

Cardiovascular Med Update



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North Central Heart
A Division of Avera Heart Hospital

Disclosures

Nothing to disclose

Objectives

- Review commonly used cardiovascular medications
- Understanding appropriate monitoring of medication
- Update on new cardiac medications

Who is on the front line?



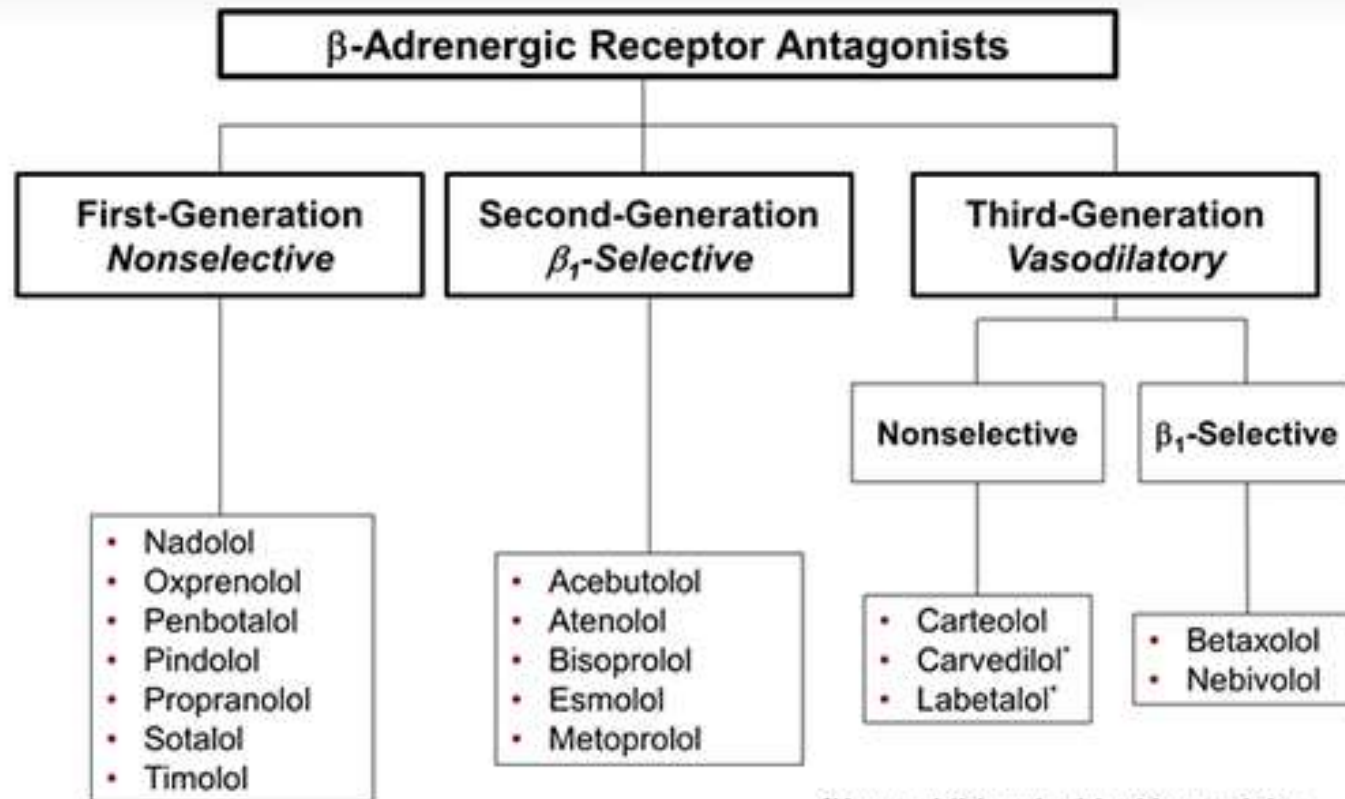
Med Reconciliation Matters

- Every visit, every time
- Have patients bring pills to visit
- Verify with pharmacy if needed
- Never ask “Everything the same as last time?”
- Helps to avoid lots of errors, confusion and phone calls



Beta Blockers

3 Generations of β -blockers



*Have additional α -blocking activity.

Manrique C, et al. *J Clin Hypertens*. 2009;11:369-375.^[1]



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Uses

❖ Nonselective

- Non-cardiac uses (Migraine, Tremor, Glaucoma)
- Cardiac uses heart rate control or hypertrophic cardiomyopathy

❖ Selective

- S/P Myocardial infarct (MI)/ Acute Coronary Syndromes (ACS)
- Anti-angina
- Tachycardia (ST or AF)/ Arrhythmia (PVCs)
- Hypertension
- Heart Failure
- Hypertrophic Cardiomyopathy

Side Effects

- Fatigue
- Bradycardia
- Hypotension
- Bronchospasm/Wheezing (non selective)
- Sexual dysfunction
- Worsening PVD-claudication, cold extremities, exacerbate Raynaud's

Pearls

❖ Only 3 indicated for heart failure

- Metoprolol Succinate (Toprol XL) ***NOT METOPROLOL TARTRATE***
- Carvedilol (Coreg)
- Bisoprolol (Zebeta)

❖ Should be titrated up slowly to maximum tolerated dose

❖ Post MI/ACS- should be started on all pt. unless contraindicated

❖ Recommendation for those with LVEF <40% indefinitely

❖ With normal LVEF-continue for 3 years

❖ Acceptable to continue beyond 3 years with normal EF

2017 ACC/AHA/HFSA Heart Failure Guidelines

Calcium Channel Blockers

Actions

	Dihydropyridines	Non-Dihydropyridines
Examples	Amlodipine, Felodipine, Nifedipine, Nicardipine	Diltiazem, Verapamil
Effect on SVR	Decrease	Decrease (possibly less than with dihydropyridines)
Effect on contractility (<i>inotropy</i>)	No effect	Decrease
Effect on sinus node rate (<i>chronotropy</i>)	No effect	Slows
Effect on AV node conduction velocity (<i>dromotropy</i>)	No effect	Slows
Effect on conduction within the atria and ventricles	No clinically significant effect	No clinically significant effect

Uses

❖ Dihydropyridines (Amlodipine, Nifedipine, Felodipine, Nicardipine)

- Potent vasodilator
- Little effect on contractility (squeeze) or conduction (heart rate)
- Hypertension
- Chronic stable angina

❖ Non-dihydropyridines (Diltiazem, Verapamil)

- Less potent vasodilator
- Greater depressive effect on contractility and conduction
- Hypertension
- Chronic stable angina
- Cardiac arrhythmias

Side Effects

- **Peripheral Edema**
 - Redistribution of fluid from vascular space to interstitium
 - Increase permeability of capillary beds (leaky vessels)
 - Dose dependent
- **Worsening heart failure** (non-dihydropyridines)
 - Negative inotropic effects (decreased heart muscle contraction)
- **Increased cancer risk?**
 - Identified by some observational studies (low power)
 - Most data does not support
- **Increased GI bleed risk?**
 - Not supported by evidence

PEARLS

- ❖ Non-dihydropyridines should not be used in heart failure
 - Decrease ventricular contractility (heart squeeze)
- ❖ Peripheral edema is common and dose dependent
- ❖ Does not “convert” atrial fibrillation, slows A-V conduction (rate control)

ACE Inhibitors

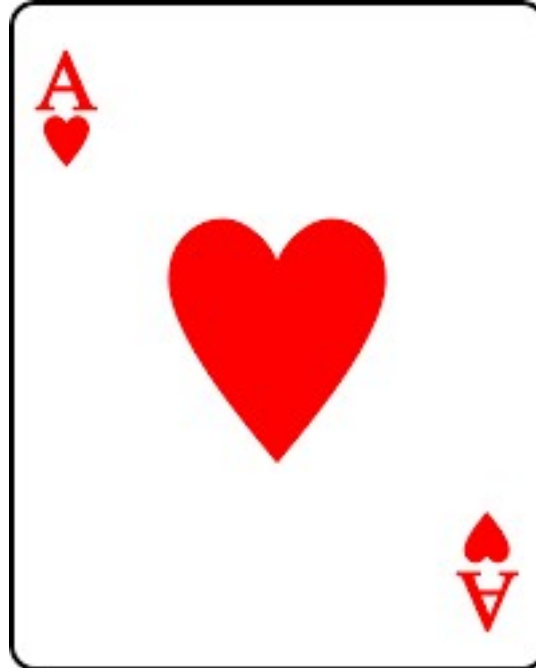
Brands	Generic
Aceon	Perindopril
Altace	Ramipril
Accupril	Quinapril
Capoten	Captopril
Vasotec	Enalapril
Prinivil, Zestril	Lisinopril
Lotensin	Benazepril
Univasc	Moexipril
Monopril	Fosinopril
Mavik	Trandolapril



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Uses

- Hypertension
- Myocardial Infarction (remodeling- reduces scar formation)
- Heart Failure
- Endothelial dysfunction (constriction & dilation of blood vessels)
- Diabetes (protection of kidneys)
- Scleroderma (auto immune connective tissue disorder)
- Migraines



Side Effects

- Dry hacky cough/ tickle in throat
 - Recommend changing to an ARB
- Hyperkalemia
 - Recommend BMP 2 weeks after starting or dose increases
- Dizziness
- Headache
- Loss of taste



PEARLS

- **Do NOT** use during pregnancy **Category X**
- NSAIDS decrease the effectiveness of ACE
- African American patients tend to have less blood pressure reduction when used as monotherapy (consider combination with thiazide diuretic)
- Use cautiously with chronic kidney disease
- Should check BMP after dose increases
- Should **NOT** be used in combination with Angiotensin Receptor Blocker(ARB)
- ❖ **May need to educate that it has uses outside of blood pressure**
 - **Provides protection for kidneys in diabetics**
 - **Reduces the pressure against which the heart pumps in HF**

Angiotensin Receptor Blockers

Angiotensin II Receptor Blockers

- Candesartan (Atacand)
- Eprosartan (Tevetan)
- Irbesartan (Avapro)
- Losartan (Cozaar)
- Olmesartan (Benicar)
- Telmisartan (Micardis)
- Valsartan (Diovan)

Side Effects

Same as ACE inhibitors except for cough

*All trade / brand / generic names are specific to the USA



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PEARLS

- Do not use in combination with ACE-I
- Olmesartan (Benicar) tends to reduce blood pressure most
- Losartan tends to reduce blood pressure least
- Monitoring similar to ACE-I



Direct Renin Inhibitors

❖ Aliskiren (Tekturna)

- Antihypertensive
- Inhibits conversion of angiotensin to angiotensin I
- Not commonly used
- No advantages or recommendations for specific conditions

Alpha Blockers

- Doxazosin (Cardura)
- Prazosin (Minipress)
- Terazosin (Hytrin)
- Used 4th line for HTN as adjunct therapy and another compelling indication (Benign prostatic hyperplasia)



Angiotensin Receptor- Neprilysin Inhibitors (ARNi)

- Sacubitril/Valsartan (Entresto)-currently only one on market
- Mechanism of action-Inhibits neprilysin which degrades vasoactive peptides= Blood vessel dilation, decreased extracellular fluid (ECF)



Considerations

- 36 hour washout of ACE-I prior to initiation
- 25/26mg daily is initial dosing
- BMP 1-2 weeks following initiation / titration
- Titration by doubling dose every 2-4 weeks
- Cost ~\$4500/yr
- Most common side effect is hypotension



Cholesterol Meds

- Statins
- Cholesterol Absorption Inhibitor
- Resins (bile acid sequestrants)
- Fibrates
- Niacin
- Omega-3 Fatty Acid Ethyl Esters
- Marine-Derived Omega 3 Polyunsaturated Fatty Acids (PUFA)
- PCSK9 Inhibitors



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Statins

Table. Classification of Statin Therapies

Statin	High-Intensity	Moderate-Intensity	Low-Intensity
	Lowers LDL >50%	Lowers LDL 30% to 49%	Lowers LDL <30%
Atorvastatin	40 mg – 80 mg	10 mg – 20 mg	
Rosuvastatin	20 mg – 40 mg	5 mg – 10 mg	
Lovastatin		40 mg	20 mg
Simvastatin		20 mg – 40 mg	10 mg
Pravastatin		40 mg – 80 mg	10 mg – 20 mg
Fluvastatin (XL)		80 mg	
Fluvastatin		40 mg (twice daily)	20 mg – 40 mg
Pitavastatin		2 mg – 4 mg	1 mg

LDL=low-density lipoprotein.

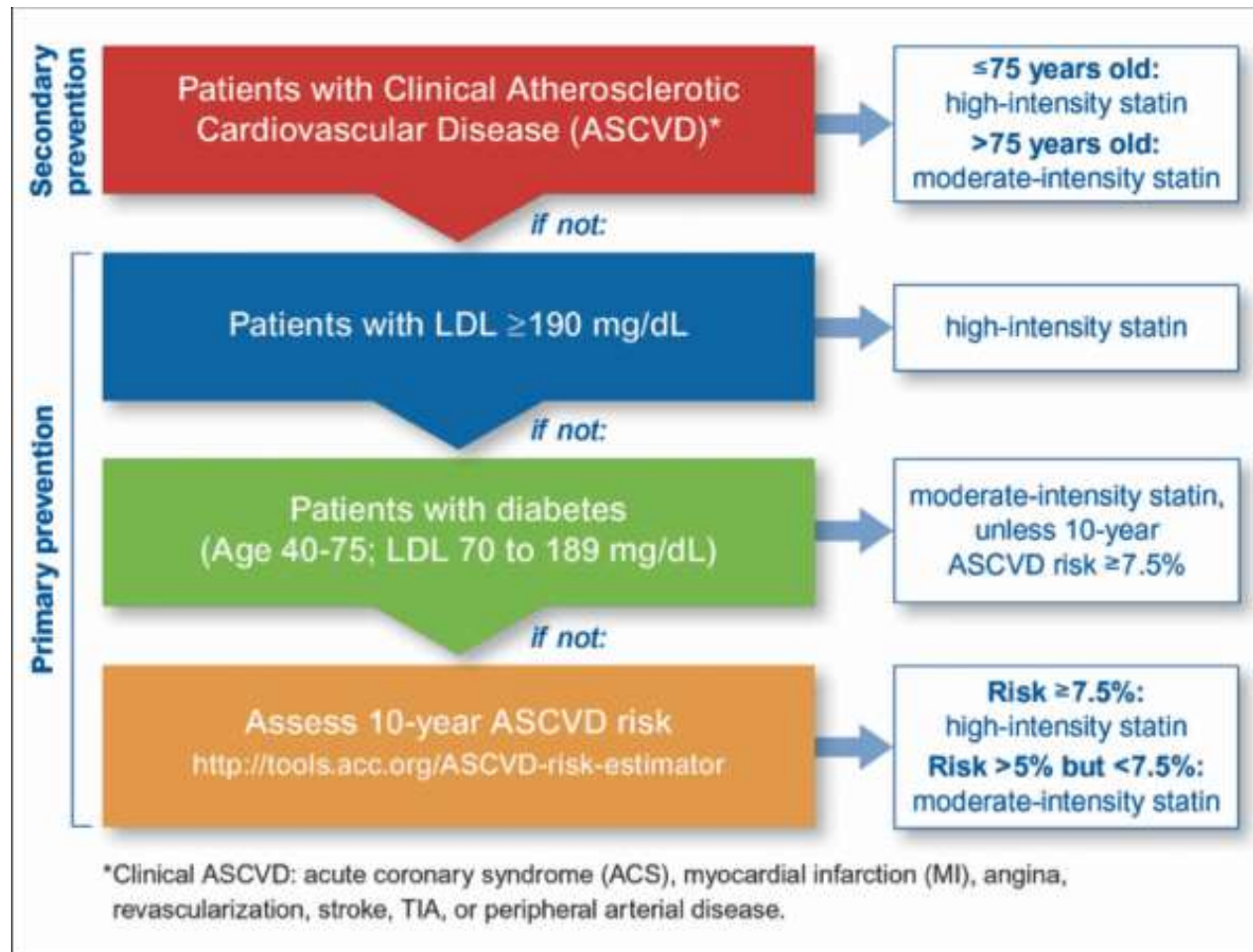
Source: *Circulation*. 2013;129(25 suppl 2):S1-S45.



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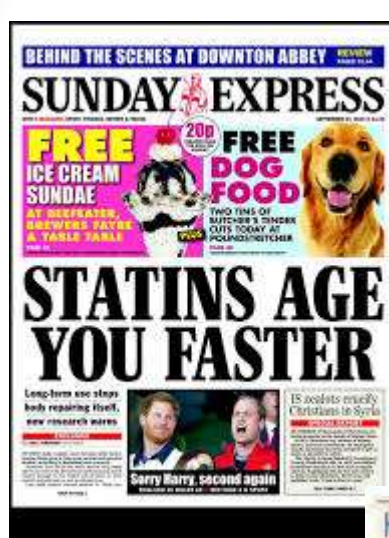
Who should get?



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(ACC 2018 Guideline on the Management of Blood Cholesterol)

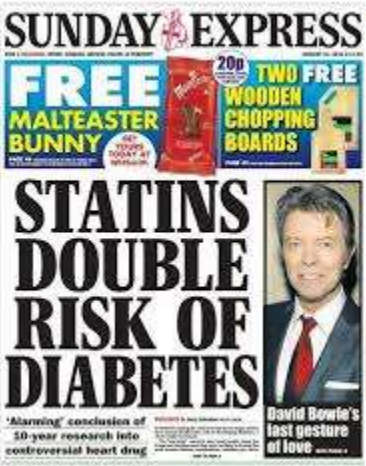
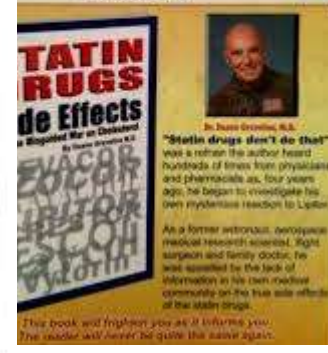
Bad Rap



\$STATIN NATION The Great Cholesterol Cover-Up



STATIN DRUGS Side Effects and the Misguided War on Cholesterol



Women exhausted due to statin drugs



Side Effects

What does the data say?

- ❖ Myalgia (muscle pain)/ Muscle weakness- most common
 - 29% of statin users report symptoms
 - Most RCT show muscle pain occurs at same rate in placebo
 - Most are able to take an alternative statin
- ❖ Rhabdomyolysis (muscle breakdown)-very rare (a few cases per million)
 - Risk is higher when used in high doses or combination with other meds
- ❖ Liver function elevations
 - If mild can continue meds
 - If 2-3X normal values can cut dose or change statin

❖ Increase in blood sugar

- If baseline sugar borderline may uncover diabetes
- Benefits of statin outweigh

❖ Memory loss

- Rare but can occur
- Resolves when meds stopped
- Some evidence that statin improve brain function in pt. with dementia

Other Cholesterol Meds

- ❖ **Cholesterol Absorption Inhibitor –ezetimibe (Zetia)**
 - Inhibits cholesterol absorption in small intestine
 - Statin intolerant or as adjunct
 - Decreased LDL 13-20%
 - GI side effects

- ❖ **Resins (bile acid sequestrants)- cholestyramine (Questran), colesevelam (Welchol), colestipol (Colestid)**
 - Binds bile acids in gut-prevents reabsorption of cholesterol
 - Constipation and GI side effects
 - No strong data that reduces ASCVD events
 - Contraindicated if TG >300
 - Fat soluble vitamin malabsorption (ADE&K)

- ❖ **Fibrates-gemfibrozil (Lopid), fenofibrate (Tricor), fenofibric acid (Trilipix)**
 - Decreases secretion VLDL and TG
 - Used with elevated TG
 - Concurrent use with statins = ↑ risk muscle / liver problems

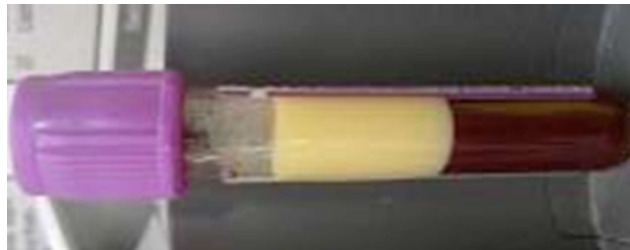


❖ **Niacin (Slo-Niacin, Niacor, Niacinol)**

- Raises HDL, Decreases LDL and TG
- Flushing, itching, hyperglycemia, GI upset, liver function abnormalities
- No data that it reduces CV events
- Potential harm when used with statin

❖ **Omega-3 Fatty Acids (Lovaza, Icosapent ethyl, Vascepa)**

- Decrease triglyceride, may elevated HDL
- Belching, fishy aftertaste
- Indication for TG > 500 despite diet modifications
- Reduce-IT trial-No data to support ↓ mortality in CVD or Pancreatitis
- Vital trial – not effective for primary prevention of CV disease



PCSK9 Inhibitors

❖ alirocumab (Praluent) , evolocumab (Repatha)

- PCSK9 is a pro-protein convertase involved in degradation of LDL
- A mutation of PCSK9 gene reduces the number of receptors and decreases the ability to clear LDL (bad cholesterol) from plasma
- These meds cause “Recycling” of receptors that clear LDL

- Injectable every 2 weeks
- **Adjunct to maximum tolerated statin or ezetimibe**
- 2018 ODYSSEY trial shows reduction in CV events
- Recent price drop from \$14,000 to \$5850/ year
- Minimal side effects-runny nose, injection site irritation
- For improved pre-authorization
 - Specify pt. on a low fat diet (<7% of kcal) ,exercise 150 min/wk, on “max tolerated statin”, list what meds failed, specify exact symptom in record



Nitrates

- ❖ Sublingual nitro, isosorbide dinitrate (Isordil), isosorbide mononitrate (Imdur), transdermal nitroglycerin
 - Dilation of coronary vasculature
 - Reduces myocardial O2 demand
 - Lowers blood pressure
 - Used in acute on chronic angina
 - Dinitrate used in combination with hydralazine for heart failure in pt who can't take ACE-I or African American patients
 - Most common side effect-head ache, usually dissipates after 3 days
 - Can cause dizziness, hypotension



Ranolazine

❖ Ranexa

- Mechanism of action unknown
- Used in chronic stable angina
- Anti-arrhythmic effects on atrial fibrillation and ventricular tachycardia
- Does not affect hemodynamics
- Can prolong QT interval – monitor EKG



Aldosterone Antagonists

❖ Spironolactone (aldactone), eplerenone (Inspra)

- Used in heart failure NYHA class II-IV with $EF \leq 35\%$
- Inhibits aldosterone thus decreasing sodium / fluid retention
- Monitor carefully for hyperkalemia, hyponatremia, renal function
- K+, Creat- 1 week, monthly X 3, then quarterly X 1 year then every 6 months
- Causes gynecomastia

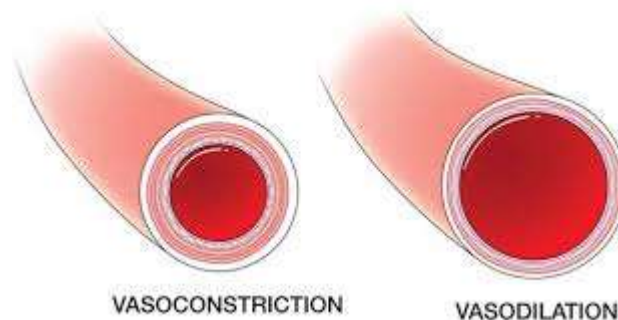


Arterial Vasodilators

❖ Hydralazine

❖ Minoxidil

- 3rd or 4th line therapy for HTN
- Used in CKD pt. who cannot tolerate higher ACE/ARB
- Hydralazine used in combo with Isordil for HF
- Dose adjustment for renal function
- Contraindicated in angina syndromes



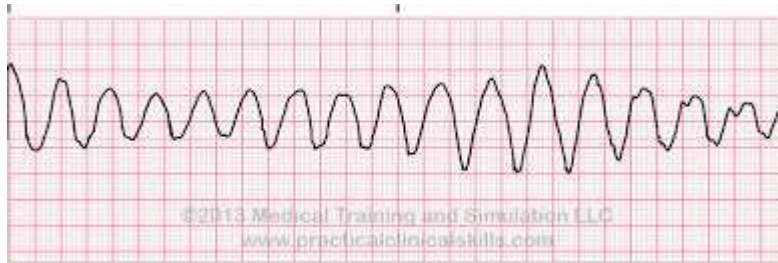
Antiarrhythmics

Vaughn Williams Classification of Antiarrhythmics				
Class		Mechanism		Examples
I	Sodium channel blockers	A	++/+++ Na channel blockade, prolonged refractoriness	• Quinidine • Disopyramide • Procainamide
		B	+ / ++ Na channel blockade, little effect on refractoriness	• Lidocaine • Phenytoin • Mexilitine
		C	+++ Na channel blockade, slight prolongation of refractoriness	• Flecainide • Propafenone
II	Beta-adrenergic blockers	Indirect Ca channel blockade by attenuation of adrenergic activation		• Propranolol • Esmolol • Sotalol
III	Potassium channel blockers	Prolong action potential refractoriness, delay repolarization		• Amiodarone • Ibutilide • Dofetilide • Dronedarone
IV	Calcium channel blockers	Directly inhibit Ca channel opening, slow SA pacemaker and conduction		• Verapamil • Diltiazem

PEARLS

- Most require Cardiology input / monitoring
- All require serial EKGs
- Some require lab monitoring
- EKG required after dose titration
- Have potential for pro-arrhythmic affects
- Some require hospitalization for initiation
- Use antibiotics with caution-pro-arrhythmic





- Washout of one med may be required before starting a new one
- Amiodarone requires baseline PFTs serial CXR, Thyroid studies, Liver function
- Amiodarone affects warfarin metabolism
- Dofetilide (Tikosyn) should not be refilled by anyone outside of cardiology
- If more than 3 doses of dofetilide (Tikosyn) missed, need to hospitalize for restart

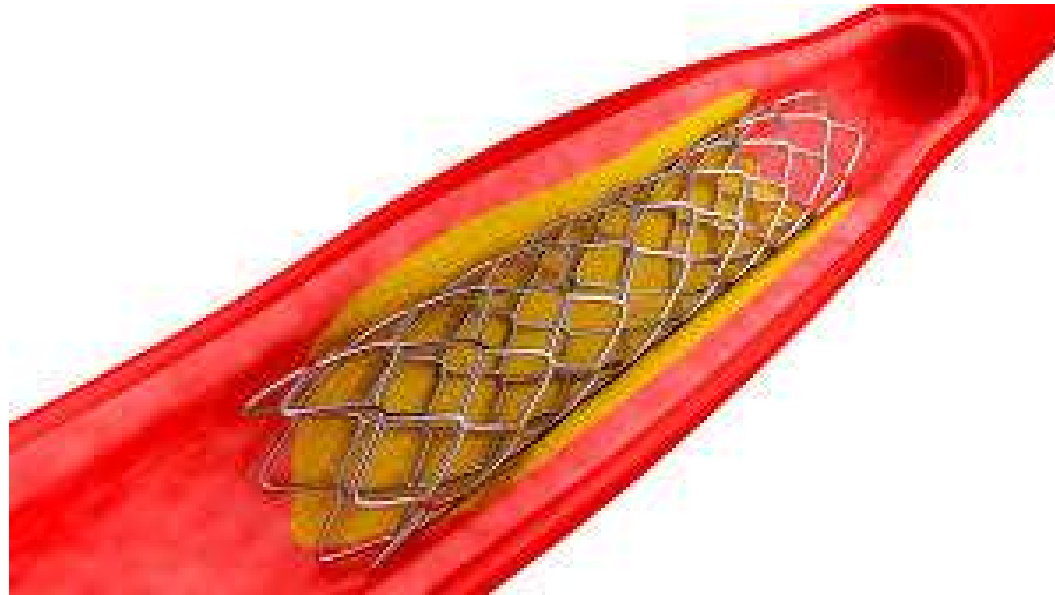
Oral Platelet Inhibitors

- ❖ Aspirin
- ❖ clopidogrel (Plavix)
- ❖ prasugrel (Effient)
- ❖ ticagrelor (Brilinta)
- ❖ ticlodipine (Ticlid)
- ❖ dipyridamole (Persantine)



Uses

- Inhibits platelet aggregation
- Acute coronary syndromes
- S/P stenting
- Chronic CAD
- CVA



PEARLS

- Duration of treatment highly patient dependent
- Commonly 1 year post drug-eluting stent or ACS in addition to ASA
- **STOPPING EARLY CAN LEAD TO ACUTE STENT THROMBOSIS**
- Can potentially be interrupted at 6 months but recommend Cardiology input
- Triple anticoagulation should peak your attention- may be indicated but verify
- PEGASUS trial showed ticagrelor superior to clopidogrel in ACS- this has driven increased use
- If cost is an issue-changing to clopidogrel requires loading dose
- Typically held 5-7 days before elective procedures

Anticoagulants

❖ Warfarin (Coumadin, Jantoven)

- Individualized dosing
- Requires INR monitoring
- Adverse affects- bleeding/ bruising
- Levels affected by other meds (antibiotics, amiodarone)
- Levels affected by diet (Vitamin K)
- Long duration of action (hold 3-5 days prior to procedures)
- Vitamin K is reversal agent
- Cost effective if labs not included in equation



❖ Direct Oral Anticoagulants (DOAC)

- Apixiban (Eliquis) BID dosing
- Dabigatran (Pradaxa) BID dosing
- Rivaroxaban (Xarelto) daily dosing
- Edoxaban (Savaysa) daily dosing



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- Used in treatment or prevention of venous thromboembolism (VTE), non-valvular a-fib (a-fib not caused by mitral valve abnormalities or mechanical valve replacement)
- Doesn't require lab testing to monitor levels
- Shorter duration of action
- Normalization of coag factors in 24-48 hours
- Contraindication for mechanical valves or valvular atrial fibrillation
- May require dose adjustment for renal fx, weight, age
- Monitor renal function to assure correct dosing
- Usually more costly but improving
- Reversal agents available but not widely (very costly)
 - Pradaxabind- for Dabigatran
 - Andexxa- for Apixiban & Rivaroxaban



Diuretics

❖ Loop-monitor electrolytes, esp K⁺

- Furosemide
- Bumetanide
- Torsemide-better GI absorption, bioavailability

❖ Thiazide- watch for hyponatremia

- Hydrochlorothiazide
- Chlorthalidone



but pineapple is a diuretic

❖ **Potassium Sparing**- Closely monitor electrolytes, renal fx

- Spironolactone (Aldactone)
- Triamterene
- Amiloride
- Used in heart failure NYHA class II-IV with $EF \leq 35\%$
- Inhibits aldosterone thus decreasing sodium / fluid retention
- K+, Creat- 1 week, monthly X 3, then quarterly X 1 year then every 6 months
- Causes gynecomastia

❖ **Other**

- Metolazone (Zaroxolyn)- potent, “rocket booster”, electrolyte derangement, avoid daily dosing
- Indapamide (Lozide)



PEARLS

❖ Uses

- Heart failure with Reduced Ejection Fraction (HFrEF)
 - Heart Failure with Preserved Ejection Fraction (HFpEF)
 - Hypertension
 - Spironolactone (Acne, PCOS)
-
- Do not refill without confirming lab monitoring
 - Discourage self- dosing
 - If orthostatic consider dose decrease
 - Will not likely help peripheral edema not related to HF



Digoxin

❖ Mechanism of action-blocks AV nodal conduction

- Slows ventricular response to high rate atrial arrhythmias
- DOES NOT “CONVERT” AFIB TO SR
- Has no effect on sinus rate



❖ Uses

- Rate control with atrial fibrillation
- Adjunct with Flecainide for AV nodal blocking
- HFREF for symptomatic patients despite GDMT
- Therapeutic digoxin level 0.5 -0.8 ng/mL
- No more than 0.125mg daily if age >70 or CKD

Ibravidine (Corlanor)

- Used to slow HR in heart failure NYHA class II- III (symptomatic)
- Must already be on GDMT (Guideline Directed Medical Therapy)
- Heart rate >70 at rest despite max dose β Blocker
- Contraindicated in atrial fibrillation
- Inappropriate sinus tachycardia



Questions



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