General Principles of Hemostasis

Kristine Krafts, M.D.
Hemostasis is a balancing act!

- **pro-clotting**: plugs up holes in blood vessels
- **anti-clotting**: keeps clotting under control
Pro-Clotting

\[ \text{Pro-Clotting} \]

\[ + \quad \text{Proteins} \quad + \quad \text{Fibrinogen} \quad = \quad \text{clot} \]
Pro-Clotting

vessels  platelets  cascade
Pro-Clotting

Blood vessel constricts.

- Blood loss decreases
- Platelets and factors meet
Pro-Clotting

Platelets form a plug.

- Proteins are exposed
- Platelets adhese
- Granules release contents
- Platelets aggregate
- Phospholipids are exposed
Pro-Clotting

Fibrin seals up plug.

- Tissue factor is exposed
- Cascade begins
- Cascade makes fibrin
- Fibrin solidifies plug
Coagulation Cascade

Intrinsic

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

Extrinsic

- exposed TF → VIIa
- VII

IXa

- Final common pathway
  - X
  - V → Va

Xa

- prothrombin → thrombin
- fibrinogen → fibrin → clot
Fibrinogen → fibrin → clot
fibrinogen ➔ fibrin ➔ clot

thrombin ➔ prothrombin ➔ thrombin

Intrinsic

Extrinsic

thrombin ➔ exposed TF ➔ VIIa ➔ VII

IXa ➔ Xa ➔ X ➔ Xa

VIIIa ➔ VIII ➔ IX ➔ IXa

XI ➔ XIa ➔ IX ➔ IXa

V ➔ Va ➔ X ➔ Xa

XI ➔ XIa ➔ IX ➔ IXa ➔ Xa ➔ X ➔ VII ➔ VIIa ➔ exposed TF ➔ thrombin ➔ prothrombin ➔ thrombin ➔ fibrinogen ➔ fibrin ➔ clot
Intrinsic

thrombin

IXa

IX

VIII

VIIa

X

V

Extrinsic

exposed TF

TF

VII

prothrombin

thrombin

fibrinogen

fibrin

clot
Intrinsic

thrombin

IXa

IX

VIII

VIIIa

TF

VIIa

exposed TF

VII

X

V

Va

prothrombin → thrombin

fibrinogen → fibrin → clot
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

IXa

Extrinsic

exposed TF

TF → VIIa

VII → VIIa

X → Xa

V → Va

prothrombin → thrombin

fibrinogen → fibrin → clot
Intrinsic

- Thrombin
- IX → IXa
- VIII → VIIIa
- X

Extrinsic

- Exposed TF
- VIIa
- TF
- VII

- Prothrombin → Thrombin
- Fibrinogen → Fibrin → Clot
The diagram illustrates the intrinsic and extrinsic pathways of blood clotting.

**Intrinsic Pathway:**
- XI → Xla
- IX → IXa
- VIII → VIIIa
- Xa
- Prothrombin → thrombin
- Fibrinogen → fibrin → clot

**Extrinsic Pathway:**
- Exposed TF
- VIIa
- TF → VII
- Xa

Thrombin is a key enzyme in the process, converting fibrinogen to fibrin and forming a clot.
Intrinsic

IX

Extrinsic

TF VII

VIII → IX → X

V → X

thrombin → fibrin → clot
tissue factor
↓
fibrin
↓
clot
Intrinsic

thrombin

XI ➔ Xla

IX

VIII ➔ VIIIa

IXa

Extrinsic

exposed TF

TF VIIa

VII

V ➔ Va

Xa

prothrombin ➔ thrombin

fibrinogen ➔ fibrin ➔ clot
busy
distracting
sinful

thrombin
XI → XIa
IX → IXa
VIII → VIIIa

IXa

Xa

X

V → Va

prothrombin → thrombin
fibrinogen → fibrin → clot
The diagram illustrates the coagulation cascade. The Intrinsic pathway starts with thrombin activating XI to XIa, which activates IX to IXa. IXa then activates VIII to VIIIa. The Extrinsic pathway begins with exposed TF activating VIIa to TF VIIa. Xa activates X, which further acts as a catalyst in the process. Thrombin converts prothrombin to thrombin, and fibrinogen to fibrin, leading to clot formation.
The diagram illustrates the intrinsic (SIN) and extrinsic (SEX) pathways of blood clotting.

- **SIN** (intrinsic):
  - VIII
  - IX
  - X
  - Thrombin
  - Fibrin
  - Clot

- **SEX** (extrinsic):
  - VII
  - TF
  - X
  - Thrombin
  - Fibrin
  - Clot
Anti-Clotting

cascade inhibition
Anti-Clotting

cascade inhibition
• TFPI
• ATIII
• Proteins C, S

clot lysis
Anti-Clotting

clot

plasminogen + t-PA → plasmin

→ clot →
Hemostasis Outline

- The big picture
- Laboratory tests
Platelet Lab Tests

Count
• Done by particle counter
• 150 – 450 x 10^9/L

Morphology
• Size
• Granulation
Platelets
Normal Platelets

granulomere

hyalomere
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
Intrinsic

IX

SEX extrinsic

TF VII

VIII

V

thrombin

fibrin

clot
Intrinsic

VIII

IX

V

X

thrombin

fibrin

clot

Extrinsic

TF

VII

The PT is increased in:

- ↓ VII, X, V, II, I
- Coumadin
- Heparin
- DIC
When should you order a PT?

- Never!
- Order an INR instead.
What is an INR?

Just a corrected PT.
When should you order an INR?

- To assess liver function
- To monitor Coumadin therapy
- To diagnose DIC*
- To assess pre-op status

* Disseminated intravascular coagulation
Partial Thromboplastin Time

- Plasma + phospholipid
- Measures intrinsic pathway
- APTT = same thing
**SIN**

**trinsic**

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**Extrinsic**

- **IX**
- **VIII**
- **V**
- **X**

**thrombin**

**fibrin**

**clot**

- **TF VII**
The PTT is increased in:

- hemophilia A
- hemophilia B
- DIC
- heparin

The clotting process involves:

- Thrombin
- Fibrin
- Clot
When should you order a PTT?

- To investigate a history of abnormal bleeding
- To monitor heparin therapy
- To diagnose DIC
- To assess pre-op status
Fibrin Degradation Product Assay

- Measures FDPs (including D-dimers)
- VERY sensitive!
Anti-Clotting
fibrinogen fibrin cross-linked fibrin

Thrombin

XIII

cross-linked fibrin
fibrinogen → fibrin → cross-linked fibrin

plasmin → FDPs → D-dimers
FDPs are increased when there is:

- A nasty thrombus
- Minor clotting
When should you order an FDP assay?

- Not to *rule in* a clot...
- but to *rule out* a clot.