🩸 Heparin + Warfarin

💉 Heparin

🔑 Key Concept

- Fast-acting anticoagulant
- Works by activating antithrombin → inhibits clotting factors
- Short half-life → ideal for acute settings ⚡

💡 Mechanism of Action

- Heparin binds and activates antithrombin (ATIII) → ATIII inhibits → Thrombin (Factor IIa) + Factor Xa → ↓ Fibrin formation → Anticoagulation 🩸

📌 Clinical Uses

- Pulmonary embolism (PE) 🎯
- Deep vein thrombosis (DVT)
- Acute coronary syndrome (ACS)
- Myocardial infarction (MI)
- Safe in pregnancy 🤰 (does NOT cross placenta)

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- Drug of choice for immediate anticoagulation

🧪 Monitoring

- PTT (partial thromboplastin time) ⏱️ → Increased when heparin is effective

- Heparin inhibits factors II (thrombin) and X → disrupts the intrinsic pathway → leads to prolonged PTT (which assesses the intrinsic pathway)

❗ Adverse Effects

1️⃣ Bleeding

- Most common ⚠️

🔄 Reversal

Heparin overdose → Give Protamine sulfate 🛡️ → Neutralizes heparin

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2️⃣ Heparin-Induced Thrombocytopenia (HIT) 🚨

🔬 HIT Types

Feature	HIT Type I	HIT Type 2

Onset	1–2 days	5–10 days
Mechanism	Nonimmune	IgG-mediated
Severity	Mild	Severe
Platelets	>100,000	Markedly ↓
Risk	Low	High thrombosis risk

🔄 Flowchart: HIT Type 2 Mechanism

Heparin → Binds platelet factor 4 (PF4) → Forms heparin-PF4 complex → IgG antibodies form → Antibody binds complex → Platelet activation → Thrombosis ⚠️ → Platelet consumption → ↓ Platelet count

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⚠️ Key Clinical Insight

- Paradoxical thrombosis despite low platelets ❗

📌 Management of HIT

HIT suspected → STOP heparin immediately → Start alternative anticoagulant (Argatroban, a DTI) → Avoid warfarin initially ⚠️

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- Most common with unfractionated heparin
- Platelet drop + thrombosis = think HIT

3️⃣ Other Adverse Effects

- Osteoporosis (long-term use) 🦴
- Drug interactions
- Type IV renal tubular acidosis

🔬 Heparin Variants

1️⃣ Low-Molecular-Weight Heparin (LMWH)

(Enoxaparin, Dalteparin)

💡 Mechanism

- Preferentially inhibit Factor Xa

📌 Key Points

- More predictable pharmacokinetics
- Less monitoring needed
- Cleared by kidneys ⚠️

2️⃣ Fondaparinux

💡 Mechanism

- Selectively inhibits Factor Xa only

🎯 Key Advantage

- Does NOT bind PF4 → Safe in HIT ✅

🔄 Flowchart: Heparin Variants

Unfractionated heparin → Inhibits IIa + Xa → Monitor PTT → Safe in renal failure

LMWH → Mainly inhibits Xa → Renal clearance → Less monitoring

Fondaparinux → Only inhibits Xa → No HIT risk

🔥 Summary Table

Drug	Target	Monitoring	Special Feature
Heparin	IIa + Xa	PTT	Reversible
LMWH	Xa	None	Renal clearance

Fondaparinux	Xa only	None	No HIT

🎯 Must-Know Points

- Heparin → activates antithrombin → inhibits IIa & Xa
- Monitor PTT
- Reversal = protamine sulfate
- HIT type 2 = immune-mediated + thrombosis
- LMWH → Xa selective
- Fondaparinux → safest in HIT

💊 Warfarin

🔑 Key Concept

- Oral anticoagulant for chronic use
- Works by inhibiting vitamin K recycling

- Slow onset, long half-life ⏳

💡 Mechanism of Action

- Warfarin inhibits vitamin K epoxide reductase (VKORC1) → Prevents regeneration of active vitamin K → ↓ γ-carboxylation of clotting factors

Affected Factors:

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

Effect: ↓ clotting ability → anticoagulation 🩸

🎯 Mnemonic

In Computer Science = "2 + 7 is 9, not 10"

🧪 Monitoring

- PT/INR (extrinsic pathway) ⏱️ → Increased in warfarin therapy
- Concept: Warfarin inhibits vitamin K-dependent factors (II, VII, IX, X) → factor VII has the shortest half-life → extrinsic pathway is affected first → leads to prolonged PT/INR.

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- Factor VII has shortest half-life → PT rises first

📌 Clinical Uses

- Chronic anticoagulation
  - Atrial fibrillation (stroke prevention) 🎯
  - DVT/PE prophylaxis

⚠️ Important

- Contraindicated in pregnancy → Crosses placenta → teratogenic 👶

❗ Adverse Effects

1️⃣ Bleeding

- Most common ⚠️

2️⃣ Teratogenicity

- Causes fetal abnormalities 👶

3️⃣ Skin/Tissue Necrosis 🚨 (VERY high-yield)

🔄 Flowchart: Warfarin-Induced Hypercoagulability

Warfarin started → ↓ Protein C (short half-life) but clotting factors still present → Temporary hypercoagulable state → Microthrombi formation → Skin/tissue necrosis

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🎯 Key Insight

- Occurs in first few days
- Especially with high initial doses

🛡️ Heparin Bridging

🔄 Flowchart: Bridging Concept

Warfarin started → Initial hypercoagulability → Add heparin → Immediate anticoagulation → Prevents thrombosis → Warfarin becomes effective → Stop heparin

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- Always bridge with heparin when starting warfarin in high-risk patients

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💊 Drug Interactions

- Metabolized by CYP2C9 → Many drug interactions ⚠️

Examples:

- ↑ Warfarin effect → antibiotics, amiodarone
- ↓ Effect → enzyme inducers (e.g., rifampin)

🔄 Reversal of Warfarin

📊 Reversal Strategy

Situation	Treatment
Mild bleeding	Vitamin K
Severe bleeding	Fresh frozen plasma (FFP)
Rapid reversal	Prothrombin complex concentrate (PCC)

🔄 Flowchart: Reversal

Warfarin toxicity → ↓ clotting factors → Give Vitamin K (slow reversal) + FFP / PCC (rapid factor replacement) → Restore coagulation 🛡️

🎯 Must-Know Points

- Warfarin inhibits VKORC1 → ↓ vitamin K-dependent factors
- Affects II, VII, IX, X + Protein C/S

- Monitor PT/INR
- Initial hypercoagulability → skin necrosis
- Bridge with heparin
- Reversal: Vitamin K, FFP, PCC
- Contraindicated in pregnancy

⚖️ Heparin vs Warfarin

📊 Core Comparison Table

Feature	Heparin	Warfarin
Route	Parenteral (IV, SC) 💉	Oral 💊
Site of Action	Blood	Liver
Onset	Rapid (seconds) ⚡	Slow (depends on factor half-lives) ⏳

Duration	Hours	Days
Monitoring	PTT (intrinsic pathway)	PT/INR (extrinsic pathway)
Placenta / Pregnancy	Does NOT cross (safe)	Crosses (teratogenic)
Reversal	Protamine	Vitamin K

💡 Conceptual Understanding

🔄 Flowchart: Why Heparin Works Faster

Heparin given → Directly activates antithrombin → Immediate inhibition of IIa & Xa → Rapid anticoagulation (seconds) ⚡

🔄 Flowchart: Why Warfarin Is Slow

Warfarin given → Inhibits vitamin K recycling → No new clotting factors produced

BUT

Existing clotting factors still present → Must wait for degradation → Delayed onset (days) ⏳

🧠 Key Differences Explained

❓ Site of Action

- Heparin → acts in blood directly
- Warfarin → acts in liver (blocks synthesis)

👉 This explains:

- Fast vs slow onset

2️⃣ Monitoring

- Heparin → PTT
  - Intrinsic pathway (IIa, Xa inhibition)
- Warfarin → PT/INR
  - Extrinsic pathway (Factor VII affected first)

3️⃣ Pregnancy Safety ⚠️

Drug given to pregnant patient

- Heparin → Large, charged molecule → Cannot cross placenta → Safe

- Warfarin → Small molecule → Crosses placenta → Teratogenic

4️⃣ Duration & Clinical Use

- Heparin → Short duration → Used for acute/emergency anticoagulation

- Warfarin → Long duration → Used for chronic therapy

🎯 Exam Pearls

- Heparin = hospital, acute, IV
- Warfarin = outpatient, long-term, oral
- Heparin safe in pregnancy; warfarin NOT
- Heparin = PTT, Warfarin = PT/INR
- Always bridge with heparin when starting warfarin

-> The End <-