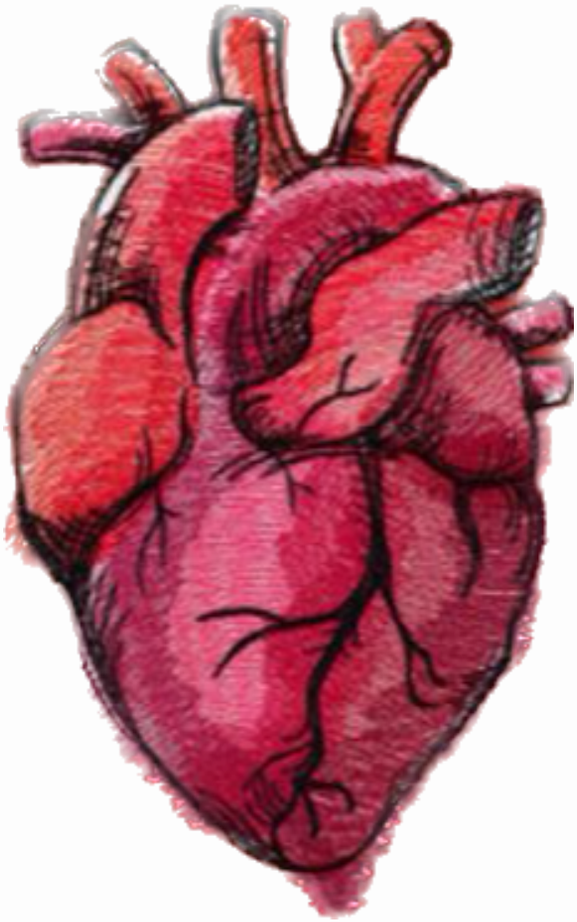
النادي الطبي

CARDIOVASCULAR SYSTEM



SUBJECT : _____

LEC NO. : 4

DONE BY : Raneem&Tabark

وَقُل رَّبِّ زِدْنِي عِلْمًا

Angina

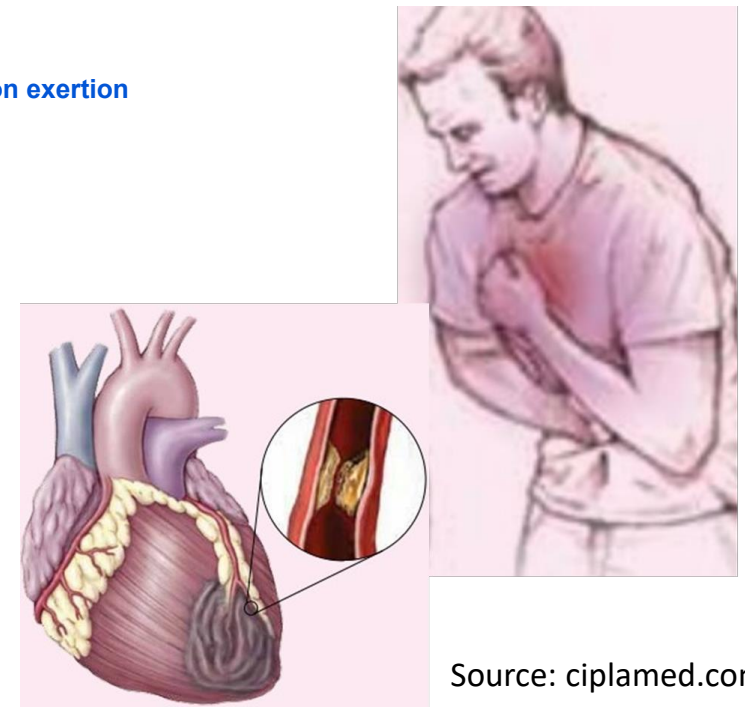
*الاعراض الي بيجي فيها المريض :

طبيعة الوجع بتختلف من مريض لتاني

Chest pain or discomfort occurs when some part of the heart muscle **does not get enough blood supply**. Specially on exertion

بسبب ال

Patients may describe it as an **intense pressure or a squeezing pain** in their chest. The pain may **radiate to the shoulders, arms, neck, jaw, or back.**



Source: ciplamed.com

Angina

Risk Factors:

•Elevated LDL-cholesterol, age, cigarette smoking; high blood pressure, sedentary lifestyle, obesity, type 2 diabetes.

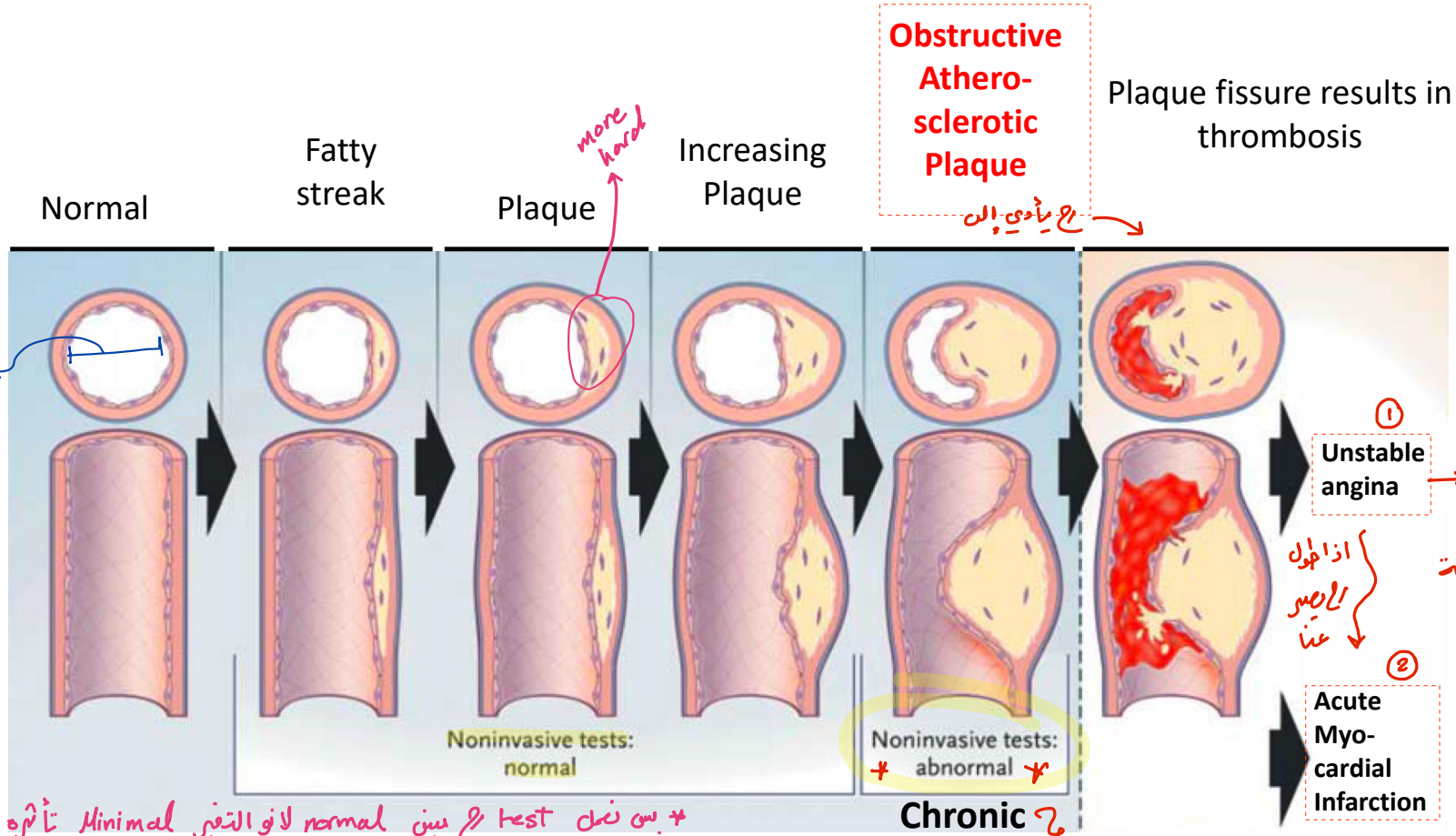
Occurrence:

•About 6 million Americans suffer from chronic angina

•About 400,000 new cases are reported each year

Very common in America and Jordan

Progression of Coronary Atherosclerosis



Modified From: N Engl J Med (2005) 352:24

Types of Angina

Chronic stable angina, also called 'angina of effort' and 'exertional angina', is the most common form and is a result of coronary artery disease.

→ more obstructive

Unstable angina is caused by the rupture of an atherosclerotic plaque. Chest pain is felt in the absence of exertion due to blockage of a coronary artery.

لانو ال **treatments** الو مختلف عن الباقي+مهم نعرف تشخيصه ،لانو بدي اعالجه عن طريق ال **VD** مش اني بدي اشيل **plaque** لانها مش موجودة إصلا ← مهم نعرفوا !!

Coronary Artery Spasm (aka Variant angina; aka Prinzmetal's Angina) is caused by contraction of smooth muscles in the wall of a coronary artery that leads to narrowing of the vessel and obstruction of blood flow. This is a **rare condition**.

Spontaneous Coronary Artery Dissection (SCAD) occurs when a tear or rupture forms in one of the coronary arteries, slowing or blocking blood flow to the heart. This is a **rare condition**.

ال **wall of coronary artery** بصير إلها **separated layer** من ال **wall** فـ يصير الدم يتجمع فيها **between the wall**

بيصل هنا

Major Determinants of Myocardial Oxyger Consumption

شو الشغلات الي بتخلي الo_2 الي بوصل للخلايا مش كافي

ليه منحكي باثو ،وهون بدنا نحكي شوية فسيو ،،،عشان نفهم ال treatment لكل نوع لانهم رح يشتغلو على هذول النقاط

بحكيلي عن طريق اعرف كم بدي O_2 ← 6+3 $^{2+1}$

1. Doubling **heart rate** approximately doubles O_2 consumption; زيادة ال demand لأسباب فسيولوجية او مرضية

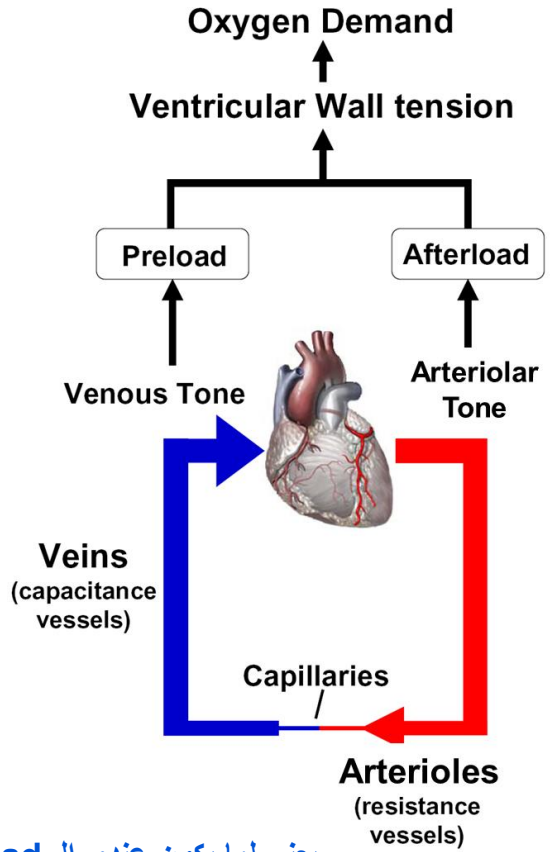
2. Increasing **contractility** increases O_2 consumption.

3. Increasing **afterload**, due to the increase in tension development (ventricle must work harder to eject blood).

لانو بس يكون عندي ال afterload عالي اذا بدي more contraction حتى يصير عنا ejections

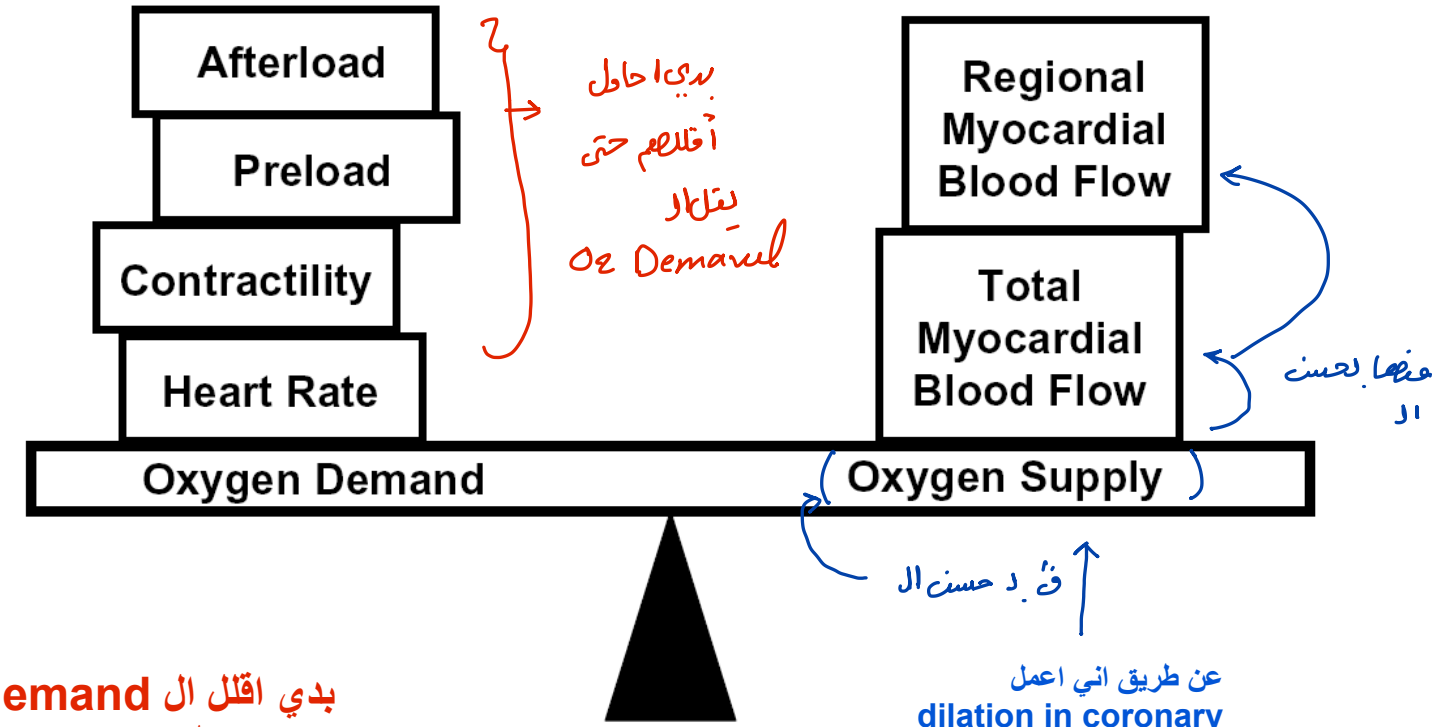
4. Increasing **preload** (ventricular end-diastolic volume), because the ventricle is forced to contract against a larger volume, resulting in increased ventricular wall tension.

يعني لما يكون عندي ال preload فلل ف الventricular فل بالدم ف الwallعليه tension كثير عالي ف رح احتاج قوة عالية حتى اعمل pump



In a Healthy Heart, Oxygen Supply is in Balance with Oxygen Demand

**هون منحكي عن تأثير الدوا كيف يكون



بدي احاول أقللهم حتى يقلل O2 Demand

منها بحسن ال

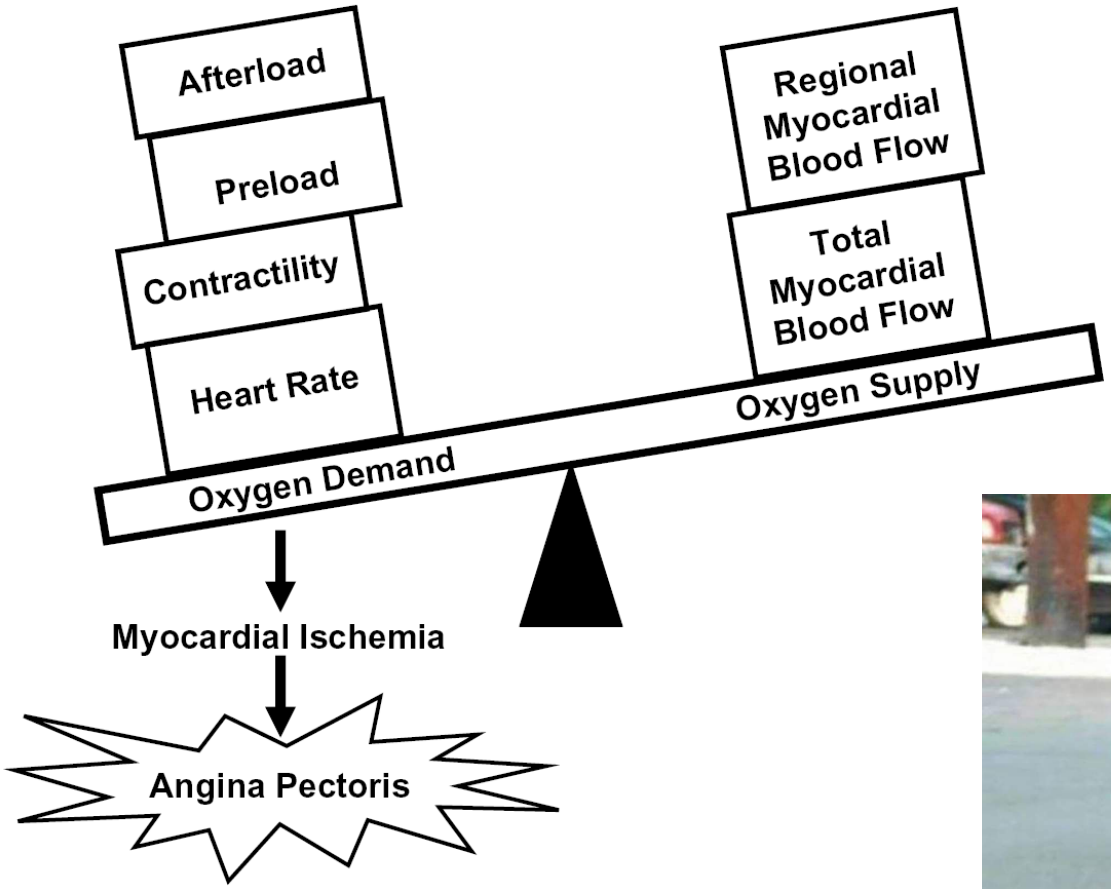
ف بـ د حسن ال

عن طريق اني اعمل dilation in coronary artery

بدي اقلل ال oxygen demand
واحسن ال oxygen supply

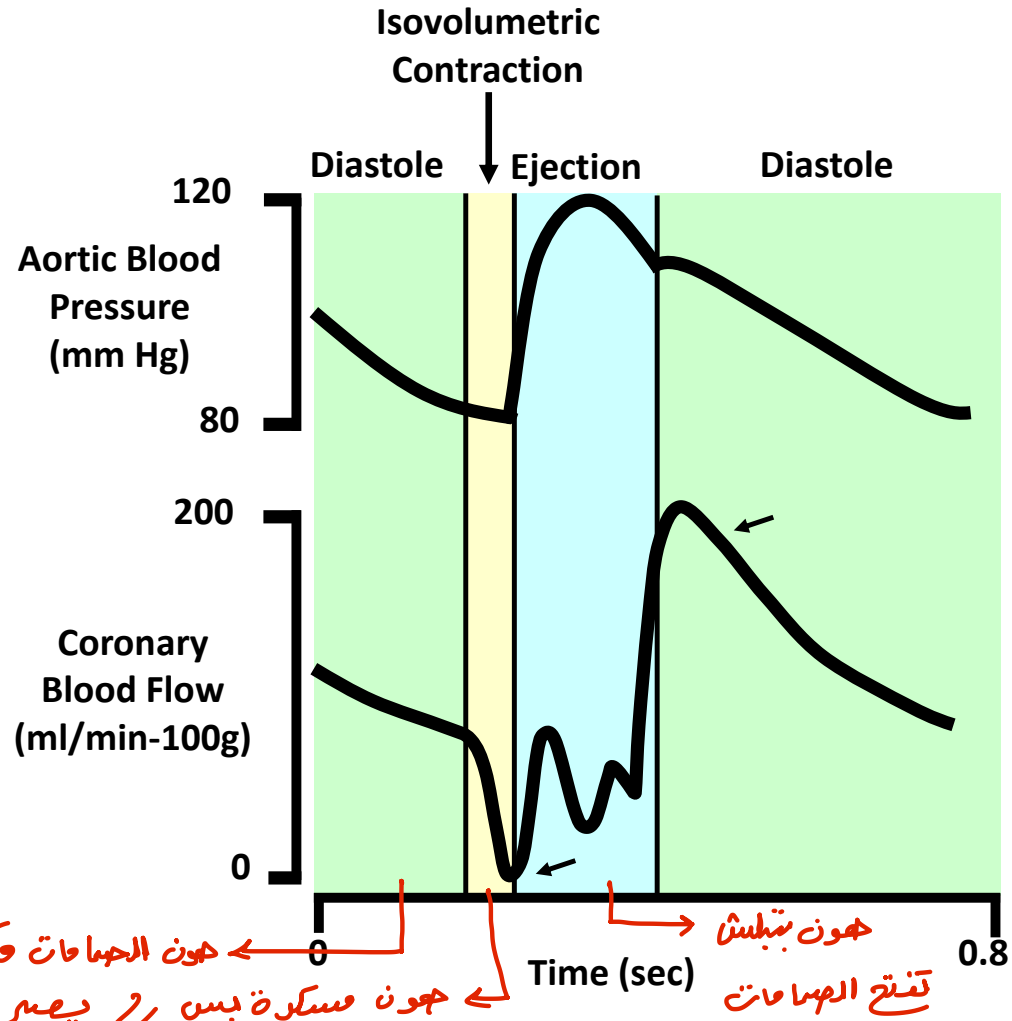
قراده

Angina Results From an Imbalance Between Oxygen Supply and Demand

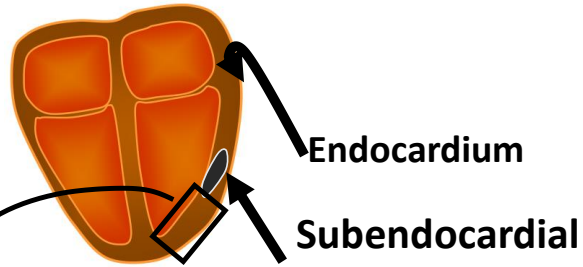


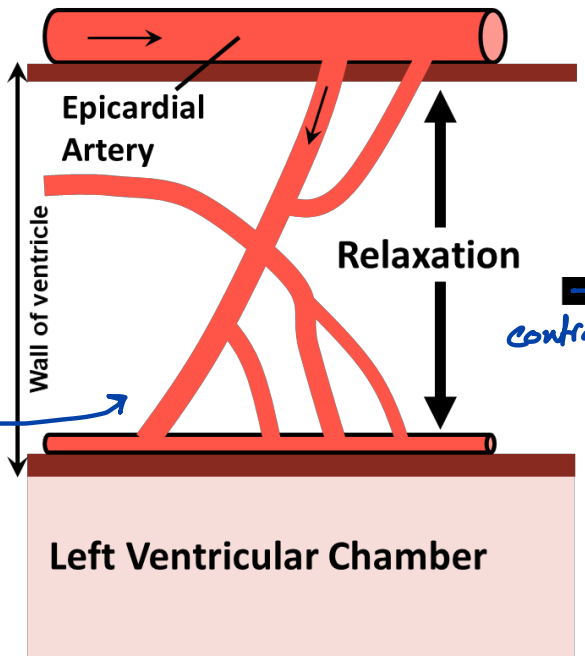
Coronary Blood Flow

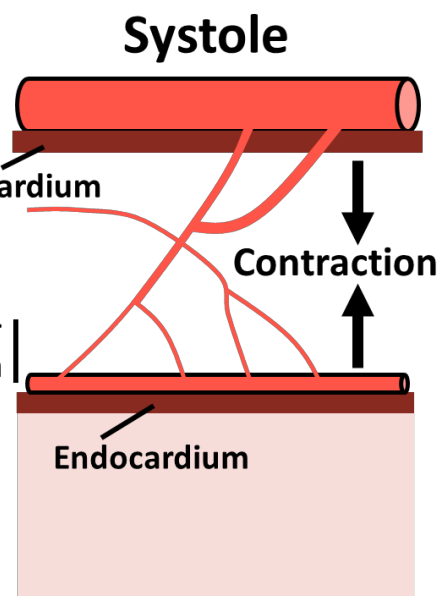
بفرق عن ال systemic circulation



Coronary Blood Flow







branch حصون ال
عاطلة ريلاكس

main blood مشان هيك ال
supply رح يصير في مرحلة
early diastolic ال

بعدين
بصير contract

ف تخيت الدم
الواصل ع
تقل

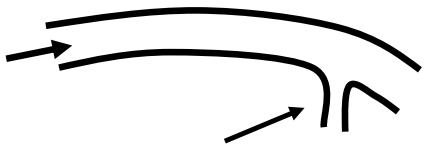
Coronary Flow Reserve

عنا endogenous factors بتسمح لهاي ال coronary artery
انها تعمل dilation لما يصير عنا exertion ،لانو احنا عنا more
demand،،فهون الجسم بسستم حالو وبفرز ماتيريال من ال
endogenous molecules تسمح بالتوسع

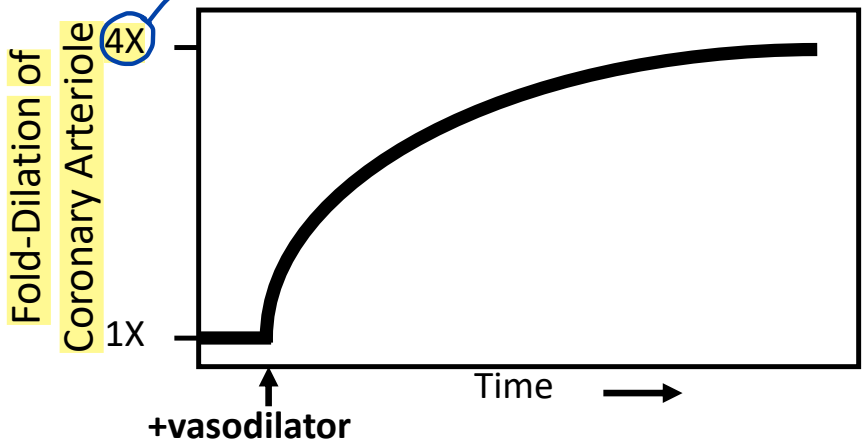
bloodsupply / O2 حميلح بحسن ال

safety Margin

Normal Epicardial Artery



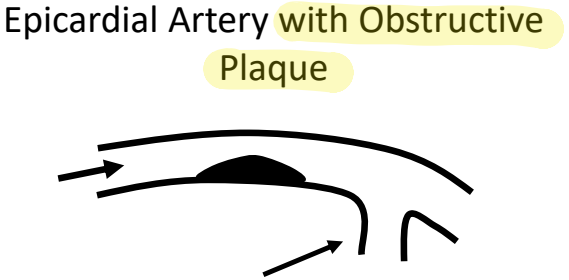
Arteriole can dilate upon exertion, or if a vasodilator is administered.

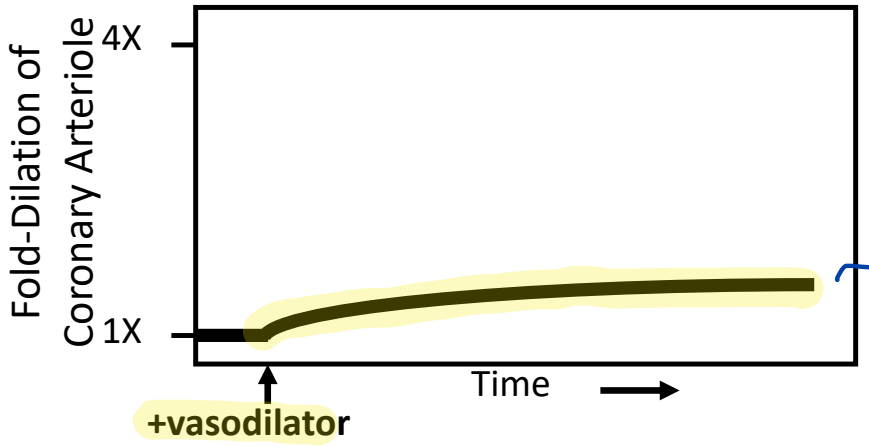


Coronary flow reserve relates to the ability of the coronary arterioles to dilate and **increase blood supply to the heart.** Coronary flow can be thought of as a **'safety margin'.**

* الحالة فوق كانت لرجال، جاب في حالة التسكير؟؟

Coronary Flow Reserve





dilation يصل لأقصى ما يقدر حتى قبل الـ exertion

أما بعد الـ exertion يدوب يزيد شوي

* Arteriole in **ischemic region is maximally dilated** and is unable to dilate further upon exertion, or when a vasodilator is administered.

* With obstructive plaque, the coronary arterioles in the ischemic region are fully dilated even at rest in order to supply sufficient blood to the heart muscle. This means there is very little safety margin if oxygen demand increases (as with exercise).

Lines of Treatment

1. General measures: علاج الاعراض المصاحبة angina للـ

- **Manage comorbidities** such as hypertension (diuretics), dyslipidemia (statins), thrombosis, and type 2 diabetes. → best control لازم نعمل
- **Associated conditions** as anemia, valvular heart disease should be corrected .

2. **Antianginal** drugs.

الجراحة قسطرة

3. Other measures: **PCA** (Percutaneous coronary angioplasty), **Grafting** (Aorto-coronary bypass grafting), **Aspirin 75 mg daily indefinitely**

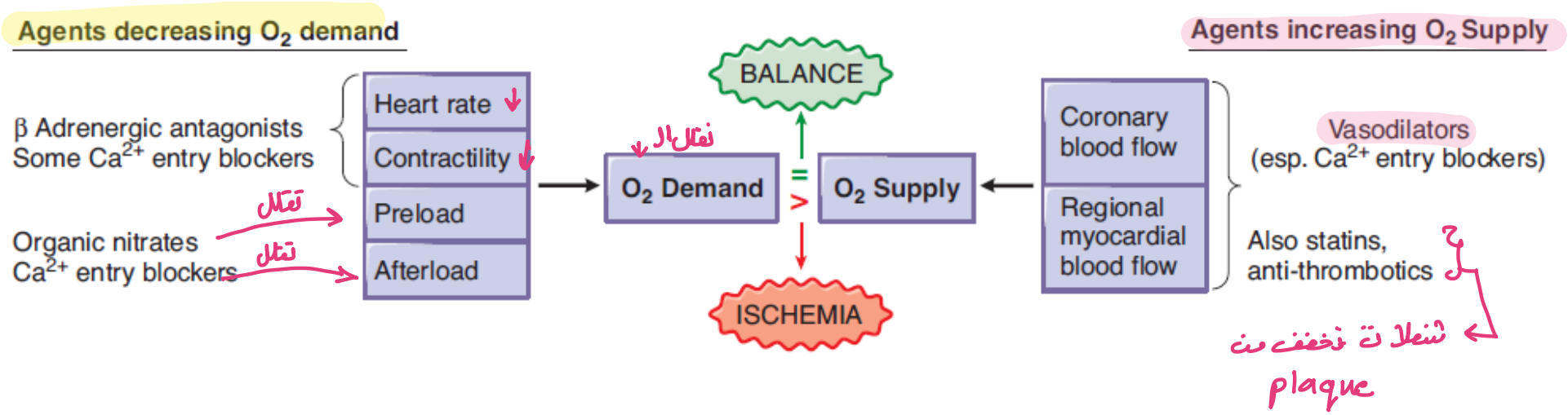
baby dose

Drugs for Chronic Stable Angina

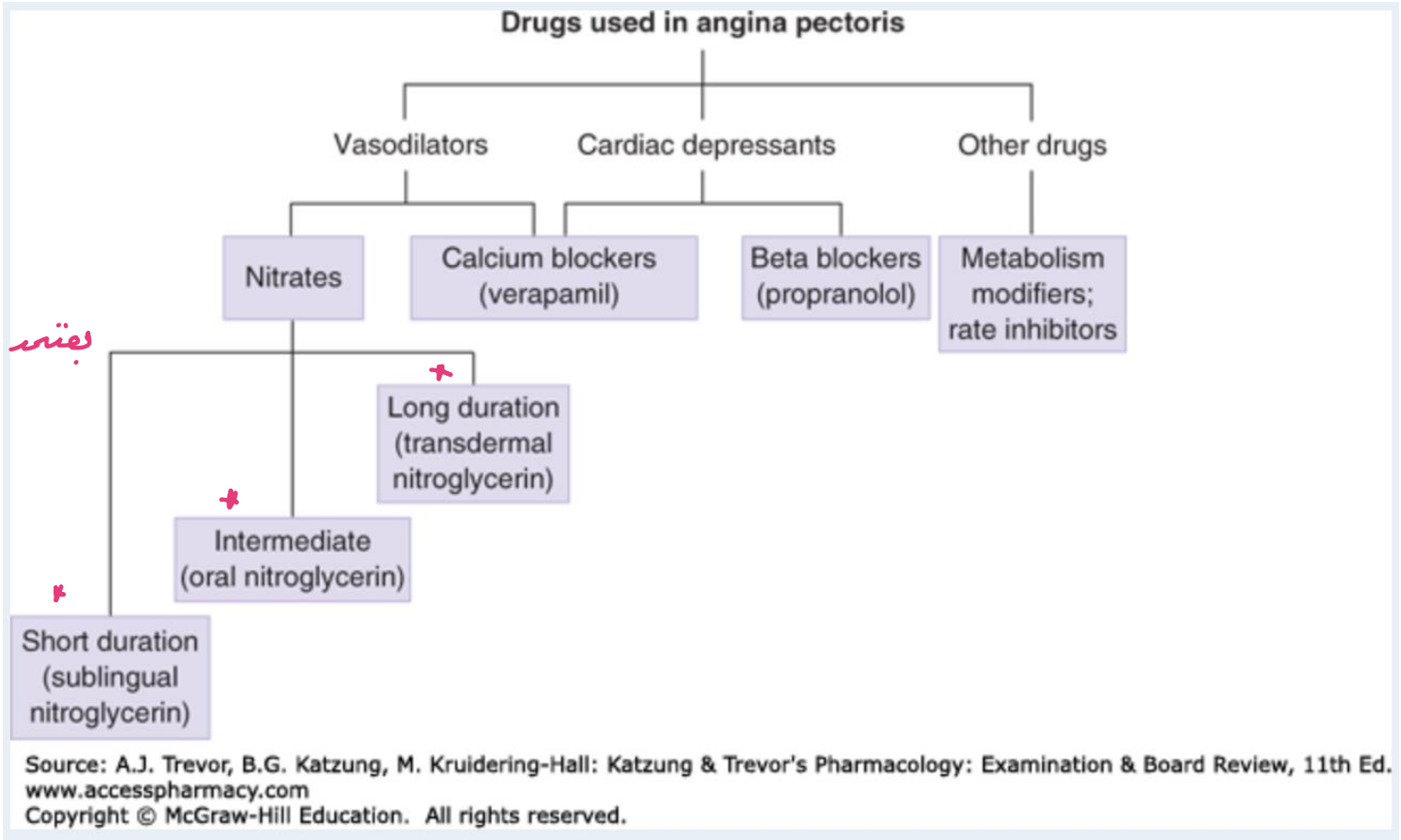
علاج ال Angina
هو الحالة زي القسطرة

Antianginal drugs are used **to relieve the symptoms of pain/discomfort associated** with cardiac ischemia by restoring the balance between oxygen supply and demand.

1. **Beta-Blockers**
2. **Calcium Channel Blockers (CCBs)**
3. **Organic nitrates**
4. **Newer antianginal drugs**: Ranolazine


Agents decreasing O_2 demand
β Adrenergic antagonists
Some Ca^{2+} entry blockers
Heart rate
Contractility
Organic nitrates
Ca^{2+} entry blockers
Preload
Afterload
BALANCE
O_2 Demand
=
>
O_2 Supply
ISCHEMIA
Agents increasing O_2 Supply
Coronary blood flow
Regional myocardial blood flow
Vasodilators
(esp. Ca^{2+} entry blockers)
Also statins, anti-thrombotics

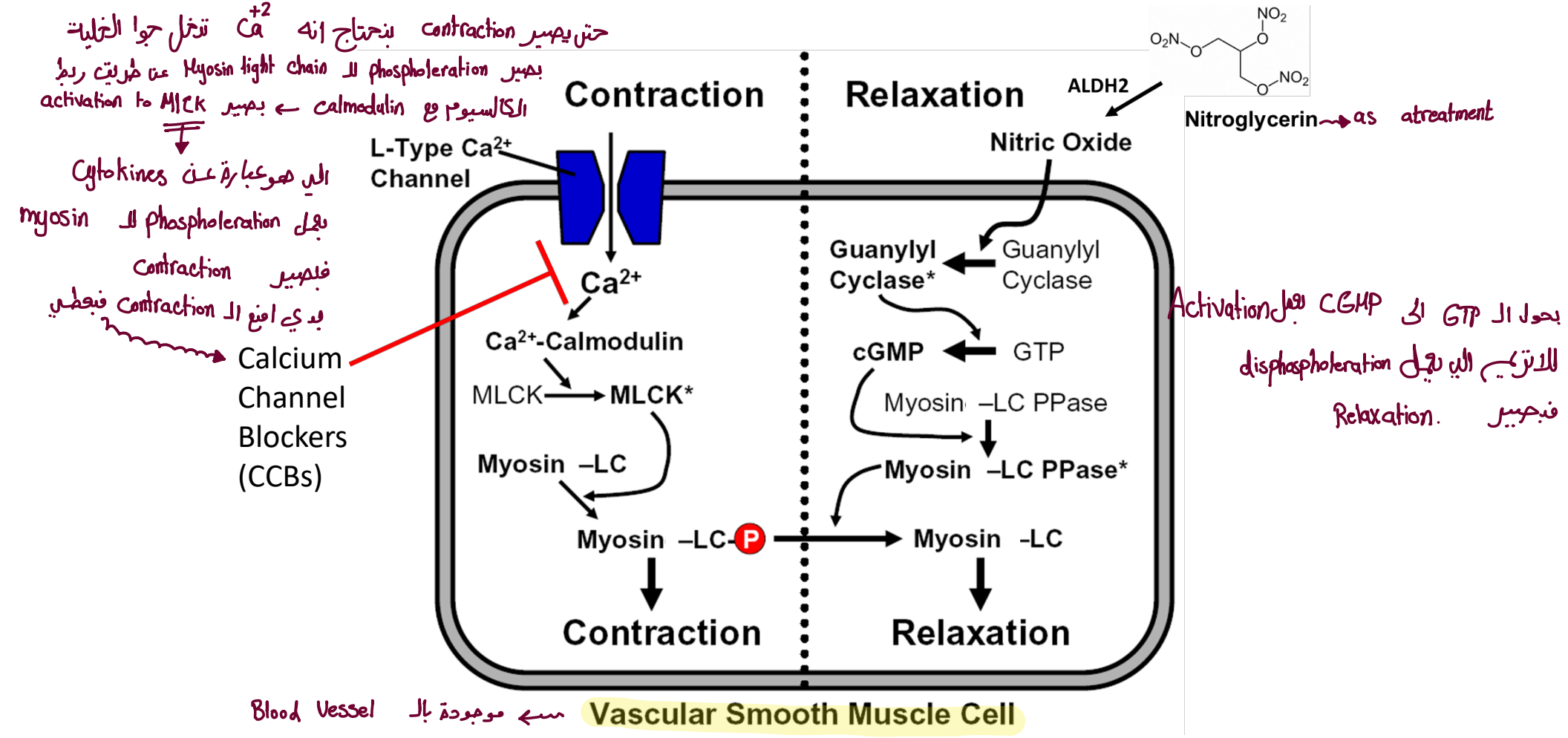
Drugs for Chronic Stable Angina



يعتمد وعلى المريض

Source: A.J. Trevor, B.G. Katzung, M. Kruidering-Hall: Katzung & Trevor's Pharmacology: Examination & Board Review, 11th Ed.
www.accesspharmacy.com

Drugs for Chronic Stable Angina



Calcium Channel Blockers (CCBs)

Nitroglycerin → as atreatment

Beta-Blockers

β-receptore → 2 Type → cardio selective
→ non cardio selective

Beta-Blockers

- **β_1- receptors** are located mainly in the **heart**. While **β_2-receptors** are located mostly in **lung** and blood vessel cells, though heart cells also have some.
- The prototypical drug in the group is **Propranolol,** a non-selective beta-blocker (may cause bronchospasm due to block of β_2 receptors)
- All β -blockers are nonselective at high doses and can inhibit β2 receptors
- Propranolol has been largely replaced by cardioselective Beta-blockers, such as **atenolol**, **metoprolol.**

Beta-Blockers

- Beta-blockers are also used in the management of **heart failure, hypertension, and cardiac arrhythmias**

- Beta-blockers competitively **inhibit the action of norepinephrine and epinephrine**.

Beta-Blockers

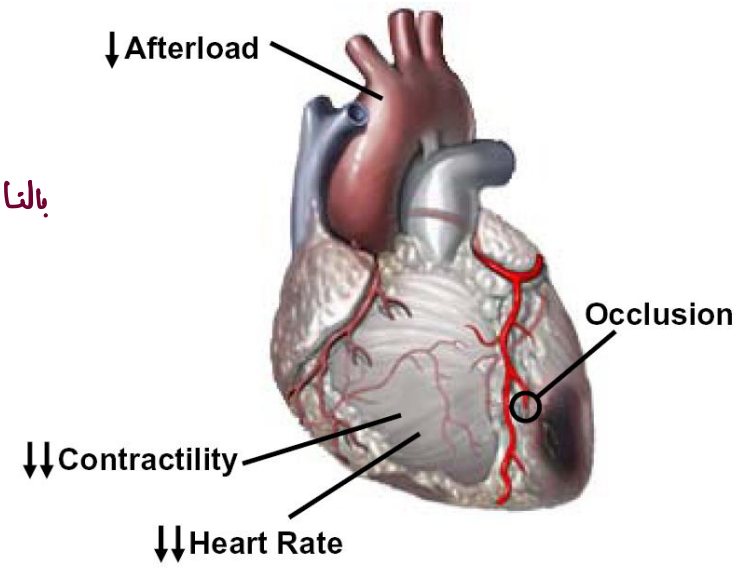
* مريض عنده Sever Angina (لدرجة مايقدر يمشي) فلما اعطيه الـ β-Blocker بخفف الاعراض وبصير يقدر يعمل الـ minor exercise (daily activity) اما لو كان Athletic (رياضي) ما بنفع لأنو بس اعطيه β-Blocker ببطل قادر يعمل الـ exercise

تأثيرها على القلب

تأثيرها على الـ blood Vessel ← بتمنع الـ contraction فبصير Vasodilation

- β1 blocker decreases the heart rate and contractility. Overall, **the workload on the heart is reduced, which also reduces oxygen consumption.** → بالتالي حسنت (خففت) الـ Symptom of Angina

- β_1 blockers decrease the release of renin by the kidneys, which reduces circulating Angiotensin II levels and **reduces afterload** (overall Beta blockers have very little effect on preload).



Beta-Blockers

- β -Blockers can **reduce both the frequency and severity of angina attacks.**
- β -Blockers can be **used to increase exercise duration and tolerance in patients with effort-induced angina.**
- β -Blockers are recommended as **initial antianginal therapy** in all patients unless contraindicated. usually first choice
- β -Blockers reduce the **risk of death and MI in patients who have had a prior MI and also improve mortality in patients with heart failure with reduced ejection fraction.**

بتقلل arrythmia ← من ال

Beta-Blockers

adrenlgic

- β -Blockers should be avoided in patients **with severe bradycardia**.

- β -Blockers can be used in patients with diabetes, peripheral vascular disease, and chronic obstructive pulmonary disease, as long as they are monitored closely.

- When a non-selective beta-blocker is used, **bronchoconstriction can occur**. Therefore, non-selective beta-blockers are contraindicated in patients with asthma or chronic obstructive pulmonary disease.

Side Effects of Beta-Blockers

- The common side effects of beta-blockers are extensions of their mechanisms of action and **include bradycardia, reduced exercise capacity, hypotension, and atrioventicular (AV) nodal conduction block.**

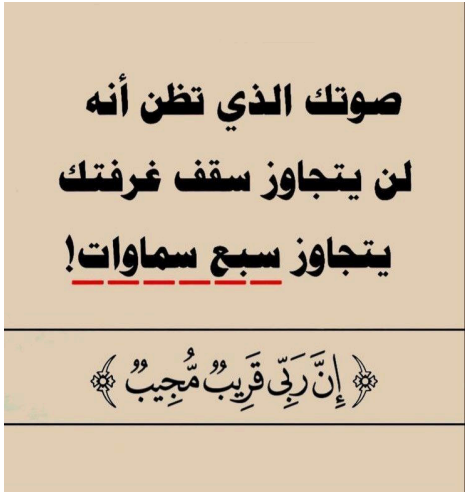
Afterload ↓
cardiac output ↓

حكينا عنها قبل
انه بيطل يقدر يعمل
التمارين اللي متعود عليها

- It is important not to discontinue β -Blocker's therapy abruptly. The dose should be gradually tapered off over 2 to 3 weeks to avoid rebound angina, Ml, and hypertension **due to upregulation of receptors.**

receptor الـ فجأة رح يكون فاذا وقفت الدوا upregulation receptor يعمل الجسم بيلش B-blocker احنا لما نعطي
B- agonist اكثر من الطبيعي بالتالي بصير زي كأني اعطيت

Calcium Channel Blockers



Calcium Channel Blockers (CCBs)

بشتغلوا على الـ Smooth muscle اللي بال blood vessel و heart

- Block the voltage gated L-type calcium channel primarily in **arteriolar smooth muscle cells and cardiac tissue.**

- CCBs fall into two broad classes (chemical structure) , the **dihydropyridines** and the **non-dihydropyridines.**

- **Amlodipine**, **Nifedipine**, **Verapamil**, **Diltiazem.**

Calcium Channel Blockers (CCBs)

calcium blocker الـ ف بس اعطي Calcium influx Angina معناها بزيد الـ اذا حد عنده calcium الي زاد بقلل الـ

- Calcium is essential for muscular contraction. **Calcium influx is increased in ischemia because of the membrane depolarization that hypoxia produces.** In turn, this promotes the activity of several ATP-consuming enzymes, thereby **depleting energy stores and worsening the ischemia.**
- The calcium channel blockers protect the tissue by inhibiting the entrance of calcium into cardiac and smooth muscle cells of the coronary and systemic arterial beds. All calcium channel blockers are, therefore, arteriolar

2→ Vasodilation و↓ Contraction in heart

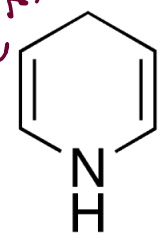
- All calcium channel blockers lower blood pressure.

The dihydropyridines (CCBs)

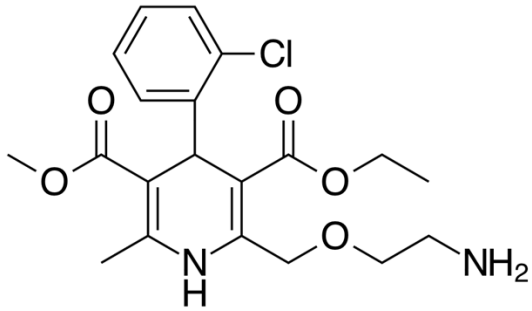
Are more selective for vascular L-type calcium channels **primarily in arterioles.**

Amlodipine, **Nifedipine.**

شغلهم على القلب قليل بالاكتر شغلهم arterioles يكون على ال



Dihydropyridine ring



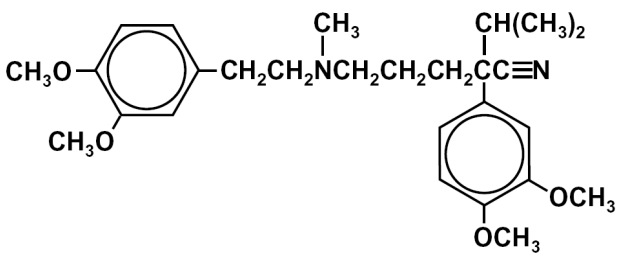
Amlodipine

Non-dihydropyridines Calcium Channel Blockers (CCBs)

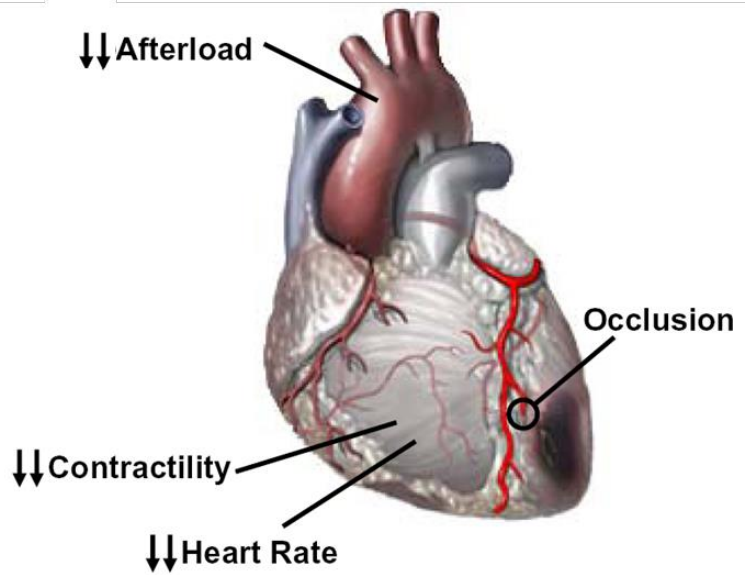
- Relax vascular smooth muscle (causing vasodilation) which decrease the afterload.
- Decrease myocardial contractility.
- Decrease heart rate.
- **Verapamil, Diltiazem.**

اكثر واحد بشتغل على القلب

intermediat effect



Verapamil



Non-dihydropyridines Calcium Channel Blockers (CCBs)

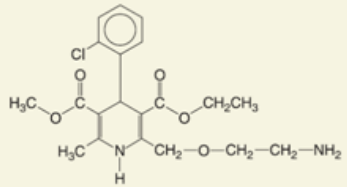
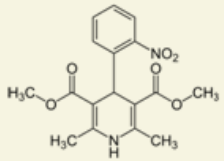
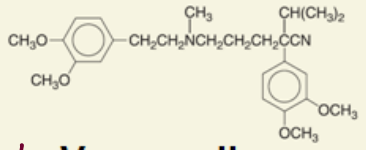
- *Verapamil* is contraindicated in patients **with preexisting depressed cardiac function or AV conduction abnormalities**.
- *Diltiazem* also slows AV conduction, decreases the rate of firing of the sinus node pacemaker, and is also a coronary artery vasodilator.

- Non-dihydropyridine calcium channel blockers **can worsen heart failure** due to their negative inotropic effect, and their use should be avoided in this population.

Summary

Table 27–2

Ca^{2+} Channel Blockers: Chemical Structures and Some Relative Cardiovascular Effects[a]

CHEMICAL STRUCTURE Generic name (trade name)	VASODILATION (ARTERIOLE FLOW)	SUPPRESSION OF CARDIAC CONTRACTILITY	SUPPRESSION OF AUTOMATICITY (SA NODE)	SUPPRESSION OF CONDUCTION (AV NODE)
 **Amlodipine**	5 التأثير كبير	1 التأثير قليل	1	0 no effect
 **Nifedipine**	5	1	1	0
 **Verapamil** (Non)	4	4	5	5

[a]Relative effects are ranked from *no effect* (0) to *prominent* (5). NR, not ranked. (Modified from Julian, 1987; Taira, 1987.)

heart failure ما يجمعهم لمرضى ال

Diltiazem is intermediate in its actions

Indications of Calcium Channel Blockers in Angina

- **Alternative** to **beta-blockers** in presence of **contraindications** to them.
- **With beta-blockers in resistant angina using nifedipine**
- **Prinzmetal's angina due to acute coronary spasm**

↳ الـ main mechanism انه بتعمل
بتقلل blocker الـ اعطيت فاذا spasm
Vasodilation ← contration الـ

هو مطلوب التفاصيل

Calcium channel blocker induced gum hypertrophy: no class distinction

A 49 year Afro-Caribbean man, with a 10 year history of resistant hypertension, was referred for further management on the following medications: amlodipine 20 mg, atenolol 200 mg, and enalapril 60 mg daily. Other treatments comprised: two-weekly modecate injections, procyclidine, and nocturnal temazepam 10 mg for stable schizophrenia. He had acquired a degree of renal impairment (creatinine clearance of 64 ml/min) as a result of his hypertension, but was not actively requiring dialysis. Pronounced gum hypertrophy with bleeding was a key initial clinical finding (below left). Withdrawal of the dihydropyridine calcium channel blocker resulted in slow regression of the gum hypertrophy. The blood pressure continued to be poorly controlled despite the use of six different antihypertensive drug classes (β blocker, α blocker, angiotensin II receptor blocker, potassium sparing diuretic as well as a loop diuretic, and a centrally acting agent). A non-dihydropyridine calcium channel blocker (diltiazem XL 240 mg daily) was therefore prescribed to try to improve the blood pressure. Unfortunately the gum features worsened again over a period of three months. They resolved several months after calcium channel blocker withdrawal (below right).

Gum hypertrophy is a well recognised side effect of dihydropyridine calcium channel blockers, with few reports following non-dihydropyridine calcium channel blockers. This case illustrates that it may occur with both major classes of calcium channel blockers and resolve following their cessation.

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A Cox
M D Feher
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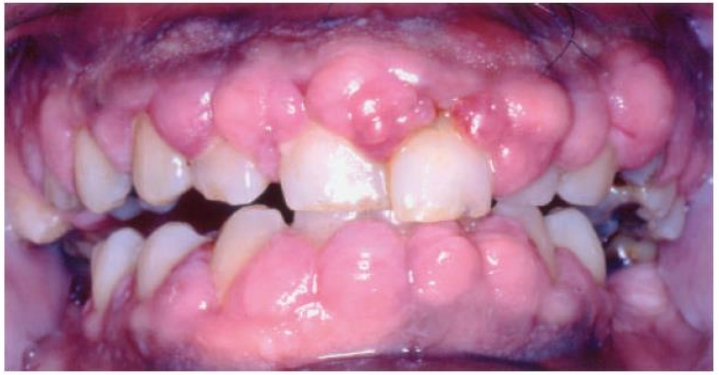
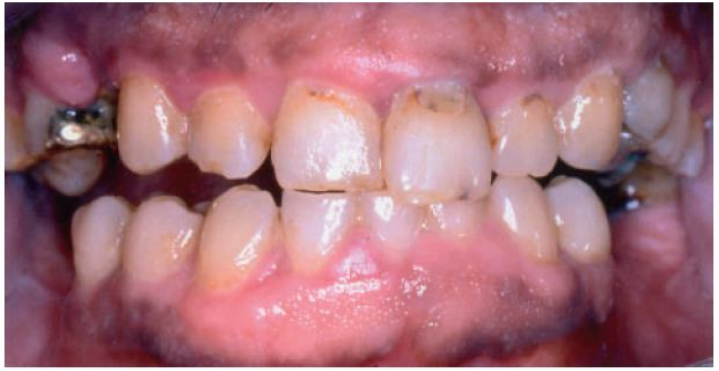
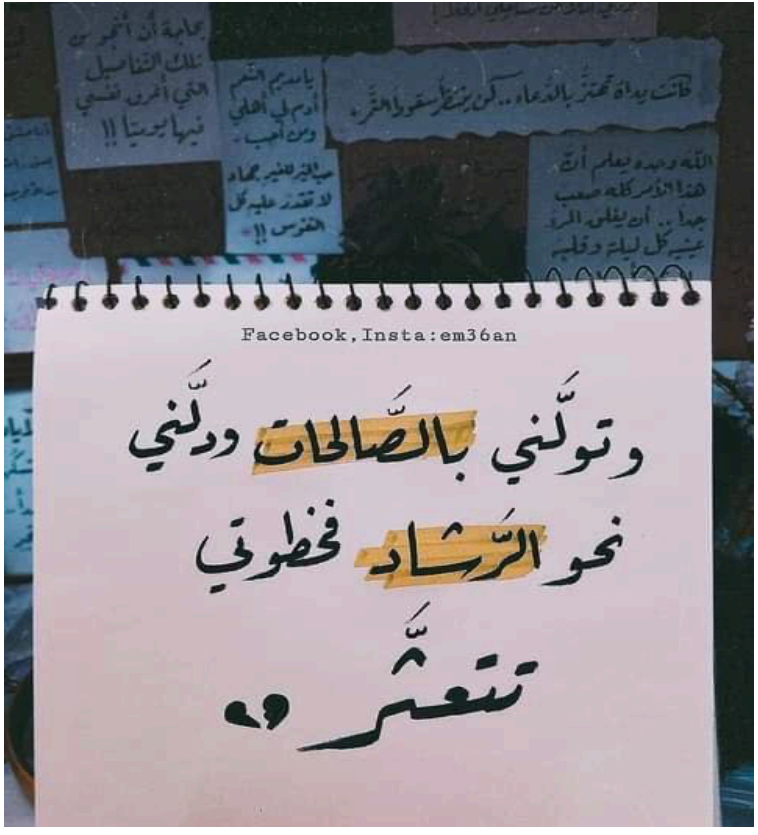


With CCB



After withdrawal of CCB

Heart 2004 90: 16
doi: 10.1136/heart.90.1.16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نحو الرّشاد فخطوتي
تتعثّر ،،