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Cardiovascular Pharmacology I

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Beta-blockers

β_1 -selective antagonists

→ act on the heart...

→ used for HF.

- Atenolol, Metoprolol, Esmolol, Bisoprolol allowed in the asthma - COPD pt... [OLD]..
- Used for hypertension
 - Blockade → ↓ CO → ↓ BP
- Metoprolol: systolic heart failure
 - Blocks sympathetic stimulation of heart
 - Reduces mortality

* 3 drug used in HF :- to decrease the mortality rate...

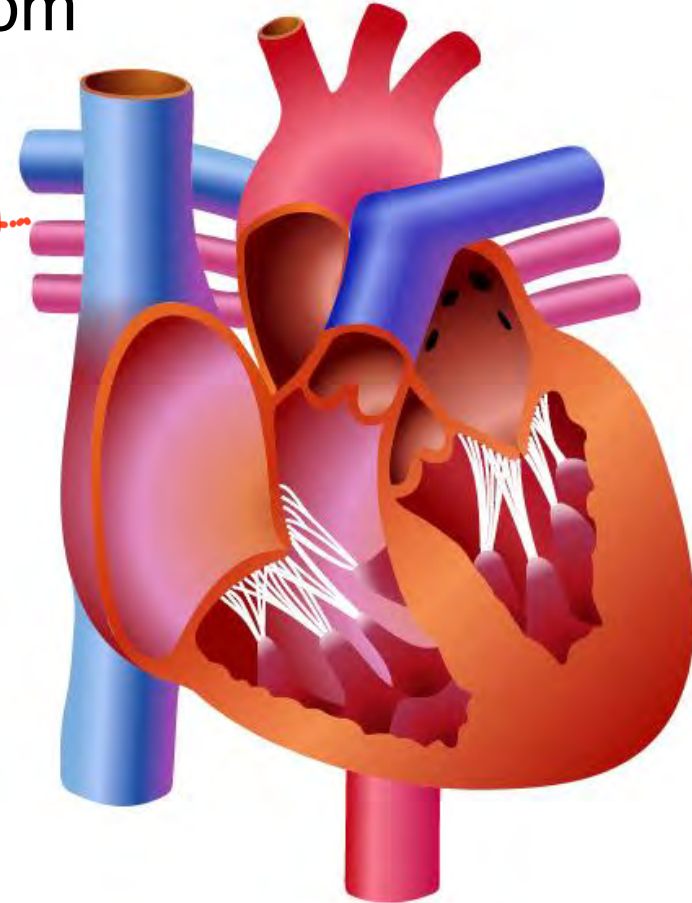
- 1- metoprolol...
- 2- bisoprolol...
- 3- carvedilol...

* B2 R presented in portal circulation...

* B2 act on the lung...

→ so contraindicated in OLD...

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Beta-blockers

$\beta_1\beta_2$ (nonselective) antagonists

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* DM pt may be presented with sympathetic hypoglycemic symptoms ^[neuro] mimic to the hypoglycemic symptoms ^{فقدان الشهية، غثاس، تعرق، خفقان، خفقان} ^{non selective β . blocker} ^{Tremor & sweating.}

Contraindicated in DM

Cardio - ^{القلب} ^{نظام} ^{الدم}

System... • Propranolol, Timolol, Nadolol

• Nadolol, Propranolol: Used in portal hypertension

- Beta 1 blockade: $\downarrow$ CO, $\downarrow$ ECV $\rightarrow$ $\downarrow$ BP in portal vein $\rightarrow$ $\downarrow$ risk of bleeding...
- Beta 2 blockade: $\downarrow$ portal blood flow $\rightarrow$ $\downarrow$ risk of rupture of veins...

• Timolol: Used in glaucoma

- Beta 1 and Beta 2 $\rightarrow$ aqueous humor production

• Propranolol: hyperthyroidism $\rightarrow$ used for it:-

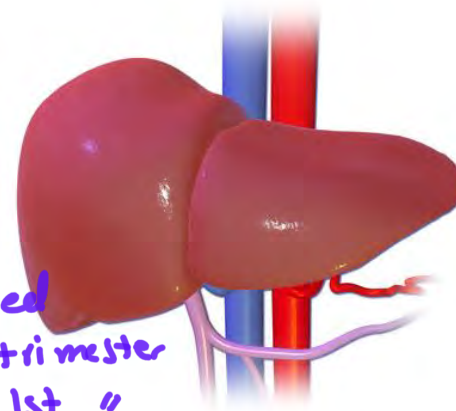
- Blocks T4 $\rightarrow$ T3 conversion
+ decrease the tremor...

1- hydrocortisol

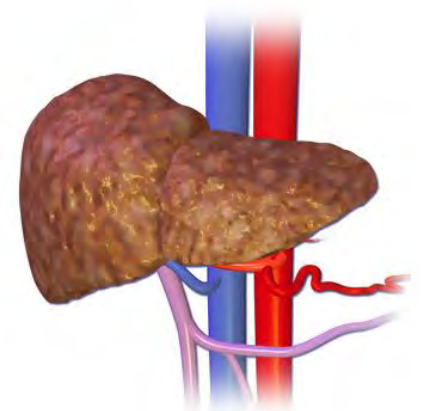
2- PTU $\rightarrow$ Contraindicated in 2nd, 3rd trimester indicated in 1st "

3- propranolol...

hepatotoxicity
agranulocytosis...



Normal Liver



Liver Cirrhosis

* The side effect of propylthiouracil [PTU]:-

Beta-blockers

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✓ $\beta_1\beta_2\alpha_1$ nonselective blockers...

* pregnancy + HTN we give them:-
1- methyl dopa...
2- labetalol...
3- hydralazine... Coral CCB...

- Labetalol: hypertensive emergency or preeclampsia

- Rapid reduction in blood pressure

HT:- ① nitrate...
or ② Labetalol...
or ③ nitroglycerine...

- Carvedilol: systolic heart failure

used in HF

- Blocks sympathetic stimulation of heart

- Reduces mortality in HF pt.



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Beta-blockers

Side effects

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- **Fatigue, erectile dysfunction, depression** النعيم
 - More common with older beta-blockers (propranolol)
- **Hyperlipidemia**
 - Mild increase in triglycerides
 - Mild decrease in HDL
 - Effect varies with different beta-blockers



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Beta-blockers

Side effects

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- Caution in diabetes due to:-
- ① • Blockade of epinephrine effects
 - Epinephrine raises glucose levels
 - Blockade → hypoglycemia + masked the symptoms..
- ② • Blockade of hypoglycemia symptoms
 - ↓ glucose → sweating/tachycardia
 - Symptoms "masked" by beta-blockers



Victor/Flickr

لیجے کہ یہ کہہ دینا کہ یہ بال Complication دیکھنا دھوکہ
ہاں اس سے وہ خارج ہو...

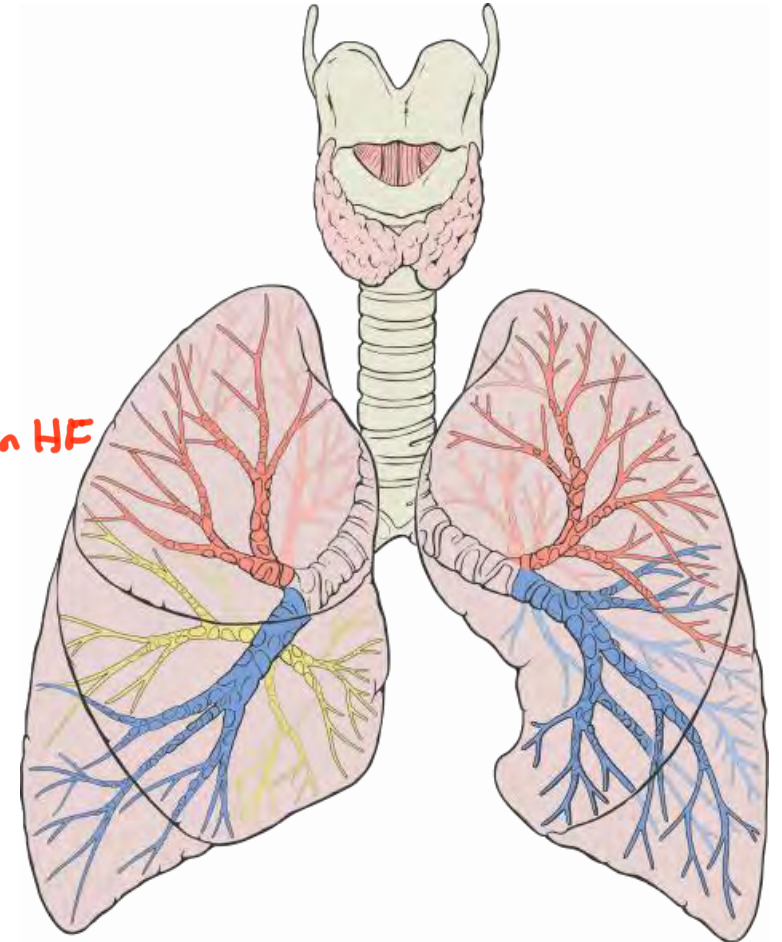
* ACE inhibitors :- nephro-protective → decrease the Albumen urea...
↳ used in DM pt

Beta-blockers

Side effects

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- **Caution in asthma/COPD**
 - B2-receptors: bronchodilators
 - B2-blockade may cause a flare [broncho constriction]
 - B1-blockers ("cardioselective") often used
- Decompensated **heart failure** *B1 blocker contraindicated in HF*
 - B1-blockers lower cardiac output → worsening of symptoms
 - Commonly used in compensated heart failure
 - Mortality benefit



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Beta-blockers

Overdose

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- Depression of myocardial contractility → shock
- Bradycardia/AV block
- Treatment: **glucagon** the antidote for B-blocker.

ATropine if HR lowered due to B-Blocker



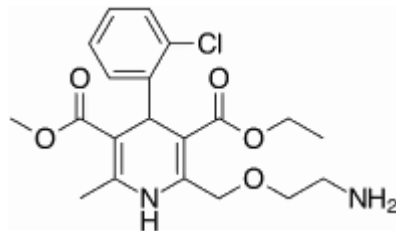
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Calcium Channel Blockers

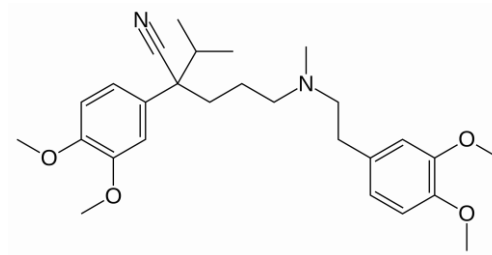
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dihydropyridines → amlodipine
nondihydropyridines → phenylalkylamine...
benzothiazepine...

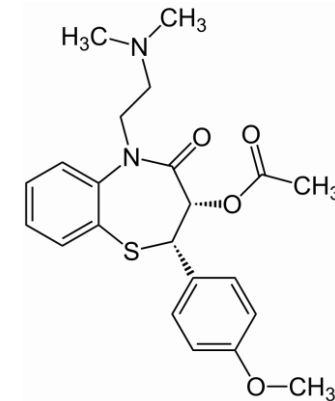
- Three major classes of calcium antagonists
 - dihydropyridines (amlodipine)
 - phenylalkylamines (verapamil)
 - benzothiazepines (diltiazem)
- Vasodilators and negative chronotropes/inotropes So we use it in HTW...



Amlodipine



Verapamil

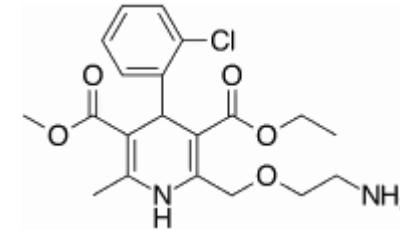


Diltiazem

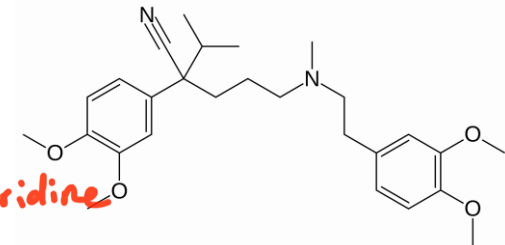
Calcium Channel Blockers

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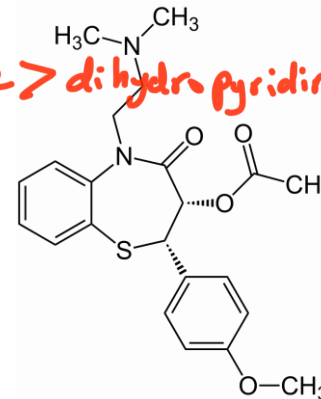
TPR:- total peripheral resistance..



Amlodipine



Verapamil



Diltiazem

- act on vessels..*

Dihydropyridines (nifedipine) *or amlodipine* → vasodilators

 - Main effect: ↓ TPR/BP *so 1st line in HTN in Black pt..*
- act on Heart*

Non-dihydropyridines (verapamil, diltiazem)

 - Similar to β 1-blockers *CCB + B-Blocker*
 - Main effects: ↓ HR; ↓ contractility → *↓ remodeling of the heart*
- Vascular smooth muscle effects** *← dihydropyridine > non dihydropyridine*

 - Nifedipine > Diltiazem > Verapamil
- Heart rate/contractility effects** *non dihydropyridine > dihydropyridine*

 - Verapamil > Diltiazem > Nifedipine

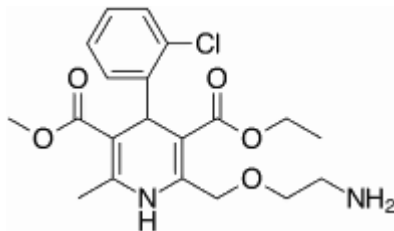
Calcium Channel Blockers

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Dihydropyridines (amlodipine)

* Pt presented to ER with 220/120 give him Cordine [nitroglycerine] this lead to severe headache [side effect] due to meningeal VD ..

- Used for **hypertension**
- Flushing, headache, hypotension [side effects]
 - Peripheral vasodilation lead to meningeal VD → headache..
- Key side effect: edema due to VD
 - Pre-capillary arteriolar vasodilation
 - Flood capillaries with fluid → edema pitting



Amlodipine



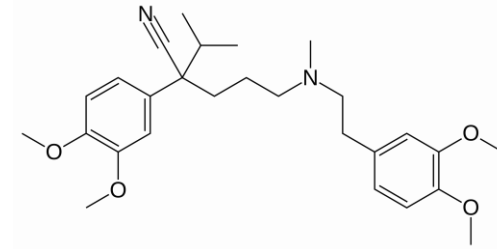
James Heilman, MD/Wikipedia

Calcium Channel Blockers

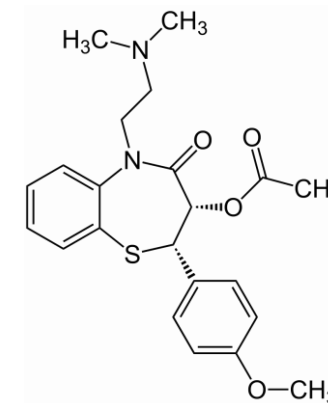
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Verapamil, diltiazem

- Used for **hypertension**
- Also used in **heart disease** *via ↓ HR, contractility.*
 - Arrhythmias (atrial fibrillation)
 - Stable angina (lower oxygen demand)
- Potential side effect: **negative inotropes**
 - Contraindicated in heart failure *or in pt take B-blocker.*



Verapamil



Diltiazem

Calcium Channel Blockers

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Other Side Effects

* hypercalcemia side effect:-

- 1- abdominal groan..
- 2- renal stone..
- 3- pains in bones..
- 4- psychic moans..

- Constipation as hypercalcemia.

- Most commonly with verapamil

- Hyperprolactinemia

- Seen with verapamil
- Blocks calcium channels CNS → ↓ dopamine release → ↑ prolactin
- Galactorrhea - amenorrhea.
- Leads to hypogonadism
- Men: ↓ libido, impotence
- Pre-menopausal women: irregular menses

* Thrombocytopenia in CCB or hypercalcemia due to:-

↳ pancreatitis - decrease the healing of ulcers - chronic constipation.



Elya/Wikipedia

Calcium Channel Blockers

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Other Side Effects

- **Gingival hyperplasia**
 - Seen in all types CCB *especially with dihydropyridine*
 - Also with phenytoin, cyclosporine 



Vaughan Williams Classification

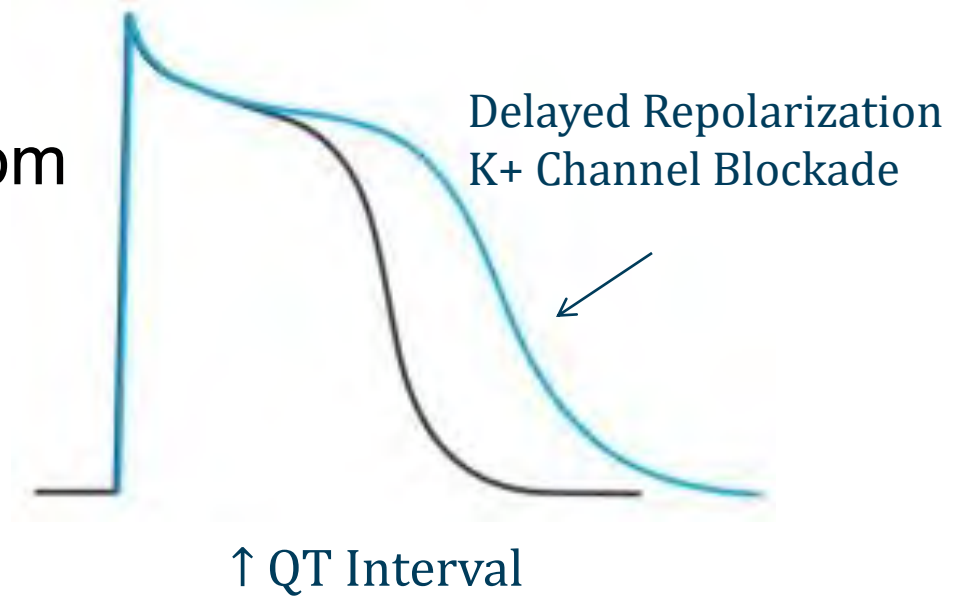
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Anti-arrhythmic medication:-

<u>Class I</u> <i>act on Na⁺ channels</i> Quinidine } Procainamide } Ia Lidocaine } Mexiletine } Ib Flecainide } Propafenone } Ic	<u>Class II</u> Beta-blockers ✓
<u>Class III</u> <i>act on K⁺ channels</i> Amiodarone <i>mc</i> Sotalol Dofetilide Ibutilide	<u>Class IV</u> Ca-channel Blockers ✓ (Verapamil/Diltiazem)

Amiodarone

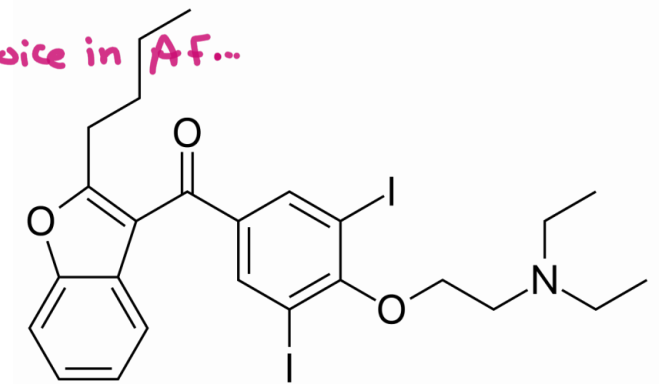
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- **Class III drug**
 - K channel blocker *via delayed the repolarization by CCB.*
 - Prolongs QT interval *↗*
- Also has class I, II, and IV effects
 - Class II, IV: Slow HR *lead to Bradycardia.*
- Highly effective drug
- Suppresses ^{acute} atrial fibrillation *so the Amiodarone is drug of choice in AF...*
- Suppresses ventricular tachycardia *[V-tac].*

* QT prolongation causes:-

- 1- drugs :- class III antiarrhythmic.
- 2- infection..
- 3- antibiotics: macrolides..

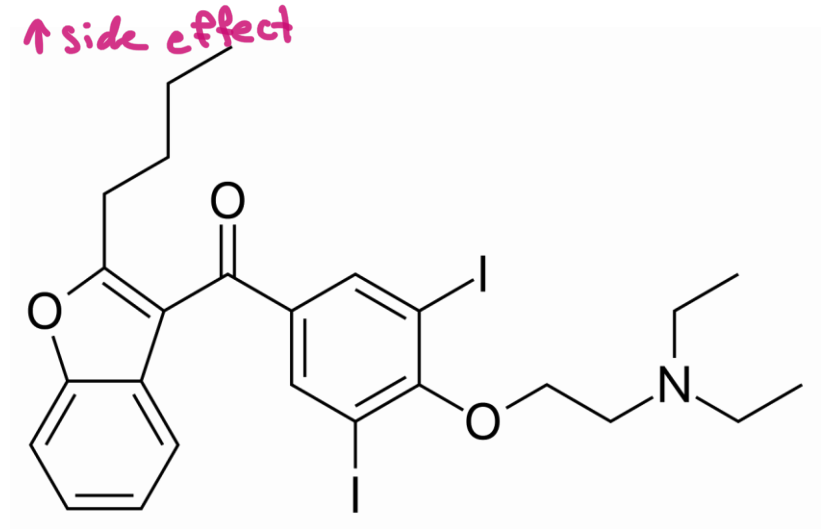


Amiodarone

Amiodarone

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- Highly **lipid soluble** →
- Accumulates in liver, lungs, skin, other tissues so has ↑ side effect
- Half-life **about 58 days**
- Once steady state reached, very long washout
- Safe in renal disease (biliary excretion^{liver})
→ So in renal failure not need dose adjustment... or CKD



Amiodarone

Amiodarone

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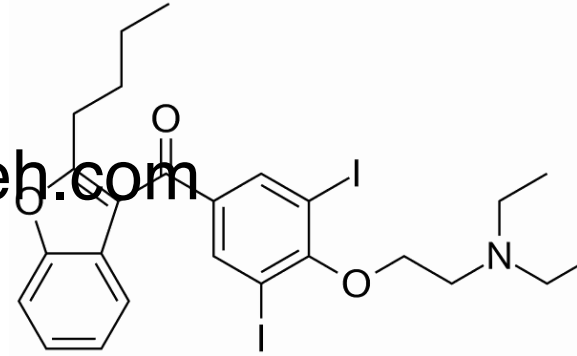
↑side effect كلما ازيد المريض دواء اكثر يعني [dose related]

- Many potential side effects related to accumulation
- Less likely at lower dosages
- Risk accumulates over time
- Young patients on indefinite therapy at greatest risk
- Often used in older patients

Amiodarone

Side Effects

- **Hyper and hypothyroidism** *کانه يکتنه دغ تر کيښه يود*
 - Contains iodine
- **Increased LFTs** *[liver fx tests] may lead to liver cirrhosis*
 - Usually asymptomatic and mild
 - Drug stopped if elevation is marked
- **Skin sensitivity to sun**
 - Patients easily sunburn



Wikipedia/Public Domain

Amiodarone

Side Effects

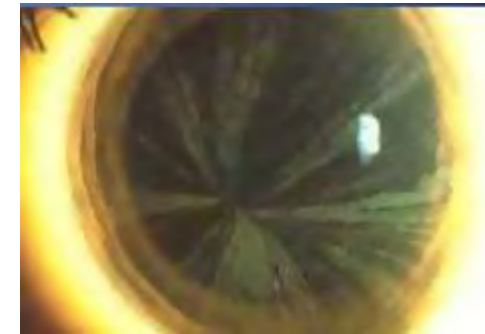
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* Vancomycin lead to red man \$...
* Chloramphenicol lead to baby grey \$...

- **Blue-gray discoloration** 
 - Less common skin reaction
 - "Blue man syndrome"
 - Most prominent on face
- **Corneal deposits** *بجوف د فلشز مناز light*
 - Secretion of amiodarone by lacrimal glands
 - Accumulation on corneal surface
 - Appearance of "cat whiskers" on cornea
 - Does not usually cause vision problems
 - See in many patients on chronic therapy



Abby Crawford/Youtube/Public Domain



Amiodarone

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Side Effects

- **Pulmonary fibrosis** *restrictive lung dz...*
- Most common cause of death from amiodarone
- Foamy macrophages seen in air spaces
- Filled with amiodarone and phospholipids
- “Honeycombing” pattern on chest x-ray
 - Bi lateral*
 - as Covid 19*



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Amiodarone

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Side Effects

- When starting amiodarone [Baseline]
 - ✓• Chest X-ray
 - ✓• Pulmonary function tests (PFTs)
 - ✓• Thyroid function tests (TFTs)
 - ✓• Liver function tests (LFTs)