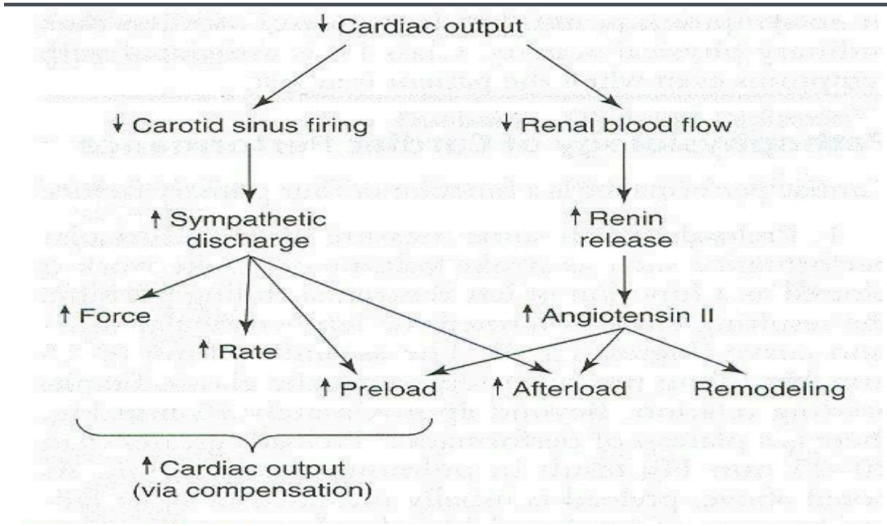
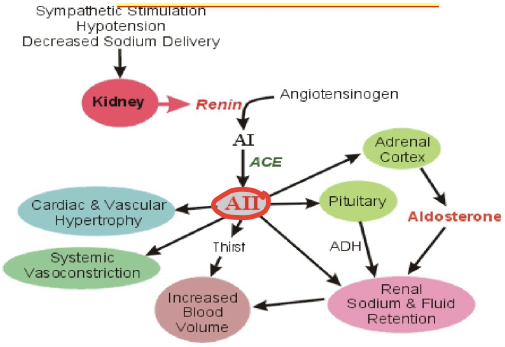
All drugs in Pharma (Final)

Done by: Mays Qashou





☆ CHF is a progressive condition where the heart's ability to pump blood effectively declines over time. This leads to decreased cardiac output (CO), triggering the body's compensatory mechanisms, which initially support circulation but eventually worsen the disease.

☆ Key Compensatory Mechanisms:

1. Baroreceptor Reflex and Sympathetic Activation: Decreased CO reduces carotid sinus firing, activating the sympathetic nervous system.

▪ Results:

1. Increased heart rate (chronotropy).
2. Increased force of contraction (inotropy).
3. Increased preload (blood volume entering the heart).
4. Increased afterload (resistance to pumping).

2. Renin-Angiotensin-Aldosterone System (RAAS):

1. Further increased preload and afterload.
2. Cardiac remodeling (structural changes in the heart).
3. Reduced ejection fraction (EF), worsening heart function, and increasing mortality risk.

☆ Impact on the Heart:

While these mechanisms temporarily improve CO, they increase the workload on the heart, leading to progressive weakening, worsening heart failure,.

The aim of antiheart faliure drugs is to decrease the symptoms and slow disease progression and improve survival

1. Anti-Heart failure drugs

Drug name	MOA	Indecations	Side effects
1. ACE Inhibitors (prils)	Inhibit angiotensin-converting enzyme, reduce angiotensin II, decrease preload and afterload.	- All stages of left ventricular failure; symptomatic and asymptomatic HF. - For most patients, ACE inhibitors are started first with low initial dose of beta blockers.	Dry cough, hyperkalemia, angioedema, fetal toxicity (contraindicated in pregnancy)
2. Beta blocker: Bisoprolol, carvedilol or nebivolol [low doses]	Inhibit sympathetic activation, reduce heart rate and myocardial demand.	Chronic HF due to left ventricular systolic dysfunction; used with ACE inhibitors.	In the short term they can produce decompensation with worsening of heart failure and hypotension. (Contraindicated in asthma, AV block, and low systolic BP (<90 mm Hg)).
3. ARBs (sartan)	Block angiotensin II receptors, reducing vasoconstriction and aldosterone release.	Alternative to ACE inhibitors for HF when intolerant (e.g., due to cough).	Hyperkalemia, renal dysfunction.
4. Diuretics:	Reduce the symptoms of volume overload by: 1. Decreasing extra cellular volume. 2. Decreasing the venous return.	- Diuretic therapy should be considered for heart failure patients with dyspnea or oedema. - Loop diuretics like furosemide and bumetanide are the most effective while Thiazides are effective in mild cases only.	Hypokalemia and hyperuricemia.
5. Spironolactone [potassium-sparing diuretic]	**- Aldosterone antagonist**; prevents sodium water retention which helps decrease fluid buildup in the body. - Prevents myocardial remodeling.	- Advanced or severe HF with reduced ejection fraction and fluid retention.	Hyperkalemia, gynecomastia (an increase in breast tissue in males), CNS effects (confusion), peptic ulcers. Eplerenone can be substituted for spironolactone in patients who develop gynecomastia.
6. Digoxin [cardiac glycosides]: it's taken from a plant called foxglove digitalis. An antidote for digoxin is called: Digifab (digoxin immune fab).	Digoxin inhibits the Na^+/K^+-ATPase pump, preventing potassium (K^+) from entering cardiac cells and causing sodium (Na^+) to accumulate inside the cell. This disrupts the sodium gradient that powers the sodium-calcium exchanger, leading to reduced calcium (Ca^{2+}) export and increased intracellular calcium levels. The excess calcium improves the heart muscle's ability to contract (positive inotropic effect), enhancing stroke volume and ejection fraction, thereby restoring more effective cardiac function.		1. low therapeutic index or window (meaning the difference between a safe dose and a toxic dose is very small). 2. Low potassium levels (hypokalemia), often caused by diuretics like thiazides or loop diuretics, can significantly increase the risk of digoxin toxicity. 3.Anorexia, nausea, vomiting and diarrhea. 4. cardiac effects that include: premature ventricular contraction, ventricular tachycardia and fibrillation.

Why? 🤔

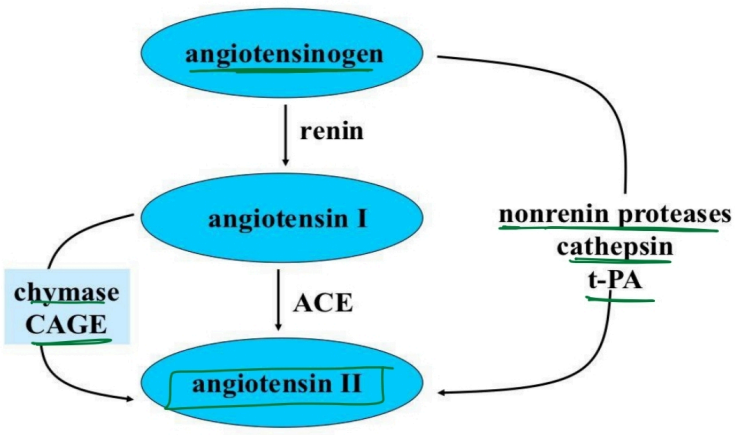
👉🏻 Because inside the cell is positive due to the accumulation of positive sodium Na+ ions, leading to an absent repolarization state, which is closer to positive, meaning that it will be easier for the cell to depolarize and generating an action potential will be easy. This makes the cell susceptible to every type of arrhythmia when patient administers digoxin.

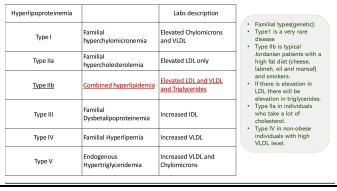
	- Digoxin is a positive inotropic drug and a negative chronotropic drug, how? It stimulates the vagus nerve, increasing acetylcholine release. Acetylcholine binds to M2 receptors in the heart, which opens potassium channels, causing potassium (K^+) to leave the cell. This hyperpolarizes the heart cells (makes them more negative), making it harder for them to fire action potentials, thus slowing the heart rate.		5. Vision changes (xanthopsia): yellowing of the vision appears as yellow holes, fatigue and headache. 6. Macrolide and tetracycline antibiotics should be avoided because they elevate digoxin serum concentration and enhance the risk for digoxin toxicity. 7. Quinidine, varapamil, and amiodarone can cause digoxin intoxication.
7. Hydralazine + Nitrates	Hydralazine reduces afterload and Nitrates reduces preload.	HF in African American patients or those intolerant to ACE inhibitors/ARBs.	
8. Dobutamine [intravenous infusion]	Beta-1 agonist; increases cardiac contractility (positive inotropic effect) and output.	Acute decompensated HF or cardiogenic shock.	Hypotension (because there will be some activation of β2 receptor (around 10%). It requires co-administration with vasopressors (noradrenaline) to inhibit hypotension.
9. Amrinone	Positive inotropic effect and increase systemic vasodilation.	Short-term treatment of refractory HF.	We stopped using this drug because it Increases mortality risk.

Important note:

- Combining ACE inhibitors (ACEIs) and ARBs is generally avoided due to the risk of hyperkalemia but may be necessary in specific cases of congestive heart failure (CHF) to block angiotensin II more effectively. While ACEIs reduce angiotensin II production, alternative pathways can still generate it. like non-renin proteases like cathepsin and tPA that can convert angiotensinogen to angiotensin II directly. Additionally, there are chymases that can convert angiotensin I to angiotensin II.

- So, ARBs complement ACEIs by blocking angiotensin II receptors. Together, they address both production and receptor activity. However, this combination should not be used with spironolactone due to a heightened risk of hyperkalemia, and potassium levels must be closely monitored when both drugs are prescribed.





Hyperlipoproteinemia		Labs description
Type I	Familial hyperchylomicronemia	Elevated Chylomicrons and VLDL
Type IIa	Familial hypercholesterolemia	Elevated LDL only
Type IIb	Combined hyperlipidemia	Elevated LDL and VLDL and Triglycerides
Type III	Familial Dysbetalipoproteinemia	Increased IDL
Type IV	Familial Hyperlipemia	Increased VLDL
Type V	Endogenous Hypertriglyceridemia	Increased VLDL and Chylomicrons

- Familial type(genetic):
- Type I is a very rare disease.
- Type IIb is typical Jordanian patients with a high fat diet (cheese, labneh, oil and mansaf) and smokers.
- If there is elevation in LDL there will be elevation in triglycerides.
- Type IIa in individuals who take a lot of cholesterol.
- Type IV in non-obese individuals with high VLDL level.

2. Antihyperlipidemic drugs

Drug name	MOA	Indications	Side effects
1. Statins: Lovastatin, pravastatin, simvastatin, fluvastatin, Atorvastatin, Rosuvastatin (important drugs) The most potent is the least dose (the rosuvastatin). They are contraindicated in pregnancy, nursing mothers, children and teenagers.	1. Statins work by inhibiting the enzyme HMG-CoA reductase [rate-limiting enzyme for cholesterol synthesis]. 2. This inhibition leads to a decrease in intracellular cholesterol, which triggers the upregulation of LDL receptors on liver cells. These receptors enhance the removal of LDL (bad cholesterol) from the bloodstream, lowering plasma LDL levels. 3. Additionally, statins reduce triglycerides, slightly increase HDL (good cholesterol), and decrease the secretion of VLDL, further lowering plasma lipid levels. - This dual mechanism of reducing cholesterol synthesis and enhancing LDL clearance helps statins effectively lower LDL cholesterol and reduce cardiovascular risk.	Hyperlipidemia, elevated LDL levels.	1. Myopathy (muscle pain and weakness) due to increased creatine kinase, especially when combined with Fibrates and Niacin. 2. Rhabdomyolysis (disintegration or dissolution of muscle). Rhabdomyolysis is rare to happen, but it can cause acute renal failure. How? By increasing myoglobin level from damaged muscle cells that lead to Glomerular blockage => acute renal failure. 3. Hepatotoxicity (increased serum transaminase). 4. G.I.T upset and Headache. 5. They interact with Warfarin and resulting in elevation of it.
2. Niacin (Vitamin B3) contraindicated in Gout, Peptic ulcer, DM and Hepatotoxicity patients	1. The most effective agent in increasing the HDL (The catabolism of HDL can be inhibited by nicotinic acid). 2. Inhibits hormone-sensitive lipase (HSL), which is a key enzyme involved in the breakdown of triglycerides in adipose tissue to fatty acids so inhibition of this enzyme will decrease the fatty acid in liver, decrease VLDL and LDL.	treatment of hyperlipidemia and hypertriglycerolemia	Cutaneous flushing, itching, burning, nausea, vomiting, GI irritation, peptic ulcer activation, hyperglycemia, hyperuricemia and elevation of liver enzymes (Hepatotoxicity). I can give the patient Aspirin or porphin to release these side effects.
3. Fibrates: Fenofibrate, Gemfibrozil and clofibrate	Activate PPARs (Peroxisome proliferator activated receptors), increasing lipoprotein lipase expression which increases the utilization of fatty acids to adipose tissue and muscle; reduce VLDL and LDL, increase HDL levels. Note: PPARs are nuclear receptors [genetic regulators that control various processes in our body, such as glucose and fat metabolism, by increasing or decreasing the expression of specific genes].	This drug is most suitable for type IV patient and type I. Treatment of hypertriglycerolemia and also useful in treating type III hyperlipidemia	1. GI disturbances, rash, urticaria. 2. Lithiasis (inhibit alpha hydroxylase, which is responsible for metabolizing the bile acid. That lead to increase the bile acid concentration the chance for binding it with cholesterol = gallstones). 3. Myositis and Myopathy. 4. Compete with anticoagulants for plasma protein binding.

Note: Statins enter the liver through a transporter called SLCO1B1. If there is a polymorphism in this transporter, as seen in some Jordanian individuals, the risk of myopathy increases because more of the drug bypasses the liver and reaches the muscles.

4. Bile acid-binding resins (Sequestrants): Cholestyramine, Colestipol	- They are resins that bind bile acid in the intestine, forming insoluble complexes that will be excreted in the feces this will Lower the bile acid level which will trigger the conversion of cholesterol into bile acid and the end result will be a reduction in cholesterol concentrations. - Good reducers of LDL [3 arrows].	1. The drugs of choice (often in combination with diet or niacin) in treating Type IIa [high LDL]. 2. We can add them to Statins in patients who do not really respond to the Statins.	1. Gastrointestinal Disturbances: constipation and nausea. 2. At high doses they impair the absorption of fat soluble vitamins (A,D,E, and K). 3. They interact with the absorption of many fat soluble drugs, for example, Tetracycline, Digoxin, Warfarin, Aspirin. - Therefore, the above drugs should be taken at least 1 to 6 hr after administration of bile acid sequestrants.
5. Cholesterol absorption inhibitors: Ezetimibe	- Ezetimibe will selectively bind to the "Cholesterol itself "inhibiting intestinal absorption of dietary and biliary cholesterol in the small intestine, resulting in an increase in the clearance of cholesterol from the blood. - Lower VLDL and LDL by one arrow [very mild and limited activity when used alone].	When combined with Statins, it will provide a **synergistic effect** towards the reduction of LDL cholesterol.	Headache and/or diarrhea

😊 Why we combine Fibrates and Statins?

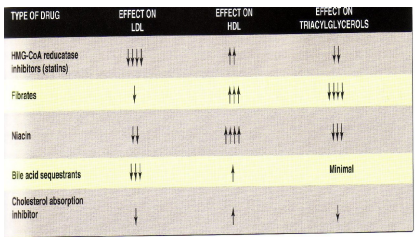
- To target both LDL (via statins) and VLDL/triglycerides (via fibrates) when no single drug provides sufficient effect.

😊 What is the difference between **Fenofibrate and Gemfibrozil** [both are fibrates] when adding them to statins?

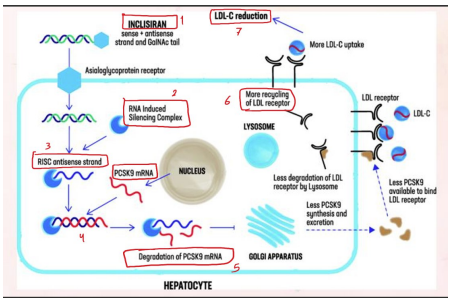
- 1. Fenofibrate: the interaction is mostly on the adverse effect (myopathy): If we prescribe fenofibrate and statin "at the same time" this will increase risk of: rhabdomyolysis (muscle breakdown, because of the overlap adverse effect of the two drugs on the muscles) and it will be dangerous for patient who have renal failure and rheumatic disease.

As a solution we give them at 2 separate times a day: one in the morning (fenofibrate) and the other in the evening (statin).

- 2. Gemfibrozil: it's contraindicated to combine it with Statins, because Gemfibrozil inhibit the CYP450 (CYP3A4 and CYP2C9) [which metabolizes the Statins], thus Statins will accumulate and this increases the risk of Myopathy. **Except for Pravastatin [which is metabolized by sulfation]** so the combination of gemfibrozil with pravastatin have fewer drug-drug interaction and we can combine them.



3. Novel Lipid-Lowering Agents

Drug name	MOA	Indications	Side effects
1. Bempedoic acid [A pro drug requires activation by an enzyme that is mainly expressed in the liver: "very-long-chain acyl-CoA synthetase-1 ". This property minimizes the exposure of the active drug to tissues other than the liver, such as the skeletal muscle. So, this property will reduce the side effects].	- Selective antagonist of ACLY. - ATP-citrate lyase (ACLY) is an enzyme that catalyzes the ATP-dependent conversion of citrate to acetyl-CoA. Acetyl-CoA is the precursor of (HMG- CoA), which is crucial for the biosynthesis of cholesterol. **Thus, the inhibition of ACLY leads to a reduction of acetyl-CoA and cholesterol synthesis, resulting in an increased number of LDLRs, causing a reduction of plasma LDL and plasma cholesterol.** - As a compensatory mechanism, the GI will increase Cholesterol absorption, however, we can inhibit this by giving Ezetimibe. - It also may cause a slight increase in HDL, carrying cholesterol from foam cells to the liver.		1. Increase blood urea nitrogen and creatinine [because this drug inhibits the transporters that secrete those solutes within the kidneys, as a result, they will accumulate in the blood]. 2. Increase uric acid [Hyperuricemia and Gout]. 3. Decrease hemoglobin [Anemia]. 4. May cause Muscle pain. 5. Hyperglycemia is not observed.
2. Evolocumab & Alirocumab	- PCSK9 inhibitors (evolocumab and alirocumab are monoclonal antibodies developed against PCSK9). - PCSK9 is an enzyme predominantly produced in the liver, binds to the LDL receptor (LDLR) present on the surface of the hepatocytes, leading to their degradation and a subsequent increase in plasma LDL-C levels. **So, inhibition of this enzyme causes an increase in LDLR number and a subsequent decrease in plasma LDL-C levels.**		Flue-like syndrome (remember they are monoclonal Abs)
3. Inclisiran [injectable drug that is given 3 times a year, it is given as a loading dose].	- PCSK9 inhibitor (Inclisiran is a synthetic small interfering RNA (siRNA), which works by targeting the PCSK9 mRNA). - 	Inclisiran can be given with Statins to increase its activity	Injection-site reaction only

Inclisiran, a double-stranded RNA molecule, targets PCSK9 to lower cholesterol levels. Once delivered into liver cells, it interacts with the RNA-induced silencing complex (RISC), which separates its strands. The active strand binds to PCSK9 mRNA, leading to its degradation. This prevents the production of the PCSK9 enzyme, which normally reduces the activity of LDL receptors by causing their degradation. Without PCSK9, LDL receptors remain active, clearing more LDL cholesterol from the bloodstream and effectively reducing cholesterol levels.

4. Volanesoren [It is an injectable drug].	- ApoC-III inhibitor (antisense oligonucleotide (ASO) (siRNA), but our target this time is APOC3 mRNA). - Apolipoprotein C-III (apoC3) is an enzyme that inhibits the lipoprotein lipase LPL, (the enzyme responsible for the lipolysis of TG in the very-low-density lipoprotein (VLDL) and chylomicron particles). **So, the inhibition of this enzyme increases the expression of LPL, thus increasing TG (triglycerides) lipolysis and reducing VLDL and chylomicrons.**	Patients with elevated plasma TG levels and patients with familial chylomicronemia syndrome (FCS).	Thrombocytopenia and injection-site reactions.
5. Evinacumab	- ANGPTL3 inhibitors (Evinacumab is monoclonal antibody against ANGPLT3). - ANGPTL3 is an enzyme that regulates plasma TG and HDL-C levels by inhibiting lipoprotein lipase (LPL) and endothelial lipase, respectively. **So, the Inhibition of ANGPTL3 preserves the function of LPL and EL resulting in a decline in TG, LDL-C and HDL-C plasma levels independently of LDLR function**.		
6. Vupanorsen	- ANGPTL3 inhibitors (Vupanorsen is an antisense oligonucleotide targeting ANGPTL3).		

😊 Don't get confused!

- **Evinacmab** is a monoclonal AB against ANGPLT3
- **Evolocumab** is a monoclonal AB against PCSK9
- **Volanesoren** is an antisense oligonucleotide (ASO) targeting APOC3 mRNA
- **Vupanorsen** an antisense oligonucleotide targeting ANGPTL3

NOTE: The idea for Volanesoren [ApoC-III inhibitor] came from studying people with a natural loss-of-function mutation in the APOC3 gene. These individuals had: 40% lower triglyceride (TG) levels AND 40% reduced risk of cardiovascular diseases (CVD). This discovery inspired the development of a drug to mimic this beneficial effect by inhibiting ApoC3, leading to lower triglycerides and reduced CVD risk.

- Remember: ***All drugs in this lecture*** (new LDL-C LOWERING AGENTS) ***are not considered first line therapy.*** They all have activities, but we use them as Add On Drugs to Statins (and others).

😊 Some Notes before going to the anti-arrhythmic drugs: [read them quickly]

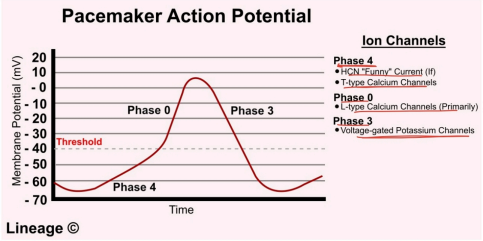
- Cardiac arrhythmias are disorders that affect the heart's rate, rhythm, and electrical impulse generation or conduction.
- Many anti-arrhythmic drugs can aggravate or generate arrhythmia.(بس مجبورين نستخدمهم)
- Many anti-arrhythmic drugs create more serious rhythm disorders than the ones being treated (proarrhythmic).
- Atrial fibrillation (AF) is a condition where the heart's normal rhythm is disturbed by irregular electrical signals, usually starting near the pulmonary veins. These signals override the usual beats from the sinoatrial (SA) node, causing the heart to beat unevenly and often too fast.
- Abnormal conditions lead to arrhythmia: 1. The circus rhythm happens around the AV node, caused by scares or fibrosis causes reentry. 2. Triggered arrythmia: Ectopic foci generate autorhythmicity that reach the AV node. 3. The autorhythmicity in the AV node itself has increased. - **All these will increase the conductivity of the AV node.**
- All atrial arrythmias (atrial fibrillation, atrial flatter, SVT) **caused by increased conductivity of the AV node EXCEPT WPW** (wolff-Parkinson-white) syndrome, since the electrical signals bypass the AV node.
- It's contraindicated to give WPW patient these four drugs: Digoxin, Beta-blocker, Calcium-channel blocker and Adenosine.
- In WPW, we can do two things:

1. Inhibit the sodium channel >> less conductivity, since the sodium channel opening causes the start of action potential.

2. Or we block the potassium channel >> less efflux of potassium, lead to increased QT interval and action potential, so less frequency of firing (less contraction).

- All Class I are Na+ channel blockers.
- Class IC is the strongest, followed by Class IA, and then Class IB (memorize them as CAB).
- Class IB has a unique feature—it decreases the action potential duration (APD) due to its preference for binding to sodium channels in their inactive state.
- Class III agents include wider ranges of voltage-dependent K+ channel blockers
- Examples: **nonselective (ambasilide, amiodarone)** and **selective (dofetilide, ibutilide, sotalol) blocker.**
- Dofetilide and ibutilide can be used in SVT, A fib, flatter, they are weak, so we don't give them in ventricular arrhythmias.
- Class IV: drugs blocking Ca2+ entry through specific Ca2+ channels (CCB).
- Examples: non-selective (Bepridil) and Selective: (Phenylalkylamines (eg, verapamil), benzothiazepines (eg, diltiazem)).

The doctor didn't mention them



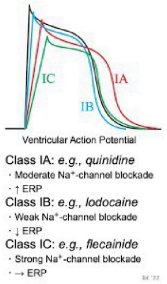
4. Class II drugs ["AV nodal dependent" Atrial arrhythmia drugs].

Drug name	MOA	Indications	SE
1. Beta-blockers (class IIa) and Calcium-channel blockers. [All beta-blockers, except for **sotalol**].	They block the L-type calcium channels, leading to prolonged phase 0, leading to decreased conductivity in the AV node.	Used as **prophylaxis** in patients have SVT, atrial flatter or atrial fibrillation.	Sinus bradycardia, AV block, Cold extremities and masks symptoms of hypoglycemia.
2. Digoxin (Class IId)	- Muscarinic M2 receptor activators. - Positive ionotropic: It increases the force of contraction of the heart by reversibly inhibiting the activity of the myocardial Na-K ATPase pump. It induces an increase in intracellular sodium that will drive an influx of calcium in the heart and cause an increase in contractility. - Increases the vagal tone increasing the release of acetylcholine, bind to M2 receptor (inhibitory GPCR) [the gamma subunit] will open the potassium channels, releasing the potassium outside, leading to hyperpolarization.	Sinus tachycardia or supraventricular tachyarrhythmia.	1. Visual changes (blurring, photophobia, disturbance in vision color). 2. GI toxicity: anorexia, nausea, vomiting. 3. Gynaecomastia, skin rashes. 4. Cardiac adverse effects: Bradycardia, AV block, Paroxysmal atrial tachycardia, Sino atrial arrest and Ventricular tachycardia.
3. Adenosine (Class IIe). [Given as a rapid IV bolus].	- Adenosine A1 receptor activator. - Acts directly on cardiac receptors (adenosine A1 receptor) causing potassium efflux and hyperpolarization of the cell membrane. Adenosine causes complete hyperpolarization, causing no conductivity in the AV node for seconds, since the half-life for adenosine is seconds. - Adenosine exerts a negative chronotropic effect by suppressing the automaticity of cardiac pacemakers, and a negative dromotropic effect through inhibition of AV-nodal conduction.	In acute supraventricular tachycardia (SVT), atrial flutter, or atrial fibrillation—especially if associated with hypotension or when the reentrant circuit involves the AV node, **Adenosine is the first-line treatment.**	1. Sinus bradycardia, sinus arrest or AV block. (Main side effect). 2. Atrial fibrillation.

5. Class I drugs [Monomorphic Ventricular arrythmia drugs and WPW].

Drug name	MOA	Indications	SE
1. Class Ia: Quinidine, procainamide, disopyramide	- Bind to the open state of Nav1.5 with moderate dissociation time constants (moderate block). - Reduce AP conduction velocity. - Increase ERP and APD. - So, they inhibit the induction and prolong the QT interval.	Supraventricular tachyarrythmias (atrial fibrillation) and **Ventricular tachycardia (Main Use).**	1. Very proarrhythmic drugs. 2. Quinidine: - Torsade's de pointes with QT interval prolongation. - Cinchonism: a syndrome of headache, dizziness and tinnitus. - May increase the plasma concentration of digoxin leading to digitalis toxicity. - GIT side effects: diarrhea, nausea, vomiting. 3. Procainamide: - Torsade's de pointes with prolonged QT interval. - Lupus-like syndrome (Like Hydralazine): rash, small joint arthralgia, and arthritis. - Pleuritis and pericarditis. - Hypotension.
2. Class Ib: lidocaine	- Bind to the Nav1.5 inactivated state with relatively rapidly dissociation time constant (weak block). - shorten both APD and ERP.	- Ventricular tachyarrhythmias. - Class IC and IB are particularly useful for patients with arrhythmias caused by QT interval elongation. - Lidocaine is local anesthetic. - Patients with MI, coronary artery disease, or congestive heart failure with low ejection fraction, **Lidocaine is the drug of choice.**	CNS effects (slurred speech, drowsiness, dizziness, muscle twitching, seizures and hypotension).
3. Class Ic: propafenone, flecainide	- Bind to the inactivated Nav1.5, from which they dissociate more slowly (strong block). - Reduce AP conduction velocity. - Maintain normal ERP and APD.	- Patient with WPW syndrome, **Class Ic is a good choice.** - Supraventricular tachyarrhythmias (atrial tachycardia, atrial flutter, atrial fibrillation). - Main use: Ventricular tachyarrhythmias resistant to other.	1. Flecainide: - Ventricular tachycardia in presence of ischemic heart disease or old MI. - Vision problems. - Headache, dizziness - Teratogenic 2. Propafenone: - Ventricular tachycardia in presence of ischemic heart disease or old MI. - Slowed sinus rate - Dizziness, chest pain, shortness of breath. - N/V, constipation/ diarrhea.

- Class Id: includes drug acting on recently reported late Na currents.



6. Class III drugs [Polymorphic ventricular arrythmia drugs].

Drug name	MOA	Indications	SE
1. Amiodarone	Blocks potassium channels, prolongs APD and ERP, minor effect on sodium and calcium channels.		1. Torsade's de pointes [Since the Class III cause QT interval prolongation]. 2. Heart block 3. Bradycardia 4. Cardiac depression. 5. lung fibrosis 6. Liver damage 7. Corneal microdeposits"bluish color on the eyes around the cornea" 8. peripheral neuropathy. 9. Amiodarone main problem is that it contains iodine, which causes one of two: 1. toxicity, by apoptosis the thyroid cells die because of its inability to utilize iodine causing hypothyroidism. 2. the cell utilizes iodine causing hyperthyroidism.
2. Sotalol (selective class III).	Potassium channel blocker, beta-blocker activity [decreasing the contractibility and conductivity and QT elongation].	If the ventricular arrhythmia is caused by sympathetic overactivation, then **sotalol is a better choice** than amiodarone.	Amiodarone and sotalol have the same side effects.

Let's explain the previous diagram and what the drug does:

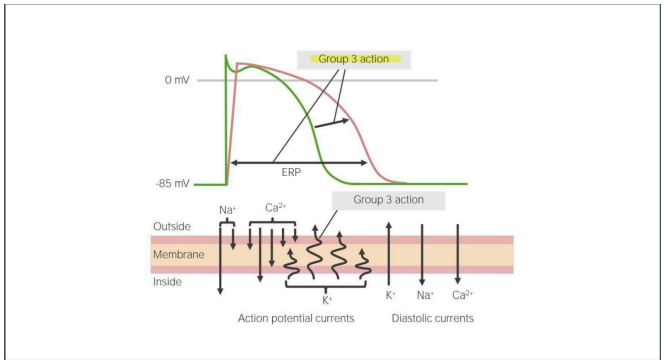
- Slope in phase 0: The drug reduces the slope of phase 0.
- Eliminates phase 1: Phase 1 is effectively deleted.
- Small changes in phase 2: There are slight alterations in the slope of phase 2.
- Blocking potassium channels: This increases the duration of phase 3.

- From this, you can see that this class exhibits a polymechanism of action.

- Some sodium channels are blocked, slightly affecting calcium channels (though not significantly).
- The most prominent effect is on potassium channels, leading to an increase in both the effective refractory period (ERP) and the action potential duration (APD).
- Conductivity decreases because the first firing relies on sodium, which is being reduced.
- The slope in phase 0 resembles that seen with Lidocaine.

- I am very strong with polymorphic application. So, if a patient has polymorphic ventricular arrhythmia originating from different sites, you need to target the treatment aggressively. However, be cautious of torsades de pointes, and ensure there is no congenital QT interval elongation or use of drugs that cause QT interval prolongation, or arrhythmias resulting from such factors.

- In a patient with MI, we can use this drug because we are addressing different types of arrhythmias.



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