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

IXa

Extrinsic

exposed TF

VIIa

Final common pathway

X

V

VIIIa

VII

prothrombin → thrombin

fibrinogen → fibrin
Intrinsic

- XI → Xla
- IX → IXa

Extrinsic

- exposed TF → VIIa → VII

Other:

- X → Xa
- V → Va
- prothrombin → thrombin
- fibrinogen → fibrin
Intrinsic

- XI → XIa
- IX
- VIII → VIIIa

Extrinsic

- exposed TF
- TF → VIIa

Thrombin Pathway:

- IXa
- X
- V → Va
- prothrombin → thrombin
- fibrinogen → fibrin
Intrinsic

Extrinsic

thrombin

IX

IXa

XI

XIIa

VIII

VIIIa

VII

IXa

TF

VIIa

exposed TF

X

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

thrombin

XI → Xla

IX → IXa

VIII → VIIIa

Extrinsic

exposed TF

TF

VIIa

VII

Xa

V → Va

prothrombin → thrombin

fibrinogen → fibrin
Intrinsic

thrombin

XIIa

IXa

VIIa

Xa

prothrombin → thrombin

fibrinogen → fibrin

Extrinsic

exposed TF

TF VIIa

VII

VIIIa

VIII

XII

IX

V

Va
Intrinsic

- XI → Xla
- IX → IXa
- VIII → VIIIa

Extrinsic

- exposed TF → VIIa
- VII → TF

Thrombin:
- IXa → Xa
- Xa → Va

Prothrombin:
- prothrombin → thrombin

Fibrinogen:
- fibrinogen → fibrin
Intrinsic

IX

VIII

Extrinsic

TF
VII

X

V

thrombin

fibrin
tissue factor
↓
fibrin
busy
distracting
sinful

simple
riveting
sexy
Intrinsic Extrinsic

- Thrombin
- IXa
- Xa
- IX
- VIII
- VIIa
- TF
- X
- V
- Va
- Prothrombin → Thrombin → Fibrinogen → Fibrin

Exposed TF

Sex

Simple riveting sexy
How to keep clotting under control

inhibit the cascade
Clot formation involves the conversion of fibrinogen to fibrin. This process is regulated by the intrinsic and extrinsic coagulation pathways. Key components include factor Xa (IXa), factor VIIa (VIIa), and thrombin. The intrinsic pathway begins with factor XIa (XIa) and factor IX (IX). The extrinsic pathway involves tissue factor (TF), factor VIIa (VIIa), and factor Xa (Xa). Protein C inactivates factors Va and VIIIa, while antithrombin (ATIII) inhibits thrombin. The final products are fibrin polymerization leading to clot formation.
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

$\text{SEX}_{\text{trinsic}}$

IX

TF VII

VIII

V

thrombin

fibrin
Partial Thromboplastin Time

- Plasma + phospholipid
- Measures intrinsic pathway
**SIN**trinsic

**Extrinsic**

- **IX**
- **TF VII**

- **VIII**
- **V**

- Thrombin
- Fibrin
- Clot
Fibrin Degradation Product Assay

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