بتلاقوا هون تفريغ كلام الدكتور،، ان شاء الله انه شامل كل اشي حكاه وركز عليه الدكتور

So, to start off, I really recommend you guys watch the lecture — it'll help you get it better. Let's get started!

بدّي أحكيلك عن دعاء تدعيه قبل الدِّراسة وأنت مزنوق وبتلمّ المادَّة^^

بعد ما تحمد الله -عزَّ وجلّ- وتثني عليه وتصلِّي على سيِّد الخلق ﷺ تقول:
"اللّهمَّ إنّي أسألك فهم النَّبيين وحفظ المرسلين والملائكة المقرَّبين..سبحانك لا علمَ لنا إلَّا ما علَّمتنا إنَّك أنت العليم..اللّهم إنِّي أستودعكَ ما سأقرأ وأحفظ وما تقع عيني عليه، فردَّه إليّ وقت حاجتي إليه."

بعدين بلّش دراسة..

وقبل ما تفتح ورقه الاسئلة في الامتحان قول:
"اللّهمَّ ردَّ لي ما استودعتك إيَّاه يا خيرَ الحافظين، اللّهمَّ لا سهلَ إلَّا ما جعلته سهلاً، وإنّك تجعل الصَّعب إذا شئت سهلاً"

« Lec 1 »

- Introduction and Basic Concepts of Hemostasis and Coagulation

- **Core physiological concepts:**
  - Hemostasis is a balance between coagulation and anticoagulation factors in the body.
  - There are natural anticoagulants such as **Antithrombin III**, **Protein C**, and **Protein S** that counterbalance coagulation factors.
  - Disorders occur when this balance shifts—either thrombosis (excess clotting) or hemorrhage (excess bleeding).
- **Thrombosis relevance:**
  - Conditions like **myocardial infarction (MI)**, **stroke**, **deep vein thrombosis (DVT)**, and **peripheral artery disease (PAD)** are common and linked to coagulation abnormalities.
  - Risk factors prevalent in Jordan include smoking (8 out of 10), hypertension, diabetes, and emerging issues like substance abuse (e.g., Captagon).
- **Pharmacological focus:**
  - Lec 1 ◦ Antiplatelets prevent platelet aggregation (clumping), mainly as prophylactic agents to stop clot formation or enlargement. (this Lec)
  - Lec 2 ◦ Anticoagulants dissolve clots or inhibit clot formation by targeting coagulation pathways.
  - Lec 3 ◦ Thrombolytic agents actively dissolve clots but carry high risk and require expert administration.

* لح نتعلم ادوية بتستهدف كل Pathway منظم :

الدكتور شرح هون بداية شوية Physiology مهمة للفهم :

- Platelet Activation and Aggregation Mechanisms

- **Endothelial cells** line blood vessels and normally inhibit platelet adhesion using substances like **nitric oxide (NO)** and **prostacyclin**.
- **Atherosclerosis** damages the endothelium, exposing **collagen** and von Willebrand factor (**vWF**), which promote platelet adhesion and aggregation.
- Platelets bind to collagen via vWF and platelet receptors (**glycoproteins IIb/IIIa**, **glycoprotein Ib**), triggering platelet activation and aggregation.
- Released platelet granules contain factors such as **thromboxane A2 (TXA2)**and **adenosine diphosphate (ADP)**, which act in an **autocrine** fashion to amplify aggregation.
- **ADP binds to P2Y12 receptors** on platelets, further enhancing aggregation and receptor expression, facilitating cross-linking by fibrinogen.

Pharmacological Targets and Mechanisms of Antiplatelet Drugs

- **Four main pharmacological targets to inhibit platelet aggregation:**
  1. **Inhibition of thromboxane A2 synthesis** (e.g., **aspirin**) by irreversibly inhibiting **cyclooxygenase (COX-1)**.
  1. **Blocking ADP receptors (P2Y12)** (e.g., clopidogrel, ticlopidine, prasugrel).
  1. **Inhibition of glycoprotein IIb/IIIa receptors** to prevent fibrinogen binding and cross-linking (not deeply covered here).
  1. **Phosphodiesterase inhibitors** (e.g., dipyridamole), which increase cyclic AMP levels to reduce intracellular calcium and inhibit platelet activation.

1. Antiplatelts

Drug name	MOA	Indications	Adverse effects	Route of adminstration
Aspirin 1	Irreversibly inhibits COX-1, preventing TXA2 production, thus reducing platelet aggregation.	Widely used as a prophylactic agent in cardiovascular diseases (MI, stroke, stents).	* Gastrointestinal irritation due to reduced protective prostaglandins in the stomach mucosa, increasing risk of ulcers and bleeding. * Contraindicated in children under 19 with viral infections due to risk of **Reye's syndrome** and in asthmatics due to bronchospasm risk.	Orally (daily dose of 100 mg).
Cangrelor Ticagrelor NOT prodrugs	ADP receptors blockers but with ↓↓ Short half-life ∴ used in emergency (Rapid Platelt ↓)		Ticagrelor: bleeding and shortness of breath (dyspnoea) •Reversible P2Y12 inhibitor	Ticagrelor(Orally) Cangrelor (IV)
Clopidogrel Ticlopidine Prasugrel Prodrugs ? Clopidogrel and prasugrel are **prodrugs** requiring activation in the liver by **CYP2C19 enzyme**. Genetic polymorphisms in CYP2C19 affect drug activation and efficacy.	**P2Y12 ADP receptor blockers**, preventing ADP-induced platelet aggregation.	* Dual antiplatelet therapy (aspirin + clopidogrel/prasugrel) is standard in patients with MI, stroke, or stent placement to prevent thrombosis. * Dose adjustments are required based on metabolic status (normal, intermediate, (poor metabolizers: receive alternative drugs))	• **Ticlopidine** is associated with serious side effects like **thrombotic thrombocytopenic purpura (TTP)**, making it less favourable clinically. • Clopidogrel and prasugrel have fewer side effects, with prasugrel generally considered more potent but more expensive, high bleeding risk	Orally - Ticlopidine: 250 mg BID orally. -Clopidogrel: oral loading dose 300 mg, maintenance dose 75 mg once daily.
Abciximab Eptifibatide Tirofiban	AlII inhibit bridging of platelet by fibrinogen [Glycoprotein IIb/IIIa inhibitors]	- percutaneous coronary intervention (PCTA) & inACSs. ?	high bleeding Risk ! ----------	Parenterally
Dipyridamole cilostazol		- with aspirin for prophylaxis in angina. - with warfarin to inhibit embolization from prosthetic heart valves.		----------

MoA
- Inhibits phosphodiesterase → ↑ cAMP → ↓Ca++ → potentiates effects of prostacyclin → platelet inhibition.
- Dipyridamole is also a coronary vasodilator

- Cilostazol is used in **intermittent claudication** (leg muscle pain due to poor blood flow), improving perfusion by vasodilation and antiplatelet effects

- **NSAIDs like ibuprofen and diclofenac** do not irreversibly inhibit COX and thus lack the same antiplatelet effect as aspirin.
- Aspirin is often given as a **"baby aspirin" low dose** daily for prophylaxis in high-risk patients, especially in Jordan due to high prevalence of hypertension, smoking, and diabetes.

- **Mechanism of side effect TTP:**
- Ticlopidine inhibits **ADAMTS13 protease**, which normally cleaves vWF multimers.
- Inhibition causes accumulation of large vWF multimers, leading to excessive platelet aggregation in small vessels, thrombocytopenia, and purpura (blue skin lesions).

• الفكرة هون انه المريض كل ما أخذ اكتر من هاد الدواء
كل ما زادت احتمالية يسكر vesicles اكبر
• طيب كيف يعبر Platelets ؟
ال Platelets بتصير تتجمع بال tissue فيتقل بالدم !

- **Patient preparation for stenting:**
  - Loading dose of clopidogrel (e.g., 300 mg or 600 mg) is given at least 2 hours before the procedure to achieve steady-state platelet inhibition.
- **Monitoring platelet activity:**
  - Laboratory tests such as **platelet aggregation assays** (e.g., VerifyNow P2Y12 test) measure platelet inhibition to ensure therapeutic effect before interventions.

عادةً ما منعملة بالاردن

ملخص سريع

Key Insights and Conclusions

- **Antiplatelet drugs primarily prevent platelet aggregation through several mechanisms:**
  - Aspirin inhibits thromboxane A2 synthesis irreversibly.
  - P2Y12 receptor blockers (clopidogrel, prasugrel, ticagrelor) inhibit ADP-mediated platelet activation.
  - Glycoprotein IIb/IIIa inhibitors prevent fibrinogen binding and platelet cross-linking.
  - Phosphodiesterase inhibitors increase cAMP to reduce platelet activation.
- **Pharmacogenetics profoundly affects the efficacy and safety of antiplatelet drugs, especially clopidogrel, necessitating dose adjustment or alternative agents.**
- **Dual antiplatelet therapy (aspirin + P2Y12 blocker) is standard in the management of MI, stroke, and patients undergoing stenting.**
- **Side effects and contraindications must be carefully considered:**
  - Aspirin contraindicated in asthma, children with viral infections, and in patients prone to GI bleeding.
  - Ticlopidine rarely used due to risk of TTP.
  - Prasugrel and ticagrelor have cardiovascular side effects and higher bleeding risk.
- **Emergency use drugs like cangrelor provide rapid platelet inhibition but are expensive and reserved for critical cases.**
- **Phosphodiesterase inhibitors like cilostazol offer benefits in peripheral arterial disease but have limited availability locally.**