General Principles of Hemostasis

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Hemostasis is a balancing act!

- pro-clotting:
  - plugs up holes in blood vessels

- anti-clotting:
  - keeps clotting under control
How to make a clot

Constrict vessel + Form platelet plug + Seal plug with fibrin = clot
Coagulation Cascade

Intrinsic

- XII → XIIa
- XI → Xla
- IX → IXa
- VIII → VIIIa

IXa

Extrinsic

- exposed TF
- VII → VIIa

TF VIIa

Final common pathway

- X
- V → Va
- Xa

Prothrombin → Thrombin

Fibrinogen → Fibrin
Intrinsic

XI → Xla
IX → IXa
VIII → VIIIa

Extrinsic

exposed TF
TF VIIa

VII

Xa

V → Va

prothrombin → thrombin
fibrinogen → fibrin
Where does tissue factor come from?

• “Hidden” cells exposed during injury
• Microparticles floating in blood
• Endothelial cells and monocytes (during inflammation)
Intrinsic

- XI → Xla
- IX → IXa
- VIII → VIIIa

Extrinsic

- exposed TF → VIIa
- VII → VIIa

- thrombin → IXa
- IXa → Xa
- Xa → thrombin

- prothrombin → thrombin
- fibrinogen → fibrin
Intrinsic

IX

VIII

Extrinsic

TF

VII

V

thrombin

fibrin
tissue factor

↓

fibrin
busy
distracting
sinful

simple
riveting
sexy
Intrinsic

- XI → Xla
- IX → IXa
- VIII → VIIIa

Extrinsic

- exposed TF
- VII → VIIa

- thrombin

- IXa → X

- Xa → prothrombin
- prothrombin → thrombin
- thrombin

- fibrinogen → fibrin
SIN

Intrinsic

thrombin

XI → Xla
IX → IXa
VIII → VIIIa

Extrinsic

exposed TF

TF VIIa → VII

IXa

IX → IXa
V → Va
VIII → VIIIa

Xa

thrombin

prothrombin → thrombin
fibrinogen → fibrin

busy

distracting
sinful
$\text{SIN}_{\text{trinsic}} \quad \text{SEX}_{\text{trinsic}}$

- VII
- IX
- VIII
- V
- TF VII
- X

Thrombin

Fibrin
How to keep clotting under control

inhibit the cascade
How to keep clotting under control

lyse the clot
Tissue plasminogen activator (t-PA)

plasminogen → plasmin

clot → fibrin degradation products (FDPs)
Hemostasis Outline

- The big picture
- Laboratory tests
Platelet Lab Tests

Count
- Done by particle counter
- 150 – 450 x 10⁹/L

Morphology
- Size
- Granulation
Platelets
Bleeding Time

Why?
• Evaluate platelet response to vascular injury
• Some platelet disorders have a long bleeding time

How?
• Inflate blood pressure cuff
• Make incision
• Time how long it takes to stop bleeding

Careful!
• Lots of things affect the test!
• Some consider the test unreliable.
Two incisions are made and the time for clotting to occur is recorded.
Coagulation Lab Tests

• Draw blood into citrate tube
• Spin tube, decant plasma
• Add reagents to plasma
• Watch for formation of fibrin
Prothrombin Time

- Plasma + thromboplastin
- Measures extrinsic pathway
- INR = a “corrected” PT
Intrinsic

\[ \text{VIII} \quad \rightarrow \quad \text{IX} \quad \rightarrow \quad \text{X} \quad \rightarrow \quad \text{thrombin} \quad \rightarrow \quad \text{fibrin} \quad \rightarrow \quad \text{SEX}^{\text{trinsic}} \quad \rightarrow \quad \text{TF VII} \]

SEX_{\text{trinsic}}
Partial Thromboplastin Time

- Plasma + phospholipid
- Measures intrinsic pathway
SIN\textsubscript{trinsic}  

Extrinsic

- IX
- TF VII

VIII

- VIII

V

- V

thrombin

- fibrin

- clot
Fibrin Degradation Product Assay

- Measures FDPs
- VERY, VERY sensitive test
- Best used to rule OUT a thrombus!

clot → fibrin degradation products (FDPs)