis (called Virchow's triad):**
  1. **Endothelial* Injury (Heart, Arteries)**
  2. **Stasis** (abnormal blood flow)
  3. **Blood Hypercoagulability**

* Endothelial cells are special type of cells that cover the inside surface of blood vessels and heart.
CONTRIBUTION OF ENDOTHELIAL CELLS TO COAGULATION

Normotension
Laminar flow
Growth factors (e.g., VEGF)

Non-adhesive, non-thrombogenic surface

Endothelium

Basal state

Turbulent flow
Hypertension
Cytokines
Complement
Bacterial products
Lipid products
Advanced glycation end-products
Hypoxia, acidosis
Viruses
Cigarette smoke

Increased expression of procoagulants, adhesion molecules, and proinflammatory factors
Altered expression of chemokines, cytokines, and growth factors

“Activated” state

No thrombosis

thrombosis
Endothelial Cell Injury and exposure of subendothelial collagen

Adherence of platelets

Release of tissue factor

Progression of coagulation event .....
Response of Vascular Wall Cells to Injury

1. Recruitment of smooth muscle cells or smooth muscle precursor cells to the intima
2. Smooth muscle cell mitosis
3. Elaboration of extracellular matrix

Endothelium

Internal elastic lamina

Smooth muscle cells

Intima

Media
RESPONSE OF VASCULAR WALL CELLS TO INJURY

- Injury results in a healing response
- Pathologic effect of vascular healing:

  Excessive thickening of the intima ➔ ➔ luminal stenosis & blockage of vascular flow
Causes of Endothelial injury

1. Valvulitis
2. MI
3. Atherosclerosis
4. Traumatic or inflammatory conditions
5. Hypertension
6. Endotoxins
7. Hypercholesterolemia
8. Radiation
9. Smoking
10. ...............etc.
ENDOTHELIAL INJURY

THROMBOSIS

ABNORMAL BLOOD FLOW

HYPERCOAGULABILITY

Turbulence

Stasis
LAMINAR BLOOD FLOW
LAMINAR VS TURBULENT BLOOD FLOW

Laminar Flow

Turbulent Flow
Stasis

- *Stasis is a major factor in venous thrombi*
- Normal blood flow is **laminar** (platelets flow centrally in the vessel lumen, separated from the endothelium by a slower moving clear zone of plasma)
- Stasis and turbulence cause the followings:

  - Disrupt normal blood flow
  - Prevent dilution of activated clotting factors by fresh flowing blood.
  - Retard the inflow of clotting factor inhibitors
  - Promote endothelial cell injury.
Causes of Stasis

1. Atherosclerosis
2. Aneurysms
3. Myocardial Infarction (Non-cottractile fibers)
4. Mitral valve stenosis (atrial dilation)
5. Hyper viscosity syndrome (PCV and Sickle Cell anemia)
6. ........
Hypercoagulability

A. Genetic (primary):
- most common >> mutations in factor V gene and prothrombin gene

B. Acquired (secondary):
- multifactorial & more complicated
- causes include: Immobilization, MI, AF, surgery, fractures, burns, Cancer, Prosthetic cardiac valves ...
...etc
MORPHOLOGY OF THROMBI

- Can develop anywhere in the CVS (e.g., in cardiac chambers, valves, arteries, veins, or capillaries).

- **Arterial or cardiac** thrombi begin at sites of **endothelial injury** or turbulence; and are usually superimposed on an **atherosclerotic plaque**

- **Venous** thrombi occur at sites of **stasis**. Most commonly the veins of the lower extremities (90%)

- Thrombi are focally attached to the underlying vascular surface.

- The propagating portion of a thrombus is poorly attached → fragmentation and embolus formation
TERMS TO REMEMBER ....
LINES OF ZAHN

- gross and microscopically apparent laminations
- represent pale platelet and fibrin layers alternating with darker erythrocyte-rich layers
- Significance? distinguish antemortem thrombosis from postmortem clots
- postmortem blood clots are non-laminated clots (*no lines of Zahn*)
Mural thrombi - in heart chambers or in aortic lumen
**CARDIAC VEGETATIONS**

= Thrombi on heart valves

**Types:**
1- infectious (Bacterial or fungal blood-borne infections)
e.g. infective endocarditis
2- non- infectious:
e.g. non-bacterial thrombotic endocarditis


**Fates of a thrombus**

- Thrombus formation
- Resolusion
- Propagation of thrombus
- Thromboembolism
- Organization
- Recanalization
- Mycotic aneurysm (discussed later)
ORGANIZED ARTERIAL THROMBUS
Fate of thrombi

1. **Propagation** ➔ accumulate additional platelets and fibrin, eventually causing vessel obstruction

2. **Embolization** ➔ Thrombi dislodge or fragment and are transported elsewhere in the vasculature

3. **Dissolution** ➔ Thrombi are removed by fibrinolytic activity (only in recent thrombi)

4. **Organization* and recanalization** ➔ Thrombi induce inflammation and fibrosis. These can recanalize (re-establishing some degree of flow), or they can be incorporated into a thickened vessel wall

*Organisation refers to the ingrowth of endothelial cells, smooth cells and fibroblasts into the fibrin rich thrombus.

5. **Superimposed infection (Mycotic aneurysm)**