Artery Academy

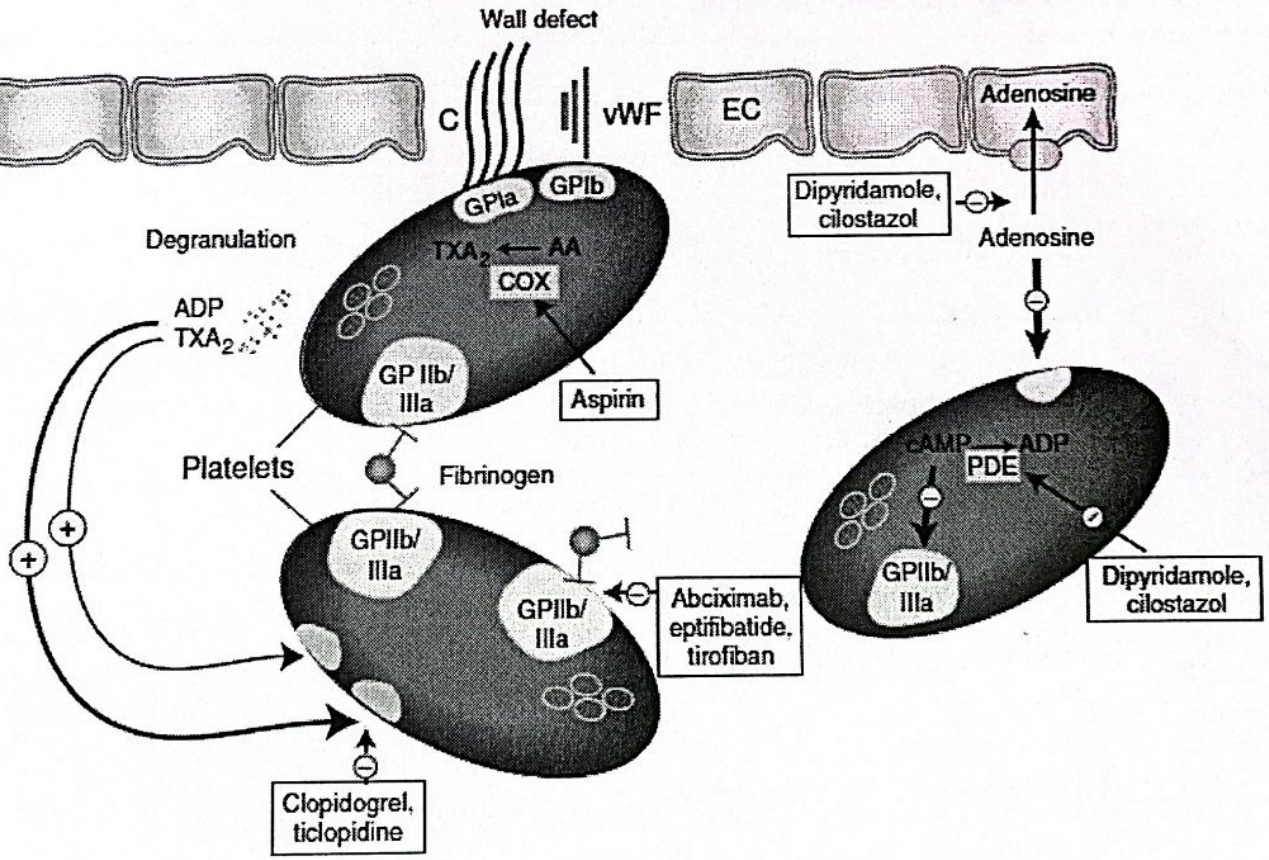
Done by Hawazen

رب اشرح لي صدري ويسر لي أمري واحلل عقدة من لساني يفقه قولي .. بسم الله

Antiplatelet Drugs

- Antiplatelet drugs include:
  1. **Aspirin** (also known as acetylsalicylic acid; ASA)
  2. Glycoprotein IIb/IIIa receptor inhibitors (**abciximab, tirofiban,** and **eptifibatide**),
  3. Antagonists of ADP receptors (**clopidogrel and ticlopidine**)
  4. **Dipyridamole** and **cilostazol.**

Antiplatelet Drugs



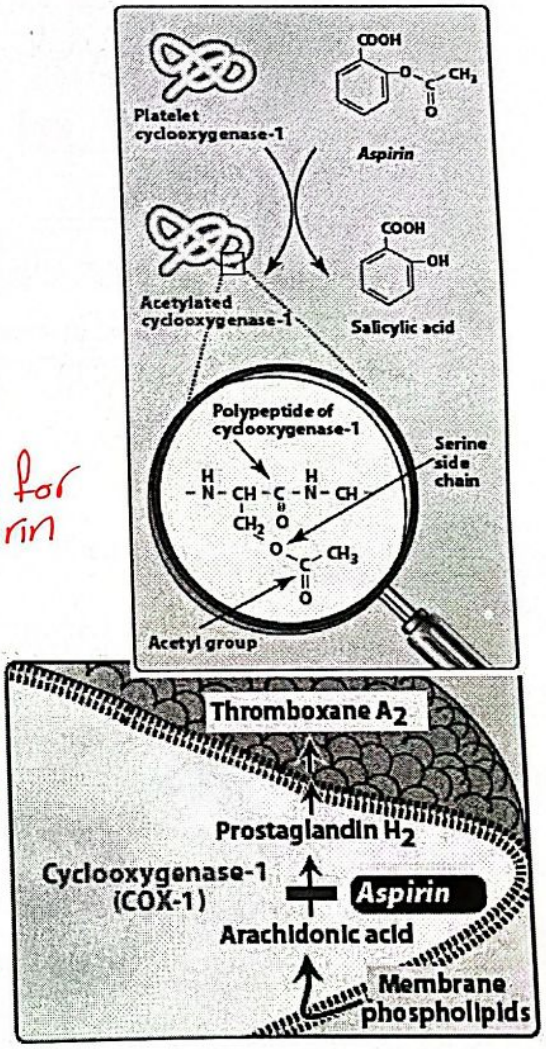
هذا الدواء الوحيد من بين كل الأدوية المذكورة يتغير الـ action على الـ platelet ويختلف باقي المجموعة عن تأثيرهم لأن الـ nonsteroidal بس الـ anti-inflammaory و pain

Aspirin

- Aspirin is part of a group of medications called nonsteroidal anti-inflammatory drugs (NSAIDs), but differs from other NSAIDs in the mechanism of action. Aspirin (but not the other NSAIDs) inhibits COX-1 in an irreversible manner.
- The **thromboxane A_2** is an arachidonate product that causes platelets to change shape, release their granules, and aggregate.
- Aspirin inhibits thromboxane A_2 synthesis from arachidonic acid in platelets by irreversible acetylation of a serine in COX-1, preventing arachidonate from binding to the active site, thus, inhibition of COX-1.

أعتبره الوحيد من المجموعة اللي يشتغل as antiplatelet

another function for Aspirin



يقوم الـ Aspirin بعمل تثبيط للـ COX-1 بالتالي توقف عندي إنتاج الـ Thromboxa A_2 (وهو مسؤول عن تغير الشكل الخاص بالـ platelet)

(شرح مبسّط للسلايد بالشابه) date / /

الـ Aspirin يعتبر مثبّط للـ COX-1 (Cyclooxygenase-1).

بتحوّل عندي الـ Arachidonic acid إلى prostaglandin H_2 من ثمّ إلى $Thromboxane A_2$

بفعل الـ COX-1 عام لهون؟

لحتى الـ Aspirin يقل تثبيط للـ COX-1 بسؤول عن كلّ هاي القمص فيقل عندي مستوى الـ $thromboxane A_2$ (معروف عنه إنه مسؤول عن ① شكل الـ platelet وتغيره)

② إفراز الـ granules

③ Aggregate

نستخدم ال aspirin primary prevention و كان Socound prevention شو الفرق بينهم؟

Aspirin

الاستخدامات الرئيسية له :-

- Aspirin is currently used in the prophylactic treatment to prevent heart attacks, strokes (brain attack), and blood clot formation in people at high risk of developing blood clots.
- Complete inactivation of platelets occurs with 160 mg of aspirin given daily. The recommended dose of aspirin ranges from 50 to 325 mg, with side effects determining the dose chosen.
- Formerly known as "baby aspirin," 81-mg aspirin is most commonly used.
- Bleeding time is prolonged by aspirin treatment, causing complications that include an increased incidence of hemorrhagic stroke as well as GI bleeding, especially at higher doses of the drug.
- Aspirin is frequently used in combination with other drugs having anticlotting properties, such as heparin or clopidogrel.

المشاكل يلي عمل يعملها الاسبرين :-

أدوية تستخدم مع ال Aspirin

① البرايمري يكون عند المريض ما صار له قبل heart attack لكن معرض إنه يصيرله بسبب عوامل معينة مثل الوراثة مثلا فهون نستخدم ال Aspirin كـ primary prevention

② السكندري هو إنه المريض صار عنده قبل heart Attack بس بدي أمنع second attack بالتالي نستخدم ال Aspirin كـ Scoundes prevention

Aspirin

أيضا هناك أنواع أخرى من ال NSAIDs بجانب ال aspirin :-

- NSAIDs, such as ibuprofen, inhibit COX-1 by transiently competing at the catalytic site. Ibuprofen, if taken concomitantly with, or 2 hours prior to aspirin can obstruct the access of aspirin to the serine residue and, thereby, antagonize the platelet inhibition by aspirin.
- Therefore, aspirin should be taken at least 30 minutes before ibuprofen or at least 8 hours after ibuprofen.
- Aspirin as other NSAIDs has antipyretic, anti-inflammatory and analgesic action, but it is the only NSAID that irreversibly exhibits antithrombotic action.

بس ما يعتبر Antipletel وهينا بس ال Aspirin

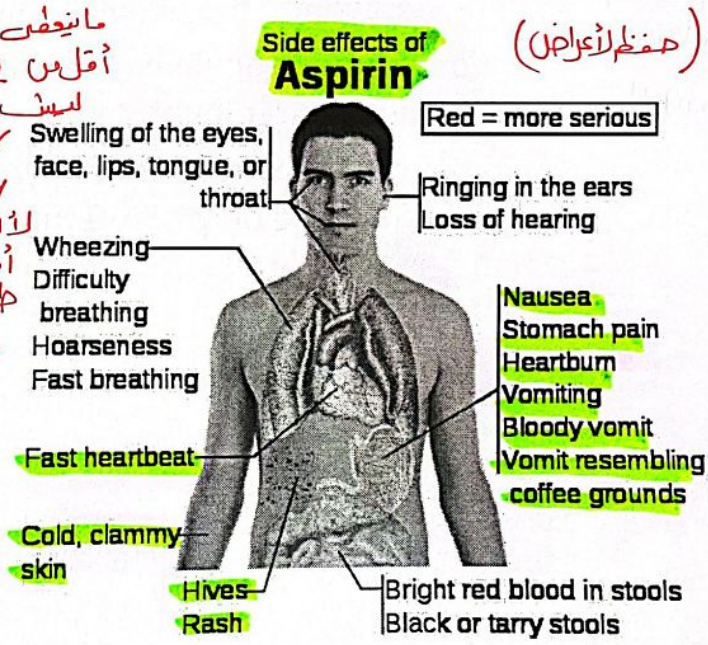
ال Ibupofen يعيقه عن ال Aspirin كيف نحل هاي المشكلة؟

من خلال إنه نعطي قبل بنص ساعة Aspirin بعدين ال Ibupofen أو ناخذ ال Ibuprofen وبعد 8 ساعات ناخذ ال Aspirin

Aspirin

Adverse effects:

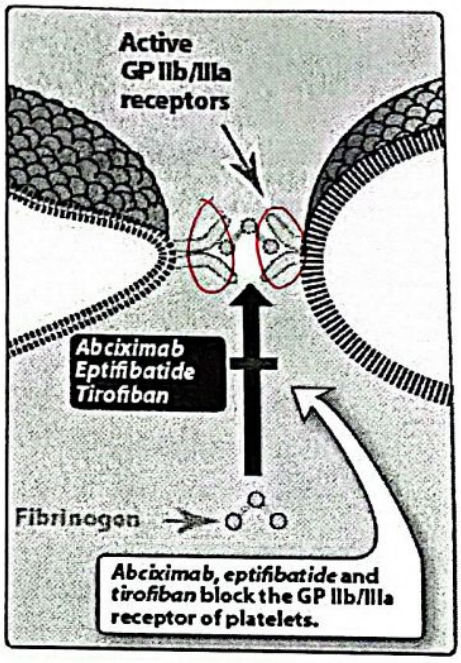
- Gastrointestinal ulcers, stomach bleeding, and tinnitus, especially in higher doses.
- In children and adolescents, aspirin is no longer indicated to control flu-like symptoms or the symptoms of chickenpox or other viral illnesses, because of the risk of Reye's syndrome.



Glycoprotein IIb/IIIa Receptor Inhibitors

حل أدويتي إلهم نفس الـ Action

- **Abciximab** is a monoclonal antibody that reversibly inhibits the binding of fibrin and other ligands to the platelet glycoprotein IIb/IIIa receptor, a cell surface protein involved in platelet cross-linking.
- **Eptifibatide** and **tirofiban** also reversibly block the glycoprotein IIb/IIIa receptor.



عندي بالصورة موضح receptor في حالة الـ rest يكونوا inactive form لأن بالكلسيوم عندي متوقف

في حالة التهاب إلهم active راح يتشكل عندي cross linking بين الـ receptor إلموجودين بالصورة فراح يقربوا لـ platelet من بعض ويعملوا clote

⇐ بالتالي هاي الأدوية بتقلل تثبيط من إنه يرتبط هدول الـ receptor ببعض.

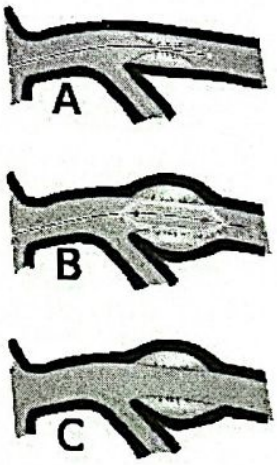
وهيك الصورة عزيزي الصيدلاني ؟ ^^

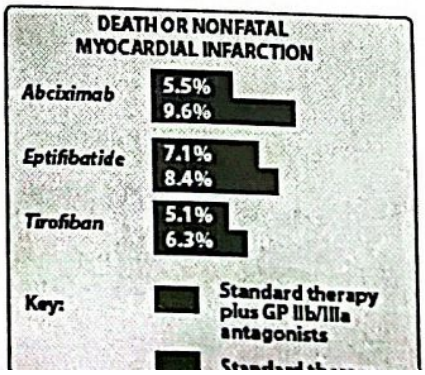
Glycoprotein IIb/IIIa Receptor Inhibitors

- **Abciximab** is given intravenously along with either heparin or aspirin as an adjunct to percutaneous coronary intervention (angioplasty) for the prevention of cardiac ischemic complications. It is also approved for unresponsive unstable angina and for prophylactic use in myocardial infarction.
- Eptifibatide and tirofiban, like abciximab, can decrease the incidence of thrombotic complications associated with acute coronary syndromes.

بنعطى

غالباً هاي الأدوية تنعطى للأشخاص إلي بدهم يعملوا قسطرة القلب.





أعتمدوا الخين !

ADP Receptor Antagonists

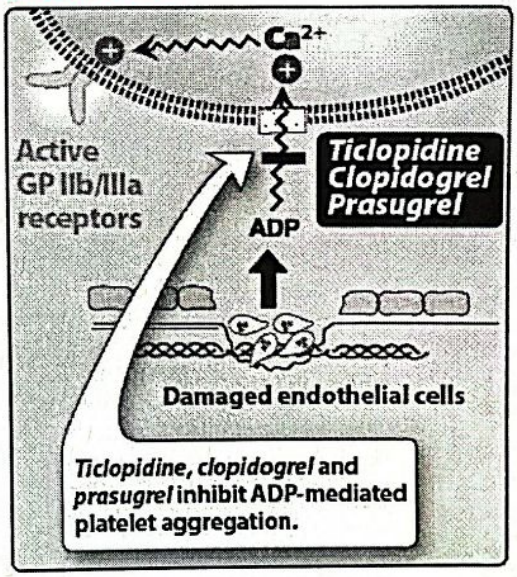
- **Clopidogrel**, **prasugrel**, and the older drug **ticlopidine** are converted in the liver to active metabolites that irreversibly inhibit the platelet ADP receptor and thereby prevent ADP-mediated platelet aggregation.
- Use of ticlopidine, clopidogrel, or prasugrel to prevent thrombosis is now considered standard practice in patients undergoing placement of a coronary stent.

هاي الأدوية يصيرلها activation بالكبد (Liver)

وهما ينعطوا pro-drug والـ active metabolite

platelet aggregation هي يلي تنع

لـ أي مريض عليه قسطرة يعطوه أحد هذه الأدوية. وينعطوا لتسع أشهر - سنة.



ADP Receptor Antagonists

- Due to **ticlopidine**'s life-threatening hematologic adverse reactions, including neutropenia/agranulocytosis, thrombotic thrombocytopenic purpura (TTP), and aplastic anemia, ticlopidine is generally reserved for patients who are intolerant to other therapies.
- Therapy with ticlopidine require frequent blood monitoring, especially during the first 3 months of treatment.
- Compared to ticlopidine, **clopidogrel** is the preferred agent in ischemic heart disease events, because there is more data to support use of clopidogrel in these cardiac patients. Furthermore, clopidogrel has a better overall side-effect profile, although TTP may also occur with this agent.
- **Prasugrel** is the newest ADP receptor antagonist. In clinical trials, prasugrel was more effective than clopidogrel in reducing cardiovascular death, nonfatal heart attack, and nonfatal stroke.

ADP Receptor Antagonists

Pharmacokinetics:

- Food interferes with the absorption of ticlopidine, but not with clopidogrel or prasugrel.
- After oral ingestion, all three of these drugs are extensively bound to plasma proteins.
- They undergo hepatic metabolism by the cytochrome P450 (CYP450) system to active metabolites.
- "Poor metabolizers" and clopidogrel:
- Genetic polymorphism of CYP450 2C19, that primarily biotransforms clopidogrel, leads to less active metabolite, variable pharmacokinetic properties and reduced clinical response in patients who are poor metabolizers.
- Tests are currently available to identify poor metabolizers, and it is recommended that other antiplatelets or different strategies be used.

Dipyrimadol and Cilostazol

شو بعملوا هدول الأدوية؟

- Dipyridamole and the newer cilostazol appear to have a dual mechanism of action:
  - They prolong the platelet-inhibiting action of intracellular cAMP by inhibiting phosphodiesterase enzymes that degrade cyclic nucleotides, including cAMP, an inhibitor of platelet aggregation, and cyclic guanosine monophosphate (cGMP), a vasodilator. (1)
  - They also inhibit the uptake of adenosine by endothelial cells and erythrocytes and thereby increase the plasma concentration of adenosine. Adenosine acts through platelet adenosine A2 receptors to increase platelet cAMP and inhibit aggregation. (2)

① يصير عندي إنه هاي الأدوية تعمل inhibiting لـ phosphodiesterase enzyems تعمل على degrade cyclic nucleotides

② يصير عندي بسبب هاي الأدوية inhibit the uptake of adenosine بواسطة Endothelial cells ويزيد Adenosine ↑ plasma concentration

Dipyrimadol and Cilostazol

- Dipyridamole is approved as an adjunct to warfarin in the prevention of thrombosis in those with cardiac valve replacement and has been used in combination with aspirin for secondary prevention of ischemic stroke.
- Cilostazol is used to treat intermittent claudication, a manifestation of peripheral arterial disease.
- The most common adverse effects of dipyridamole and cilostazol are headaches and GI problems.

لهمه عظمنا كل الأدوية يلي تعالج الـ Clotting وهو يلي يمنع جريان الدم، هما العكس

Drugs Used in Bleeding Disorders

الأسباب الرئيسية عندي للـ inadequate Clotting

- Inadequate blood clotting can result from:
  - vitamin K deficiency ← نقص فايتمين K
  - genetically determined errors of clotting factor synthesis (eg, hemophilia) ← الدم دايمًا بيكون فايت
  - a variety of drug-induced conditions → بيكون المريض ياخذ أدوية تحفز عندهم الـ bleeding
  - thrombocytopenia
- Treatment involves administration of:
  1. vitamin K
  2. preformed clotting factors → في الحالات الطارئة (في الطوارئ)
  3. Fibrinolytic inhibitors

العلاج للحالات السابقة في

- Thrombocytopenia can be treated by administration of platelets or oprelvekin, the recombinant form of the megakaryocyte growth factor interleukin-11

Vitamin K

ابتداءً بالخمائن

- Deficiency of vitamin K, a fat-soluble vitamin, is most common in older persons with abnormalities of fat absorption and in newborns, who are at risk of vitamin K deficiency bleeding. لم يكون لديهم fat عندهم قليل بالتالي الفايتمين قليل
- The deficiency is readily treated with oral or parenteral **phytonadione (vitamin K1).** نقص الفايتمين K علاجه
- Large doses of vitamin K1 are used to reverse the anticoagulant effect of excess warfarin.
- The response to vitamin K is slow, requiring about 24 hours (time to synthesize new coagulation factors). Thus, if immediate hemostasis is required, fresh-frozen plasma should be infused.

يحتاج مدة طويلة تصل إلى 24 ساعة بالتالي عكس مفعه fresh-frozen plasma لأنه تحتوي على clotting factor فنحل المشكلة بسرعة وقت.

Clotting Factors

- The most important agents used to treat hemophilia are fresh plasma and purified human blood clotting factors, especially **factor VIII (for hemophilia A)** and **factor IX (for hemophilia B)**, which are either purified from blood products or produced by recombinant DNA technology.
- These products are expensive and carry a risk of immunologic reactions.

- Hemophilia is a group of hereditary genetic disorders that impair the body's ability to control coagulation. Haemophilia A (clotting factor VIII deficiency) is the most common form of the disorder. Haemophilia B (factor IX deficiency).

Fibrinolytic Inhibitors

- Antiplasmin agents are valuable for the prevention or management of acute bleeding episodes in patients with hemophilia and others with a high risk of bleeding disorders.
- **Aminocaproic acid** and **tranexamic acid** are orally active agents that inhibit fibrinolysis by inhibiting plasminogen activation.
- Adverse effects include thrombosis, hypotension, myopathy, and diarrhea.

عن طريق الفم

ادعولي .. وربكم بالمثل ☺