# 🩸 HEMATOLOGY AND ONCOLOGY FOR USMLE 🩸

## Coagulation Disorders

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### 📌 Prothrombin Time (PT)

#### 🔎 What does PT test?

Evaluates the Extrinsic + Common pathway

Factors tested:

- VII (Extrinsic)
- X, V, II (prothrombin), I (fibrinogen) → Common pathway

#### 🧠 Mnemonic:

"Play Tennis outside" → PT = Extrinsic pathway

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#### 📊 When is PT prolonged?

- Factor VII deficiency (earliest in Vit K deficiency ⚠️)
- Warfarin therapy
- Liver disease
- DIC
- Severe vitamin K deficiency

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## 📈 INR (International Normalized Ratio)

$$INR = Patient\ PT / Control\ PT$$

- Normal = 1
- > 1 = prolonged PT
- Used to monitor warfarin therapy

💊 Warfarin inhibits:

- Factors II, VII, IX, X
- Protein C and Protein S

⚠️ Step 1 Trap:

Factor VII has the shortest half-life → PT prolongs first in vitamin K deficiency and warfarin therapy.

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## 📌 Partial Thromboplastin Time (PTT)

### 🔎 What does PTT test?

Evaluates Intrinsic + Common pathway

Factors tested:

- XII, XI, IX, VIII → Intrinsic
- X, V, II, I → Common
- (NOT VII, NOT XIII)

🧠 Mnemonic:

"Play Table Tennis inside" → PTT = Intrinsic pathway

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### 📊 When is PTT prolonged?

- Hemophilia A (VIII)

- Hemophilia B (IX)
- Hemophilia C (XI)
- Heparin therapy
- Factor inhibitors (e.g., anti-VIII antibodies)
- DIC
- Severe liver disease

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## 📌 Thrombin Time (TT)

### 🔎 What does TT measure?

Conversion of:

Fibrinogen -> Fibrin

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### 📊 TT is prolonged in:

- Anticoagulants (especially heparin)
- Hypofibrinogenemia
- DIC

- Advanced liver disease

🧠 Think: TT checks the final step of coagulation.

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## 📌 Factor XIII

Neither PT nor PTT measures

🔬 Why?

Factor XIII (Fibrin-stabilizing factor) acts after fibrin is already formed.

Sequence:
Fibrinogen → (Thrombin) → Fibrin → Factor XIII cross-links fibrin

So XIII works after the clot has formed, stabilizing it.

🧪 What measures Factor XIII?

❌ Clot solubility test (most classic test)

Also called:

- SM urea clot solubility test

- Or acetic acid clot solubility test

👉 In Factor XIII deficiency, the fibrin clot forms normally
BUT it dissolves in SM urea within 24 hours.

Because:
Factor XIII is needed to cross-link fibrin strands and stabilize the clot.

2️⃣ Specific Factor XIII activity assay

Used for confirmation in modern labs.

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## 🧪 Mixing Study — Differentiating Deficiency vs Inhibitor

🔬 Principle:

Patient plasma + Normal plasma → Repeat PT/PTT

| Result | Interpretation |
| --- | --- |
| ✅ Corrects | Clotting factor deficiency |
| ❌ Does NOT correct | Factor inhibitor present |

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🧠 Why?

If a factor is missing → normal plasma supplies it → clotting normalizes.
If an inhibitor (antibody) is present → it also inactivates factors in normal plasma → no correction.

📌 Most common acquired inhibitor = Factor VIII inhibitor

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## 🩸 Hemophilias

All are intrinsic pathway defects → ↑ PTT, normal PT

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## 🧬 Hemophilia A

- Factor VIII deficiency
- X-linked recessive
- Most common hemophilia
- Think: "Hemophilia ATE (VIII)" 🍽️

### 🧪 Labs:

- ↑ PTT
- Normal PT
- Normal bleeding time

### 🩺 Clinical Features:

- Hemarthroses (bleeding into joints 🦵)
- Easy bruising
- Bleeding after trauma/dental procedures

### 💊 Treatment:

- Desmopressin (↑ vWF → stabilizes VIII)
- Factor VIII concentrate
- Emicizumab (bispecific antibody mimics VIII function)

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## 🧬 Hemophilia B (Christmas Disease)

- Factor IX deficiency
- X-linked recessive

🧪 Labs:

- ↑ PTT
- Normal PT

💊 Treatment:

- Factor IX concentrate

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## 🧬 Hemophilia C

- Factor XI deficiency
- Autosomal recessive

🧪 Labs:

- ↑ PTT
- Normal PT

💊 Treatment:

- Factor XI concentrate

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🧾 Hemophilia Comparison Table

| Feature | Hemophilia A | Hemophilia B | Hemophilia C |
|---|---|---|---|
| Factor | VIII | IX | XI |
| Inheritance | X-linked | X-linked | Autosomal recessive |
| PT | Normal | Normal | Normal |

| | | | |
|---|---|---|---|
| PTT | ↑ | ↑ | ↑ |
| Hemarthroses | Yes | Yes | Mild/Variable |

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## 🧪 Vitamin K Deficiency

### 🧬 Mechanism

Vitamin K is required for $\gamma$-carboxylation of:

- II
- VII
- IX
- X
- Protein C
- Protein S

This modification allows calcium binding → activation of clotting factors.

Without vitamin K → Factors produced but nonfunctional

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## 📊 Lab Findings

- ↑ PT (earliest)
- ↑ PTT (later)
- Normal bleeding time

### ⚠️ Why PT increases first?

Factor VII has shortest half-life.

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## 🧠 Flowchart — Vitamin K Deficiency

Vitamin K deficiency

⬇

↓ $\gamma$-carboxylation

⬇

↓ Functional II, VII, IX, X

⬇

Extrinsic affected first (VII)

⬇

↑ PT → later ↑ PTT

⬇

Bleeding tendency 🩸

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## 🎯 USMLE Points

- Isolated ↑ PT → think Factor VII or early Vit K deficiency
- Isolated ↑ PTT → think Hemophilia
- Both PT & PTT ↑ → think DIC, liver disease, severe Vit K deficiency
- Mixing study correction = deficiency
- No correction = inhibitor

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# 🩸 Platelet Disorders

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## 🧬 Core Concept: Primary Hemostasis

Primary hemostasis = Platelet plug formation

Steps:

1. 🧲 Adhesion → Platelets bind exposed collagen via vWF
2. 🔗 Activation → Shape change + granule release
3. 🧩 Aggregation → Platelets bind each other via GpIIb/IIIa

⚠️ All platelet disorders affect primary hemostasis

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## 📌 Hallmark Clinical Features of Platelet Disorders

- ↑ Bleeding Time (BT)
- Mucosal bleeding (epistaxis, gum bleeding)
- Petechiae
- Easy bruising
- Immediate bleeding after trauma

🧠 Contrast:

- Platelet disorders → superficial bleeding
- Coagulation factor disorders → deep bleeding (hemarthroses)

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## 🧪 Lab Patterns in Platelet Disorders

| Parameter | Finding |
|---|---|
| Bleeding Time | ↑ |
| PT | Normal |
| PTT | Normal |
| Platelet Count | Usually ↓ (except qualitative disorders) |

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# 🧲 Bernard-Soulier Syndrome

## 🧬 Mechanism

Autosomal recessive defect in platelet adhesion

↓ GpIb receptor
↓ Platelet binding to vWF
↓ Adhesion to damaged endothelium

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## 🧠 Pathway Flow

GpIb defect
⬇
↓ vWF binding
⬇
↓ Adhesion
⬇
Defective platelet plug
⬇
Mucosal bleeding 🩸

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## 🧪 Labs

- ↓ Platelet aggregation
- ↑ Bleeding time
- Large platelets (giant platelets)
- Platelet count: ↓ or normal

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### 🎯 USMLE Clue

"Big platelets" + adhesion defect = Bernard-Soulier

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## 🧩 Glanzmann Thrombasthenia

### 🧬 Mechanism

Autosomal recessive defect in platelet aggregation

↓ GpIIb/IIIa (integrin $\alpha$IIb$\beta$3)
↓ Platelet-to-platelet binding (via fibrinogen)

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### 🧠 Pathway Flow

GpIIb/IIIa defect

⬇

Cannot bind fibrinogen

⬇

Cannot aggregate

⬇

No platelet clumping

⬇

Bleeding tendency 🩸

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## 🧪 Labs

- ↑ Bleeding time
- Normal PT/PTT
- Platelet count: normal
- Peripheral smear: no platelet clumping

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## 🎯 Comparison

| Feature | Bernard-Soulier | Glanzmann |
|---|---|---|
| Defect | Adhesion | Aggregation |
| Receptor | GpIb | GpIIb/IIIa |
| Platelet size | Large | Normal |
| Clumping | Reduced | Absent |

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## 🛡️ Immune Thrombocytopenia (ITP)

### 🧬 Mechanism

Autoantibodies (usually IgG) against GpIIb/IIIa

⬇

Opsonized platelets

⬇

Splenic macrophage destruction

⬇

↓ Platelet count

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## 🧪 Labs

- ↓ Platelet count
- ↑ Bleeding time
- Normal PT/PTT
- ↑ Megakaryocytes in bone marrow

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## 🧠 Causes

- Idiopathic
- Autoimmune diseases (eg, SLE)
- Viral infections (HIV, HCV)
- Malignancy (CLL)
- Drug-induced

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### 💊 Treatment

- Glucocorticoids
- IVIG
- Rituximab
- TPO receptor agonists (eltrombopag, romiplostim)
- Splenectomy (refractory cases)

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### 🎯 USMLE Pearls

- Anti-GpIIb/IIIa antibodies
- Increased megakaryocytes = bone marrow trying to compensate
- Normal PT/PTT differentiates from DIC

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## 🧪 Uremic Platelet Dysfunction

### 🧬 Mechanism

Renal failure

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Accumulation of uremic toxins

⬇

Impaired platelet adhesion & aggregation

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### 🧪 Labs

- Normal platelet count
- ↑ Bleeding time
- Normal PT/PTT

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### 🎯 Key Point

Qualitative defect — platelets present but dysfunctional

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## ⚡ Thrombotic Microangiopathies (TMA)

These disorders:

- Form microthrombi in small vessels
- Cause thrombocytopenia
- Cause microangiopathic hemolytic anemia (MAHA)

⚠️ IMPORTANT:

Unlike DIC → coagulation cascade is NOT activated

So:

- PT normal
- PTT normal
- Fibrinogen normal

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## 🧠 Pathophysiology Overview

Microthrombi formation

⬇

RBCs shear against fibrin strands

⬇

Schistocytes form

⬇

Hemolysis

⬇

↑ LDH, ↓ Hb

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## 🔬 Thrombotic Thrombocytopenic Purpura (TTP)

### 👩 Epidemiology

Typically adult females

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### 🧬 Mechanism

Deficiency or inhibition of ADAMTS13

ADAMTS13 normally cleaves large vWF multimers.

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### 🧠 Flowchart

↓ ADAMTS13

⬇

Large vWF multimers accumulate

⬇

Excess platelet aggregation

⬇

Microvascular thrombosis

⬇

MAHA + Thrombocytopenia

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## 🩺 Presentation

Classic pentad:

- Thrombocytopenia
- MAHA (schistocytes, ↑ LDH)
- Acute kidney injury
- Fever
- Neurologic symptoms

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## 🧪 Labs

- ↓ Platelets
- ↓ Hb
- Schistocytes
- ↑ LDH
- Normal PT/PTT

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### 💊 Treatment

### 🚨 Emergency!

- Plasma exchange (removes antibodies + replaces ADAMTS13)
- Glucocorticoids
- Rituximab

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## 🦠 Hemolytic Uremic Syndrome (HUS)

### 👶 Epidemiology

Typically children

## 🧬 Mechanism

Shiga toxin-producing E. coli (O157:H7)

Shiga toxin

⬇

Endothelial damage

⬇

Platelet activation

⬇

Microthrombi formation

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## 🩺 Presentation

Triad:

- Thrombocytopenia
- MAHA
- Acute kidney injury

Distinguishing feature:

- Bloody diarrhea

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## 🧪 Labs

- ↓ Platelets
- Schistocytes
- ↑ LDH
- Normal PT/PTT

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## 💊 Treatment

Supportive care
(Antibiotics may worsen toxin release ⚠️)

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## 🆚 TTP vs HUS vs DIC Comparison Table

| Feature | TTP | HUS | DIC |
|---|---|---|---|
| ADAMTS13 | ↓ | Normal | Normal |
| Trigger | Autoimmune | Shiga toxin | Sepsis, trauma, malignancy |
| PT/PTT | Normal | Normal | ↑ |
| Fibrinogen | Normal | Normal | ↓ |
| Neuro symptoms | Prominent | Mild | Variable |
| Bloody diarrhea | No | Yes | No |
| Treatment | Plasma exchange | Supportive | Treat underlying cause |

### 🎯 Exam Points

- Normal PT/PTT + MAHA = Think TTP or HUS
- Schistocytes = microangiopathic process
- If PT/PTT prolonged → think DIC instead
- Neurologic symptoms prominent → TTP
- Child with bloody diarrhea → HUS

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## 🩸 Mixed Platelet & Coagulation Disorders

These disorders affect both primary and secondary hemostasis, so lab patterns get more interesting.

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## 🧬 von Willebrand Disease (vWD)

### 📌 Core Concept

vWF has two major roles:

1️⃣ Platelet adhesion (primary hemostasis)

2️⃣ Stabilizes factor VIII (secondary hemostasis)

So deficiency affects both platelet function AND intrinsic pathway.

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🧠 Pathophysiology Flow

↓ vWF quantity/function

⬇

↓ Platelet adhesion (via GpIb)

⬇

Defective platelet plug

⬇

↑ Bleeding time

AND

↓ Protection of factor VIII

⬇

↓ Factor VIII levels

⬇

↑ PTT

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## 🧪 Lab Pattern

| Parameter | Finding |
|---|---|
| Platelet Count | Normal |
| Bleeding Time | ↑ |
| PT | Normal |
| PTT | Normal or ↑ |

⚠️ PTT increases because vWF carries factor VIII.

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## 🧬 Genetics

- Most common inherited bleeding disorder

- Usually autosomal dominant
- Typically mild

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## 🩺 Clinical Presentation

- Menorrhagia
- Epistaxis
- Easy bruising
- Prolonged bleeding after dental procedures

🧠 Think: mucosal bleeding + prolonged PTT + normal platelets.

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## 💊 Treatment

- Desmopressin (DDAVP) → releases vWF from endothelium
- vWF concentrates (severe cases)

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# ⚡ Disseminated Intravascular Coagulation (DIC)

## 📌 Core Concept

Widespread clotting factor activation → consumption → bleeding

You clot everywhere
Then you bleed everywhere

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## 🧠 Mechanism Flowchart

Trigger (sepsis, trauma, etc.)

⬇

Massive tissue factor activation, factor III (it initiates extrinsic pathway by activating VII -> VIIa)

⬇

Widespread thrombin generation

⬇

Microthrombi formation

⬇

Consumption of platelets + clotting factors

⬇

Bleeding + organ ischemia

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## 🧪 Lab Pattern

| Parameter | Finding |
|---|---|
| Platelet Count | ↓ |
| Bleeding Time | ↑ |
| PT | ↑ |
| PTT | ↑ |
| Fibrinogen | ↓ |
| D-dimer | ↑ |

| | |
|---|---|
| Smear | Schistocytes |

⚠️ Factor V and VIII levels decrease.

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🩺 Clinical Clues

- Oozing from IV sites
- Bleeding + thrombosis
- Acute organ failure

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🧠 Causes Mnemonic: SSSTOP Making New Thrombi

- Sepsis (gram negative common)
- Snake bites
- Shock/Heat stroke
- Trauma
- Obstetric complications
- Pancreatitis
- Malignancy

- Nephrotic syndrome
- Transfusion

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## 🧠 Acute vs Chronic DIC

| Type | Characteristics |
|---|---|
| Acute | Rapid consumption → life-threatening bleeding |
| Chronic | Compensated by liver → more thrombosis |

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## 🎯 USMLE Pearl

Normal PT/PTT = TTP/HUS

Prolonged PT/PTT = DIC

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## 🧬 Hereditary Thrombophilias

Autosomal dominant disorders causing hypercoagulable states.

Primary problem: too much clotting, not bleeding.

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## 🧲 Antithrombin Deficiency

### 🧬 Mechanism

Antithrombin normally inhibits:

- Thrombin (IIa)
- Factor Xa

Deficiency → reduced inhibition → thrombosis

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### 🧪 Lab Pattern

- PT normal
- PTT normal

- Heparin response blunted (heparin requires antithrombin)

⚠️ Key exam point:

Heparin ineffective because it works by activating antithrombin.

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🧠 Acquired Causes

- Nephrotic syndrome → loss in urine
- Renal failure

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## 🧬 Factor V Leiden

📌 Most Common Inherited Thrombophilia

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🔹 What does Factor V do?

Once activated:

- Factor V → Factor Va
- Factor Xa + Factor Va + $Ca^{2+}$ + phospholipids = Prothrombinase complex

📌 Function of the Prothrombinase Complex:

Converts:

Prothrombin (Factor II) → Thrombin (Factor IIa)

And thrombin then:

- Converts fibrinogen → fibrin
- Activates Factors V, VIII, XI (positive feedback)
- Activates XIII → stabilizes fibrin

🧠 Pathophysiology

Point mutation: Arg506Gln
Factor V becomes resistant to degradation by activated protein C (APC)

Normally:
Protein C inactivates Va and VIIIa

With mutation:

Factor V persists → excessive clotting

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## 🧠 Flow

APC resistance

⬇

Factor Va not degraded

⬇

Prothrombinase complex persists

⬇

↑ Thrombin

⬇

Venous thrombosis

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## 🩺 Clinical Clues

- DVT at young age
- Cerebral vein thrombosis

- Recurrent pregnancy loss

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## 🧬 Protein C or Protein S Deficiency

### 📌 Function

Protein C + S:

Inactivate factors Va and VIIIa

"Protein C Cancels, Protein S Stops" coagulation.

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### 🧠 Mechanism

↓ Protein C/S

⬇

Va and VIIIa remain active

⬇

Excess thrombin formation

⬇

Thrombosis

## ⚠️ Warfarin-Induced Skin Necrosis

Warfarin initially decreases Protein C faster than procoagulant factors

⬇

Temporary hypercoagulable state

⬇

Skin necrosis

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## 🧬 Prothrombin G20210A Mutation

### 🧠 Mechanism

Mutation in 3´ untranslated region

⬇

↑ Prothrombin production

⬇

↑ Plasma thrombin

⬇

Venous clots

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## 📊 Hereditary Thrombophilia Comparison Table

| Disorder | Mechanism | Key Clue |
|---|---|---|
| Antithrombin deficiency | ↓ inhibition of IIa & Xa | Heparin resistance |
| Factor V Leiden | APC resistance | Most common inherited thrombophilia |
| Protein C deficiency | ↓ Va, VIIIa inactivation | Warfarin skin necrosis |
| Protein S deficiency | ↓ Protein C function | Similar to Protein C deficiency |

| | | |
|---|---|---|
| Prothrombin mutation | ↑ Prothrombin levels | Venous thrombosis |

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## 🧠 Integration Table — DIC vs vWD vs Thrombophilia

| Feature | vWD | DIC | Thrombophilia (hypercoagulable states) |
|---|---|---|---|
| Bleeding | Yes | Yes + clots | No |
| Thrombosis | Rare | Yes | Yes |
| PT | Normal | ↑ | Normal |
| PTT | ↑ | ↑ | Normal |
| Platelets | Normal | ↓ | Normal |

| | | | |
|---|---|---|---|
| D-dimer | Normal | ↑ | Normal |

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## 🎯 Exam Tricks

If question shows:

- Mucosal bleeding + ↑ PTT + normal platelets → vWD
- Bleeding + thrombosis + ↑ PT/PTT + ↓ fibrinogen → DIC
- Recurrent DVT in young patient → think inherited thrombophilia
- Heparin not working → antithrombin deficiency
- Warfarin skin necrosis → protein C deficiency

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# 🩸 Blood Transfusion Therapy

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## ❑ Packed Red Blood Cells (PRBCs)

### 🔬 Dose Effect

- ↑ Hemoglobin ≈ 1 g/dL per unit
- ↑ Hematocrit ≈ 3% per unit
- Improves oxygen-carrying capacity

### 🏥 Clinical Use

- Acute blood loss
- Severe symptomatic anemia
- Hemodynamic instability due to anemia

### ⚠ Important

- Does NOT provide clotting factors
- Does NOT significantly correct coagulopathy

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## 2️⃣ Platelets

### 🔬 Dose Effect

- ↑ Platelet count ≈ 30,000/μL per apheresis unit
- (≈ 5,000/mm³ per random donor unit)

### 🏥 Clinical Use

- Active significant bleeding + thrombocytopenia
- Platelet count <10,000 (prophylaxis)
- Qualitative platelet dysfunction
- Before invasive procedures (if low platelets)

### ❗ Not useful in:

- Immune destruction (e.g., ITP) unless life-threatening bleed

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## 3️⃣ Fresh Frozen Plasma (FFP)

### 🔬 Contains:

- All coagulation factors
- All plasma proteins

### 🏥 Clinical Use

- Liver failure (cirrhosis)
- DIC

- Multiple factor deficiencies
- Immediate warfarin reversal (if PCC unavailable)

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## 4️⃣ Prothrombin Complex Concentrate (PCC)

🔬 Contains:

- Factors II, VII, IX, X
- Protein C & S

🏥 Clinical Use

- Rapid warfarin reversal
- Major bleeding with elevated INR

👉 Faster and requires less volume than FFP.

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## 5️⃣ Cryoprecipitate

🔬 Contains:

- Fibrinogen

- Factor VIII
- Factor XIII
- vWF
- Fibronectin

### 🏥 Clinical Use

- Hypofibrinogenemia
- DIC with low fibrinogen
- Massive transfusion protocol
- Factor VIII deficiency (if specific concentrates unavailable)

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## 6️⃣ Albumin

### 🔬 Effect

- ↑ Intravascular oncotic pressure
- Volume expansion

### 🏥 Clinical Use

- Post large-volume paracentesis
- Therapeutic plasmapheresis
- Severe hypoalbuminemia

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## 🚨 Blood Transfusion Complications

### 1️⃣ Infection Transmission

- Very low risk (screening is advanced)

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### 2️⃣ Transfusion Reactions

- Acute hemolytic (ABO mismatch)
- Febrile non-hemolytic
- Allergic
- Anaphylactic

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### 3️⃣ TACO (Transfusion-Associated Circulatory Overload)

- Volume overload
- Pulmonary edema
- Hypertension
- Common in elderly or heart failure patients

👉 Cardiogenic pulmonary edema

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4️⃣ TRALI (Transfusion-Related Acute Lung Injury)

- Hypoxia
- Inflammation
- Noncardiogenic pulmonary edema
- Hypotension

👉 Occurs within 6 hours

👉 Immune-mediated (anti-HLA and anti HNA antibodies)

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5️⃣ Iron Overload

- Chronic transfusions

- May lead to secondary hemochromatosis

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## 6 Hypocalcemia

- Citrate in stored blood chelates $Ca^{2+}$
- Seen in massive transfusion

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## 7 Hyperkalemia

- Old RBC units → cell lysis → ↑ $K^{+}$

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## 🧠 Exam Pearls

| Clinical Scenario | Give |
| --- | --- |
| Hb 6 g/dL | PRBC |

| | |
|---|---|
| INR 6 with bleeding (warfarin) | PCC |
| Low fibrinogen in DIC | Cryoprecipitate |
| Platelets 8,000 | Platelets |
| Post-paracentesis | Albumin |

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## 🩸 Coagulation Cascade — Factor Lists

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### 🔴 Extrinsic Pathway

*(Measured by PT)*

- Factor VII
- Tissue Factor (Factor III)

Mnemonic:

👉 "7 is outside" (Extrinsic = short pathway)

## 🔵 Intrinsic Pathway

*(Measured by PTT)*

- Factor XII
- Factor XI
- Factor IX
- Factor VIII

Mnemonic:

👉 "TENET" = 12, 11, 9, 8

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## 🟣 Common Pathway

*(Affects both PT & PTT)*

- Factor X
- Factor V
- Factor II (Prothrombin)
- Factor I (Fibrinogen)
- Factor XIII (stabilizes fibrin)

Mnemonic:

👉 "10 → 5 → 2 → 1 → 13"

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## 🟡 Vitamin K-Dependent Factors

- Factor II
- Factor VII
- Factor IX
- Factor X
- Protein C
- Protein S

Mnemonic:

👉 "1972 + C, S"

(Important: 1972 refers to 10, 9, 7, 2 — NOT factor I)

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## 🟢 Factors Produced by the Liver

👉 All clotting factors except vWF

So:

- I
- II
- V
- VII
- VIII
- IX
- X
- XI
- XII
- XIII
- Protein C
- Protein S
- Antithrombin

⚠️ Note:

- Factor VIII is produced by liver sinusoidal endothelial cells
- vWF is produced by endothelial cells & megakaryocytes

- 🔹 Positive Feedback Targets of Thrombin

1. Factor V → Va
    - Enhances the common pathway (Xa + Va → more thrombin)

2. Factor VIII → VIIIa
    - Boosts the intrinsic pathway (IXa + VIIIa → more Xa → more thrombin)

3. Factor XI → XIa
    - Activates intrinsic pathway earlier (XII → XI → IX → VIII → X → thrombin)

4. Platelets
    - Activates platelets → more PL surface for coagulation
    - Releases ADP and thromboxane A2 → recruits more platelets

Mnemonic: P-S811

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## 💊 Warfarin Inhibits

Warfarin inhibits Vitamin K epoxide reductase

→ ↓ Gamma-carboxylation of:

- II
- VII
- IX
- X
- Protein C
- Protein S

⚠️ Step 1 favorite:

- Protein C falls first → transient hypercoagulability → skin necrosis

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## 💉 Heparin Inhibits

Heparin activates Antithrombin III

Antithrombin inhibits:

- Factor IIa (Thrombin)
- Factor Xa
- Also inhibits IXa, XIa, XIIa (less emphasized)

High-yield:

- Unfractionated heparin → inhibits IIa & Xa
- LMWH (e.g., enoxaparin) → mainly inhibits Xa

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## 📌 Acute Phase Reactants

- Fibrinogen (Factor I)
- Factor VIII
- vWF

(↑ in inflammation, pregnancy, OCP use)

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## 📌 Contact Factors (Intrinsic Initiators)

- Factor XII
- High molecular weight kininogen
- Prekallikrein

⚠️ Factor XII deficiency:

- ↑ PTT
- NO bleeding

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## 📌 Natural Anticoagulants

- Protein C (inhibits Va and VIIIa)
- Protein S (cofactor for protein C)
- Antithrombin III
- TFPI (Tissue factor pathway inhibitor)

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## 📌 Lab Associations

| Condition | PT | PTT |
|---|---|---|

| | | |
|---|---|---|
| Hemophilia A (Factor VIII) | Normal | ↑ |
| Hemophilia B (Factor IX) | Normal | ↑ |
| Factor VII deficiency | ↑ | Normal |
| DIC | ↑ | ↑ |
| Vitamin K deficiency | ↑ first | ↑ later |

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## 🩸 Coagulopathies — Inheritance Patterns

| Disorder | Inheritance |
|---|---|
| Hemophilia A | X-linked recessive |
| Hemophilia B | X-linked recessive |

| | |
|---|---|
| Hemophilia C | Autosomal recessive |
| von Willebrand disease (Type 1 & 2) | Autosomal dominant |
| von Willebrand disease (Type 3) | Autosomal recessive |
| Factor V Leiden | Autosomal dominant |
| Prothrombin gene mutation (G20210A) | Autosomal dominant |
| Protein C deficiency | Autosomal dominant |
| Protein S deficiency | Autosomal dominant |
| Antithrombin III deficiency | Autosomal dominant |
| Factor XIII deficiency | Autosomal recessive |
| Afibrinogenemia | Autosomal recessive |

| | |
|---|---|
| Dysfibrinogenemia | Autosomal dominant |

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## 🩸 Platelet Disorders — Inheritance Only

| Disorder | Inheritance |
|---|---|
| Glanzmann thrombasthenia | Autosomal recessive |
| Bernard-Soulier syndrome | Autosomal recessive |
| Storage pool disease | Usually autosomal recessive |

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<-- The End -->