💊 Antiplatelets and Thrombolytics

🩸 Antiplatelet Drugs

🔑 Key Concept

- All antiplatelets work by ↓ platelet aggregation ❗
- Target different steps in platelet activation pathways

💡 Big Picture: Platelet Activation

Platelet aggregation requires:

- TXA_2 (via COX)
- ADP (P2Y12 receptor)
- GpIIb/IIIa receptor (final common pathway)

🔄 Flowchart: Platelet Aggregation Pathway

Platelet activation → COX activation → TXA_2 release → ADP release → P2Y12 receptor activation → ↑ GpIIb/IIIa expression → Fibrinogen binds GpIIb/IIIa → Platelet cross-linking → Aggregation 🩸

🎯 Drug Targets

- Aspirin → blocks TXA_2
- Clopidogrel → blocks ADP receptor
- Abciximab-type drugs → block GpIIb/IIIa

📊 Master Table

Class	Drugs	Mechanism	Clinical Use	Adverse Effects

COX inhibitor	Aspirin	↓ TXA_2	ACS, stroke prevention	GI ulcers
P2Y12 inhibitors	Clopidogrel, Prasugrel, Ticagrelor	↓ ADP signaling	Dual therapy	Bleeding
GpIIb/IIIa inhibitors	Eptifibatide, Tirofiban	Block fibrinogen binding	PCI, unstable angina	Bleeding
PDE inhibitors	Dipyridamole, Cilostazol	↑ cAMP	Claudication, stroke	Headache

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🧪 Drug-by-Drug Notes

1️⃣ Aspirin

💡 Mechanism

- Irreversibly inhibits COX enzyme → ↓ thromboxane A_2 (TXA_2) → ↓ platelet activation → ↓ platelet aggregation

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📌 Clinical Uses

- Acute coronary syndrome (ACS) 🎯
- Coronary stenting
- Stroke prevention

❗ Adverse Effects

- Gastric ulcers 🍽️
- Tinnitus 🎧
- Renal injury
- Reye syndrome (children) 🚫

🎯 Exam Pearls

- Effect is irreversible (platelet lifespan ~7–10 days)

2️⃣ P2Y12 (ADP) Inhibitors

(Clopidogrel, Prasugrel, Ticagrelor)

💡 Mechanism

- Block P2Y12 (ADP) receptor → ↓ GpIIb/IIIa expression

🔄 Flowchart: ADP Inhibition

ADP binds P2Y12 receptor → ↑ GpIIb/IIIa expression → Platelet aggregation

P2Y12 inhibitor → Blocks receptor → ↓ GpIIb/IIIa → ↓ aggregation

📌 Clinical Uses

- Same as aspirin
- Dual antiplatelet therapy (DAPT) 🎯 → Aspirin + P2Y12 inhibitor

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❗ Adverse Effects

- Bleeding 🩸

🎯 Exam Pearls

- Clopidogrel is a prodrug (CYP activation required)
- Ticagrelor = reversible (others irreversible)

3️⃣ GpIIb/IIIa Inhibitors

(Eptifibatide, Tirofiban)

💡 Mechanism

- Block GpIIb/IIIa receptor → Prevent fibrinogen binding → Final step of aggregation blocked 🚫

🔄 Flowchart: Final Step Block

GpIIb/IIIa receptor → Binds fibrinogen → Platelet cross-linking

GpIIb/IIIa inhibitor → Blocks receptor → No fibrinogen binding → No aggregation

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📌 Clinical Uses

- Unstable angina
- Percutaneous coronary intervention (PCI) 🎯

❗ Adverse Effects

- Bleeding
- Thrombocytopenia

🎯 Exam Pearl

- Most potent antiplatelet effect

4️⃣ PDE Inhibitors

(Dipyridamole, Cilostazol)

💡 Mechanism

- Inhibit phosphodiesterase (PDE) → ↓ cAMP breakdown → ↑ cAMP in platelets → ↓ aggregation

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🔄 Flowchart: PDE Inhibition

PDE normally → Breaks down cAMP

PDE inhibitor → ↑ cAMP → ↓ platelet activation → ↓ aggregation

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📌 Clinical Uses

- Intermittent claudication 🦵
- Stroke prevention
- Coronary stent restenosis prevention

❗ Adverse Effects

- Headache
- Flushing
- Hypotension
- GI upset

🔥 Comparison Table

Step	Drug	Effect
TXA_2 synthesis	Aspirin	↓ platelet activation
ADP receptor	Clopidogrel	↓ GpIIb/IIIa
Final aggregation	Eptifibatide	Blocks fibrinogen
cAMP regulation	Dipyridamole	↓ activation

🎯 Must-Know Points

- Aspirin → irreversible COX inhibition → ↓ TXA_2
- Clopidogrel → blocks ADP receptor → used in DAPT
- GpIIb/IIIa inhibitors → most potent
- Dipyridamole → ↑ cAMP → ↓ aggregation

🧠 Quick Recall

Platelet aggregation → TXA_2 → Aspirin blocks → ADP → Clopidogrel blocks → GpIIb/IIIa → Eptifibatide blocks → cAMP ↓ → Dipyridamole ↑ → Result: ↓ clot formation 🛑

💥 Thrombolytics (Fibrinolytics)

Drugs:

- Alteplase (tPA)
- Reteplase (rPA)
- Tenecteplase (TNK-tPA)

🔑 Key Concept

- Break down existing clots (NOT just prevent formation) ❗
- Activate the fibrinolytic system → dissolve thrombi

💡 Mechanism of Action

- Convert plasminogen to plasmin → Plasmin degrades Fibrin + Thrombin → Leads to clot dissolution 💀

🔄 Flowchart: Thrombolytic Action

Thrombolytic (tPA) → Converts plasminogen to plasmin

Plasmin → Breaks down fibrin → Breaks down thrombin → Clot dissolution

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🧪 Lab Effects

- ↑ PT
- ↑ PTT
- Platelets unchanged ❗

📌 Clinical Uses (TIME-SENSITIVE 🚨)

- Early myocardial infarction (MI) ❤️
- Early ischemic stroke 🧠
- Massive / high-risk pulmonary embolism (PE) 🫁

🔄 Flowchart: When to Use Thrombolytics

Acute thrombotic event → Assess timing

→ Early presentation (within window)

- Give thrombolytic
- Restore blood flow

→ Late presentation

- Avoid (risk > benefit)

🎯 Exam Pearls

- "Time = tissue" ⏱️
- Stroke → strict time window (~4.5 hours)

❗ Adverse Effects

🚨 Bleeding (MOST important)

- Risk of intracranial hemorrhage ⚠️

⛔ Contraindications

- Active bleeding
- History of intracranial hemorrhage 🧠
- Recent surgery
- Bleeding disorders
- Severe hypertension

🔄 Flowchart: Why Bleeding Occurs

tPA given → Plasmin activation → Fibrin breakdown everywhere → Loss of clot stability → Systemic bleeding

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🛡️ Reversal of Thrombolytics

💡 Strategy

- No specific antidote → use procoagulant + antifibrinolytic approach

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📊 Reversal Options

Treatment	Mechanism
Aminocaproic acid	Inhibits plasmin
Tranexamic acid	Inhibits fibrinolysis
Platelets	Replace platelets
Cryoprecipitate	Replaces fibrinogen

FFP / PCC	Replaces clotting factors

🔄 Flowchart: Reversal

Thrombolytic overdose → Excess plasmin activity → Bleeding → Give:

- Antifibrinolytics (TXA, aminocaproic acid)
- Replace clotting components

→ Restore hemostasis 🛡️

🔥 Comparison

Feature	Thrombolytics	Anticoagulants
Action	Break clots	Prevent formation
Timing	Emergency	Acute/chronic

Risk	Severe bleeding	Bleeding
Example	tPA	Heparin, Warfarin

🔑 Must-Know Points

- tPA → plasminogen → plasmin → fibrin breakdown
- Used in early MI, stroke, PE
- ↑ PT, ↑ PTT, platelets normal
- Major risk = bleeding (especially intracranial)
- Contraindicated in recent surgery, bleeding, severe HTN
- Reversal = antifibrinolytics + factor replacement

🧠 Quick Recall

Clot present → Give thrombolytic → ↑ plasmin → ↓ fibrin → Clot dissolves

🚨 Risk: bleeding → Manage with antifibrinolytics

-> The End <-