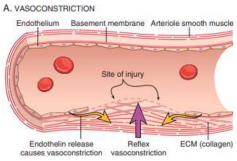
HEMODYNAMIC DISORDERS, THROMBOEMBOLISM, AND SHOCK 2

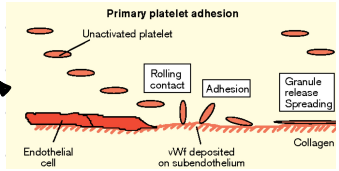
- Hemostasis is process involving platelets, clotting factors, and endothelium that occurs at the site of vascular injury and culminates in the formation of a blood clot
- MAJOR COMPONENT OF HEMOSTASIS
  1.platelates 2.Clotting factors 3.Endothelium

THE GENERAL SEQUENCE OF EVENTS LEADING TO HEMOSTASIS AT A SITE OF VASCULAR INJURY INCLUDE:

I. PRIMARY HEMOSTASIS

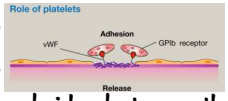


1. ARTERIOLAR VASOCONSTRICTION :
   reduces blood flow to the injured area.
   mediated by reflex neurogenic mechanisms.
   augmented by endothelin,
   this effect is transient



2. PLATELET ACTIVATION
   THE FORMATION OF THE PLATELET PLUG
   *forming the primary plug
   *providing a surface that binds and concentrates activated coagulation factors.
   *from megakaryocytes in the bone marrow into the bloodstream.

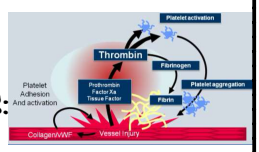
Platelets Undergo A Sequence Of Reactions After A Traumatic Vascular Injury That Culminate In The Formation Of A Platelet Plug



1. PLATELET ADHESION
is mediated via interactions with vwf, which acts as a bridge between the platelet surface receptor glycoprotein ib (gpib) and exposed collagen.

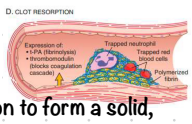
2.PLATELET ACTIVATION
A. CHANGES IN SHAPE
From smooth discs to "spiky "→ increased surface area.
alterations in glycoprotein iib/iiia that increase its affinity for fibrinogen
translocation of negatively charged phospholipids to the platelet surface
B. SECRETION OF GRANULE CONTENTS
THROMBIN/ADP/THROMBOXANE A2 (TXA2)

3. PLATELET AGGREGATION FOLLOWS THEIR ACTIVATION.
➟fibrinogen cause reversible aggregation
➟ thrombin cause irreversible aggregation (converts fibrinogen into insoluble fibrin).
➟ cytoskeleton cause contraction of the plug.



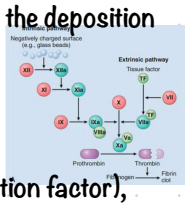
II .SECONDARY HEMOSTASIS:
DEPOSITION OF FIBRIN.
TISSUE FACTOR BINDS AND ACTIVATES FACTOR VII

III. CLOT STABILIZATION AND RESORPTION:



- polymerized fibrin and platelet aggregates undergo contraction to form a solid, permanent plug that prevents further hemorrhage.
- entrapped red cells and leukocytes are also found in hemostatic plugs,

COAGULATION CASCADE



- series of amplifying enzymatic reactions that lead to the deposition of an insoluble fibrin clot.
- each reaction step involves:
  an enzyme (an activated coagulation factor),
  a substrate (an inactive proenzyme form of a coagulation factor),
  and a cofactor (a reaction accelerator).
- these components are assembled on a negatively charged phospholipid surface, which is provided by activated platelets.

Coagulation cascade has traditionally been divided into the extrinsic and intrinsic pathways

- The prothrombin time (PT): The extrinsic pathway (factors VII, X, V, II (prothrombin), and fibrinogen).
- The partial thromboplastin time (PTT): The intrinsic pathway (factors XII, XI, IX, VIII, X, V, II, and fibrinogen).

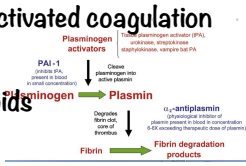
AMONG THROMBIN'S MOST IMPORTANT ACTIVITIES ARE THE FOLLOWING:

1. CONVERSION OF FIBRINOGEN INTO CROSSLINKED FIBRIN.
2. PLATELET ACTIVATION.
3. ANTI-COAGULANT EFFECTS.

FACTORS THAT LIMIT COAGULATION.

1.simple dilution:
- blood flowing at the site of injury washes out activated coagulation factors, which are rapidly removed by the liver.

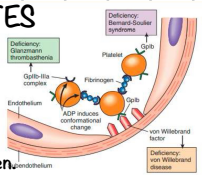
2.requirement for negatively charged phospholipids



3. fibrinolytic cascade:
- through the enzymatic activity of plasmin, which breaks down fibrin and interferes with its polymerization.

⚠ AN ELEVATED LEVEL OF BREAKDOWN PRODUCTS OF FIBRINOGEN (D-DIMERS) ARE A USEFUL CLINICAL MARKERS OF SEVERAL THROMBOTIC STATES

ENDOTHELIUM



1.PLATELET INHIBITORY EFFECTS:
📎Serve as a barrier that shields platelets from subendothelial vwf and collagen.
📎releases a number of factors that inhibit platelet activation and aggregation. among the most important are prostacyclin (pgi2), nitric oxide (no).
📎endothelial cells bind and alter the activity of thrombin, which is one of the most potent activators of platelets.
2. ANTICOAGULANT EFFECTS.
normal endothelium shields coagulation factors from tissue factor in vessel walls and expresses multiple factors that actively oppose coagulation
⚠ MOST NOTABLY thrombomodulin, endothelial protein c receptor, heparin-like molecules, and tissue factor pathway inhibitor.