Drug Treatment of Ischemic Heart Disease

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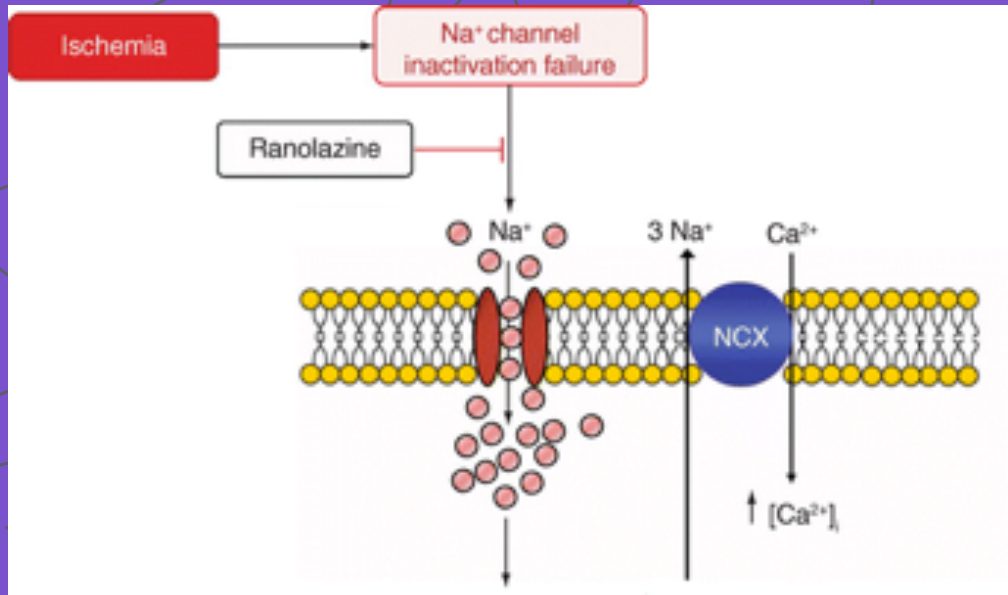
Ranolazine

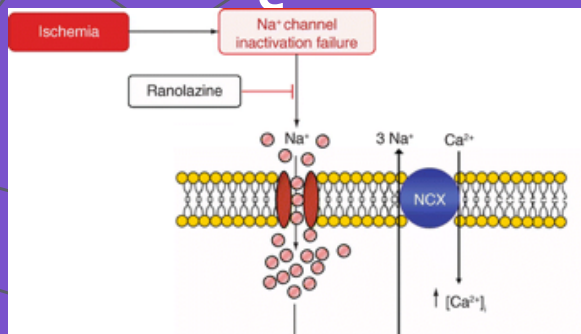
- Ranolazine is a newer antianginal drug act by reducing a late sodium current (I Na) that facilitates calcium entry via the sodium-calcium exchanger.
- The resulting reduction in intracellular calcium concentration reduces cardiac contraction
- Inhibition of late INa reduces intracellular sodium and calcium overload, thereby improving diastolic function.



Ranolazine

- Ranolazine has antianginal as well as antiarrhythmic properties.
- **USES:** patients who have failed other antianginal therapies.

- **Drug interactions:** Extensively metabolized in the liver by the CYP3A family and also by CYP2D6. It is also a substrate of P-glycoprotein.
- In addition, ranolazine can prolong the QT interval and should be avoided with other drugs that cause QT prolongation.



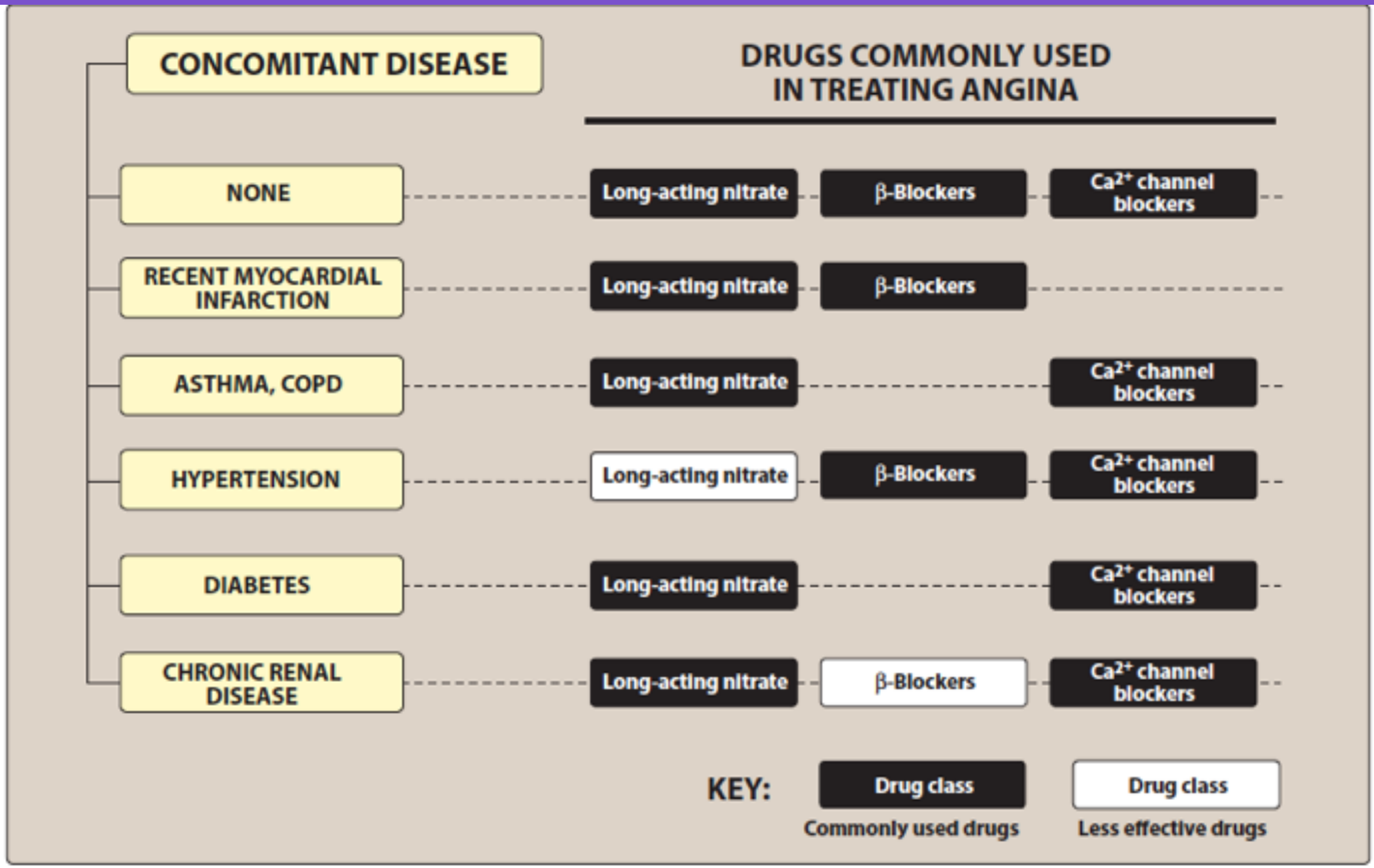
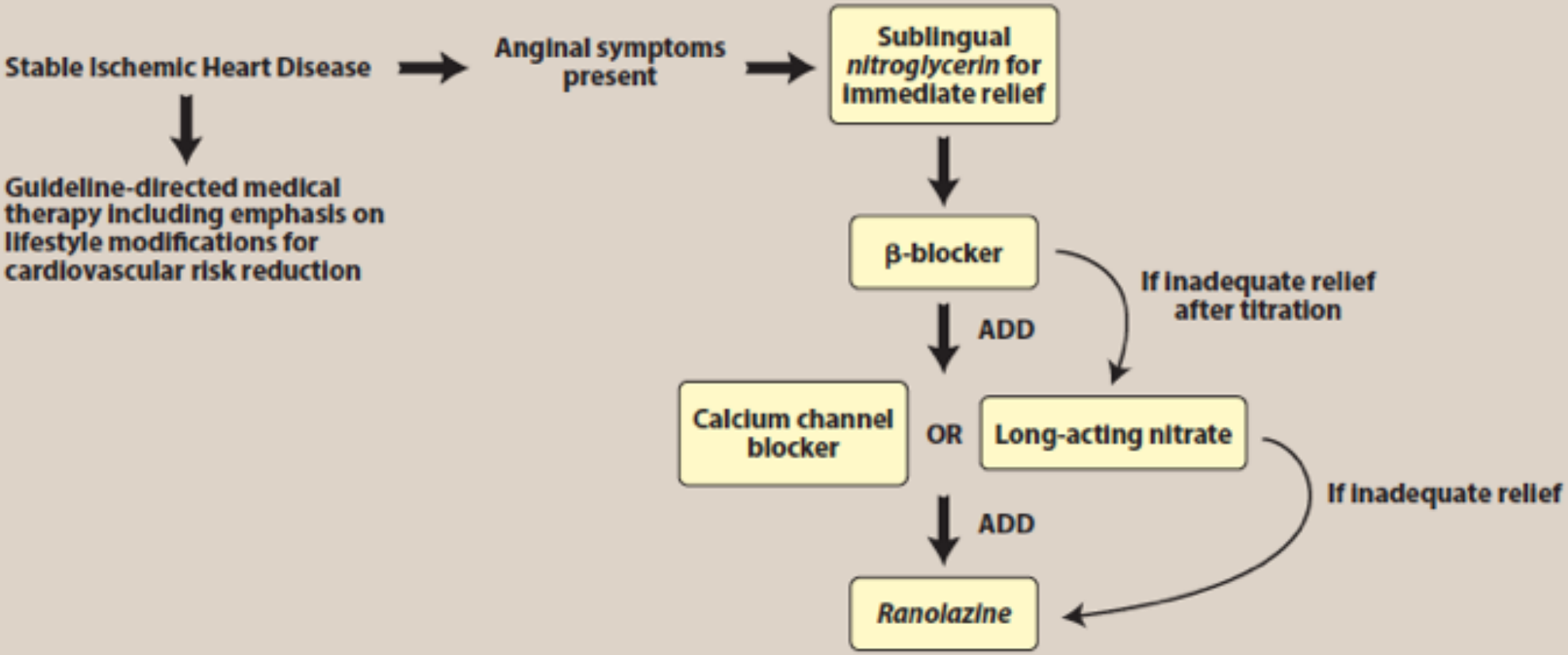

CONCOMITANT DISEASE
DRUGS COMMONLY USED IN TREATING ANGINA
NONE
Long-acting nitrate
β-Blockers
Ca2+ channel blockers
RECENT MYOCARDIAL INFARCTION
Long-acting nitrate
β-Blockers
ASTHMA, COPD
Long-acting nitrate
Ca2+ channel blockers
HYPERTENSION
Long-acting nitrate
β-Blockers
Ca2+ channel blockers
DIABETES
Long-acting nitrate
Ca2+ channel blockers
CHRONIC RENAL DISEASE
Long-acting nitrate
β-Blockers
Ca2+ channel blockers
KEY:
Drug class
Commonly used drugs
Drug class
Less effective drugs

Figure 21.3


Stable Ischemic Heart Disease
Anginal symptoms present
Sublingual *nitroglycerin* for immediate relief
Guideline-directed medical therapy including emphasis on lifestyle modifications for cardiovascular risk reduction
β-blocker
If inadequate relief after titration
ADD
Calcium channel blocker
OR
Long-acting nitrate
If inadequate relief
ADD
Ranolazine

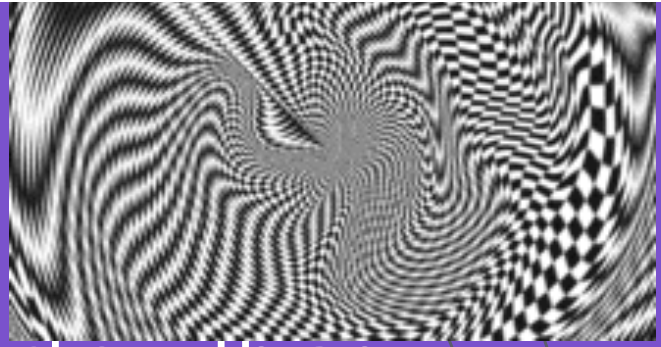
Trimetazidine:

- First cytoprotective anti-ischemic agent .
- metabolic modulators are known as pFOX inhibitors because they partially inhibit the fatty acid beta-oxidation pathway in myocardium.
- Preserves energy metabolism in cells exposed to hypoxia…. prevents the decrease in intracellular ATP levels

Ivabradine

- **Bradycardic** drugs, relatively selective If sodium channel :reduce cardiac rate by inhibiting the sodium channel in the SA node (**inhibition of pace maker current**).
- No other significant hemodynamic effects have been reported.
- USES: heart-related chest pain and heart failure
- The lack of effect on gastrointestinal and bronchial smooth muscle is an advantage of ivabradine.

Ivabradine



- Ivabradine appears to reduce anginal attacks with an efficacy similar to that of calcium channel blockers and β blockers.
- It may be as effective as the beta blocker atenolol[4] and comparable with amlodipine in the management of chronic stable angina.
- It is used in combination with beta blockers in people with heart failure with LVEF lower than 35 percent
- Side effects: luminous phenomena, bradycardia 2% and 5% of.[4] 2.6–4.8% reported headaches. first-degree AV block, ventricular extrasystoles, dizziness and/or blurred vision.

Newer Antianginal Drugs

- The Rho kinases comprise a family of enzymes that inhibit vascular relaxation and diverse functions of several other cell types. Excessive activity of these enzymes has been implicated in coronary spasm, pulmonary hypertension, apoptosis, and other conditions. Drugs targeting the enzyme have therefore been sought for possible clinical applications.
- Fasudil is an inhibitor of smooth muscle Rho kinase and reduces coronary vasospasm in experimental animals. In clinical trials in patients with CAD, ivabradineit has improved performance in stress tests.

Allopurinol

- allopurinol , represents another type of metabolic modifier.
- Allopurinol inhibits xanthine oxidase, an enzyme that contributes to oxidative stress and endothelial dysfunction.
- A recent study suggests that high-dose allopurinol prolongs exercise time in patients with atherosclerotic angina.

Dipyridamole

- Inhibits the uptake of adenosine and PDE3 inhibitor .
- Thought to be a good coronary dilator.
- Increases the blood flow to the normal area i.e. "Coronary Steal Phenomenon".
- Still used as an antiplatelet drug (in TIAs), but not better than aspirin.
- Dipyridamole enhances exercise-induced myocardial ischemia even the usual oral dosage and hence it not used as an anti-platelet agent in patients with stable angina

Others

- ACEI.
- Anticoagulants and/or Thrombolytic Therapy.
- Cholesterol Lowering Agents.
- Angioplasty
- Surgery.