ACS
Cardio Modules
Lipids
CHF
Arrhythmias
Anti-Arrythmias
Atrial Fibrillation
Cerebrovascular Disease
Pulmonary Embolism
PAH
Hemodynamics
Orientation Links

II III aVf = RCA

Goldman-Cecil Medicine https://www-clinicalkey-com.proxy.lib.ohio-state.edu/#!/browse/book/3-s2.0-C20161036684

Cardio Modules

ACS OSUMC Guideline

Alg1: Initial ED Management: Initial HSTI: high-sensitivity troponin I (hsTI)

<52M <33F → onset of symptoms 3 hours; if <3hr repeat HSTI for change <15 if >3hr and no ischemic changes on ECG and HEART score ≤3
53-115M 34-115F → repeat HSTI in 1 hr; change <15 and HEART ≤3 dc if HSTI ≥15 or HEART ≥4, admit
>115 → admission, cardio consult, consider etiologies (PE, sepsis, myocarditis, etc.)

Symptoms of Possible ACS

- chest pain / discomfort with or without radiation to the arm(s), jaw, or epigastrium - Cardiac Arrest (after Return of Spontaneous Circulation)
- shortness of breath - weakness / lightheadedness / severe fatigue - diaphoresis - nausea

Atypical sx (females): fatigue, pain between shoulder blades or epigastric area, jaw pain; diabetics may only be short of breath

Alg2: inpatient evaluation: order 12 lead ECG (done read within 10 min of symptom onset or ED arrival); establish IV access; measure vitals pulse oximetry

- ASA81 x4 chew - supplmental O2 if <90%, resp distress, hypoxemia - nitroglycerin 0.4mg sl (unless PDE5 or hypotensive); consider infusion if persistent

Alg3: STEMI Alert activated hotline 6-8111 if ECG meets one of following:

>1mm ST elevation in ≥2 contiguous limb leads >2mm ST elevation in ≥2 contiguous precordial leads New left bundle branch block (LBBB)
ST segment depression in >2 precordial leads (V1-4) suggestive of transmural posterior injury

Medications

- ticagrelor 180mg PO preferred (unless ICH) or clopidogrel 600mg PO
- heparin 60u/kg bolus (max 4000u bolus) IVP
- morphine IV considered one time dose of up to 4mg prior to cardiac cath

Cath Lab: tirofiban 25mcg/kg IVP bolus (CrCl >60 initiate 0.15mcg/kg/min; CrCl <60 0.075mcg/kg/min)
Goal: patient in cath lab <30 minutes from onset of symptoms

Alg4: UA/NSTEMI

- focused H&P (CI to anticoag/antiplatelets; alternative dx like aneurysm, PE, pneumothorax, GERD, peridcardial effusion)
- diagnostic tests (CBC, Chem 7, INR, HSTI, Chest X-ray, serial ECGs)

Medications

- ticagrelor 180mg PO preferred (unless ICH) or clopidogrel 600mg PO
- oral beta-blocker in all patients without CIs in first 24hrs (CI: HF, Shock >70yo, SBP <120, HR >110 <60; PR interval >0.24, 2nd-3rd deg heart block, asthma/airway)
- heparin 60u/kg bolus (max 4000u bolus) IVP, then 12u/kg/hr
- routine opioids and morphine not recommended

Cath: Moderate/High risk: tirofiban; do not delay transport to cath lab to administer meds

ACS Management

Invasive evaluation: angiography → coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI) or medical therapy
Assess ejection fraction: if EF<35%, consider lifevest or short-term f/u for interal cardiac defibrillator (ICD)
Antiplatelet/anticoagulant therapy: medical therapy: ASA81 daily plus ticagrelor 90mg bid or clopidogrel 75mg for at least 12mo

- see antiplatelet therapy in patients with arterial stents guideline

Blood pressure: beta-blockers, ACE/ARB, aldosterone antagonists; goal <130/80
DM: preprandial <140, random <180
Lipids: high-intensity if <75yo; LDL<100 consider LDL<70
Lifestyle: 150min/wk exercise; cardiac rehab program 1-2 weeks post-dc
Weight: goal BMI 18.5-24.9, waist <35inF <40inM; Na 2300-4000mg/day, lower caffeine; lean meats chicken turkey fish preferred over beef pork; fruits veggies
Prevention: influenza; smoking, cardiac rehab; follow up 2-3 weeks with cardiovascular medicine

AMI Quality Measures

30-day AMI mortality 30-day readmission Risk-adjusted bleeding Acute kidney injury
Prescriptions for guideline-directed medical therapy upon discharge (i.e. aspirin, P2Y12 inhibitor (e.g Clopidogrel, Prasugrel, Ticagrelor), beta-blocker, ACEI or ARB, aldosterone antagonist, SL nitroglycerin, and statin) or clear documentation of reasoning for not ordering
--Type1/2 NSTEMI's count

STEMI and NSTEMI Powerpoint

MI Complications: Dysrhythmias, Acute CHF - 60%, Cardiogenic shock (Mortality 80%), Thromboembolism (Left ventricle/leg vein), Rupture of left ventricle (7-10d)
MI Dx:

- chest pain and ACS sx (ischemic vs. non-ischemic)
- ECG changes (ST elevation vs. non-ST elevation); 12 lead ECG
- cardiac marker elevation (Troponin I and T); CK and CPK-MB (cardiac specific)

Right Dominant (85% of popuplation); Inferior Wall MI (RCA → PDA PLA) - right side of heart driven by volume = preload
Left Dominant (7.5% of population); Anterior Wall MI (LCX → PDA PLA) - left side of heart impacted by pressure = afterload
Co-Dominant (7.5% of population); RCA → PDA; LCX → PLA
Papillary muscle; anterior has two supplies LAD and circumflex; posteromedial more susceptible to ischemia (PDA); so MI involving PDA → mitral regurgitation

RCA supplies: RA, RV, RVI bottom porotion of both ventircles and back of septum
LAD supplies: anterior wall of LV, septal region, conduction path (AV node, HIS bundle, Bundle branches)
right coronary artery (RCA) posterior descending artery (PDA) posterolateral artery (PLA) left anterior descending (LAD) left circumflex (LCX)

STEMI tx plans: beta-blockers, clopidogrel, heparin IV, reperfusion (≤12hrs), fibrinolysis, PCI, ACE/ARB, statins STEMI: time is muscle!
NSTEMI tx plans: NTG, beta-blockers, clopidogrel, heparin, GP IIb/IIIa inhibitors, reperfusion, ACE/ARB, statins

Causes of ACS

indirect: ↑myocardial workload, ↓coronary arterial blood flow, hypoxemia, cocaine/ethanol toxicity
- cocaine: blocks NE/DA reuptake, release endothelin-1 (vasoconst), decrease production of nitric oxide (vasodil) = profound vasoconstriction
  - ↑myocardial oxygen demand, ↑HR BP contractility; ↓oxygen supply (vasoconstriction);
  - causes pro-thrombotic state (stimulates platelet activation, alters pro/anti-coag factors, accelerates ASHD thick/hard heart walls)
  - cocaine-associated: atherosclerotic plaque rupture, coronary vasospasms, coronary thrombus formation (stim platelet activator), coronary artery dissection

direct: STEMI (coronary thrombosis, coronary artery spasm); NSTEMI (microembolization)

Progression of plaque: healthy coronary artery, atherosclerosis begins, plaque forms, then ruptures and platelet AAA (attraction, activation, aggregation)
- platelet attraction: thin wall vessel, lipid filled and covered with fibrous cap; cap ruptures causing platelet attraction and platelets cover rupture site
- platelet activation: collagen contact, conf shape change, IIb/IIIa receptors expressed: ADP/TxA2 activate platlets; 5HT/Epi vasoconst = reduce blood flow
- platelet aggregation: part of the sequence of events leading to formation of a thrombus (clot); fibrinogen starts to web area over to stabilize clot
  - coronary thrombus leads to myocardial necrosis; 500 heart cells die every second; release structural molecules CK-MB and Troponin I and T

Rigt: RCA supply: RA, RV, bottom porotion of both ventircles and back of septum; RCA supplies SA node
Left: Circumflex artery: LA, side and back of LV; LAD and bottom of LV and front of septum; LAD supplies conduction pathway and septal wall

ACS

https://www.uptodate.com/contents/table-of-contents/hospital-medicine/hospital-cardiovascular-medicine
https://www.uptodate.com/contents/clinical-use-of-coagulation-tests
https://www.uptodate.com/contents/heparin-and-lmw-heparin-dosing-and-adverse-effects
https://www.uptodate.com/contents/warfarin-and-other-vkas-dosing-and-adverse-effects
https://www.uptodate.com/contents/direct-oral-anticoagulants-doacs-and-parenteral-direct-acting-anticoagulants-dosing-and-adverse-effects

Here are the readings and outline for October 4th. I have pointed you into the right direction for each question. For our Acute Coronary Syndrome discussion, the AMI review article and supplement is a helpful overview of all the details and then the guidelines have nice figures to help describe recommended durations and agent selection. The 2016 DAPT guidelines are the most recent guidelines to refer to for recommended durations of DAPT. The Switching article helps to switched between P2Y12 inhibitors. This part of the discussion will not focus on the intravenous agents (Glycoprotein IIb/IIIa inhibitors, thrombolytics, cangrelor).

P2Y12 inhibitors
- inhibit binding of ADP to P2Y12 receptor (↑cAMP)
- inhibits platelet activation, leading to inhibition of platelet aggregtion
(normal: ↑ P2Y12 receptor activation → Gi protein → ↓cAMP → ↑ platelet activation → ↑ GPIIb/IIIa expression → ↑ platelet aggregation)
ADP binds to P2Y12 receptor; sends signal change in GB IIb/IIIa receptor, allows fibrinogen to bind to that IIb/IIIa receptor, now aggregation

GPIIb/IIIa antagonists
inhibits platelet aggregation; bind to and inhibit binding of fibrinogen to the platelet GP IIb/IIIa

Aspirin
- inhibits COX irreversible thus ↓TXA_2 formation through preventing conversion of arachidonic acid to PGH_2.
- COX-1 consitutive (always on) → TXA_2 => platelet aggregation, vasoconstriction COX-2 inducible (turned on) → PGI_2 => inflammation, vasodilation
(normal: TXA_2 → Gq → ↑PLA_2 = platelet aggregation)

Basics of ACS

1. Define the term acute coronary syndrome (how does this differ from chronic coronary syndrome or stable ischemic heart disease)
acute coronary syndrome (ACS): unstable angina (UA), acute non-ST elevation myocardial infarction (NSTEMI), acute ST elevation myocardial infarction (STEMI)
  - applied to patients in whom there is a suspicion or confirmation of acute myocardial ischemia or infarction
chronic coronary syndrome (CCS) = stable ischemic heart disease (SIHD): based on a classic history of angina pectoris in the presence of either risk factors for or known atherosclerotic cardiovascular disease
  - angina pectoris, or angina for short, refers to chest discomfort that occurs when myocardial oxygen demand exceeds oxygen supply.
  - stable angina refers to chest discomfort that occurs predictably and reproducibly at a certain level of exertion and is relieved with rest or nitroglycerin.

https://www.uptodate.com/contents/acute-coronary-syndrome-terminology-and-classification

- Acute myocardial infarction: an event of myocardial necrosis caused by an unstable ischemic syndrome; plaque ruptures and occludes artery - forms embolus; interrupts blood flow to the heart
    - o NSTEMI: + troponin; no ST; usually results from partial occlusion
    - o STEMI: + troponin; + ST; usually results from totally occluding thrombus
    - o S/sx: chest pain/tightness, SOB, diaphoresis, radiation head, neck jaw, N/V, fatigue (women, elderly pts, pts w/ HF, and DM often present with unusual sx)
    - o Dx: clinical eval, EKG, biochemical testing, invasive/noninvasive imaging, pathological eval
    - o Type 1 = due to coronary atherothrombosis
    - o Type 2 = due to a supply-demand mismatch that is not the result of acute atherothrombosis
    - o Pathology: rupture or erosion of vulnerable plaque
- Chronic: caused by plaque obstructing artery; occurs with exercise
    - o > 1yr after ACS event (SIHD)
- Unstable angina: occurs at rest
    - o - troponin; +/- ST
- Labs: troponin, BNP (HF, PE, ESRD), EKG, electrolytes (K/Mg), Chem/SCr, coags, H/H, platelets

Left heart cath: for ACS, thru arterial side into coronary arteries, inject contrast, xray imagery – radial or femoral or brachial (rare)
Right heart cath: venous side, filling pressures in right for HF patients
CAC score
Stress tests
Echo-wall motion abnormalities changes in EKG
MRI
Nuclear

2. Referring to Figure 1 of the AMI review article, describe the difference in the pathophysiology of a non-thrombotic plaque and a thrombotic plaque.
Platelets adhere, are activated, and aggregate. Thrombin is generated, accelerating platelet activation, and fibrin formed, trapping RBCs, and forming a thrombus.
  - A totally occluding thrombus typically leads to STEMI.
  - Partial occlusion, or occlusion in the presence of collateral circulation, result in NSTEMI or UA (NSTE-ACS), often with ST-depression.

UA, NSTEMI (2/3 of AMIs), STEMI (1/3 of AMIs)

Nonthrombotic – supply-demand imbalance
- No ST-segment elevation
- No increase in biomarker level = unstable angina (demand-related)
- Increased biomarker level = non-STEMI (type 2)

ACS (atherothrombotic) - partially or fully-occluding thrombus
- No ST elevation + no increase in biomarker level = unstable angina (thrombosis-related)
- No ST elevation + increased biomarker level = non-STEMI (type 1)
- ST segment elevation + increased biomarker level = STEMI (type 1)

(see the fourth universal definition of MI document for more details on the types of MI)
Myocardial infarction implies (biochemical) evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. Myocardial typing is defined by the ACC/AHA/ESC 3rd universal definition of (acute) myocardial infarction. Myocardial infarction in the primary endpoint will include all nonprocedural MI's.
i.e., Type 1, 2 and 4b myocardial infarction and type 3 as part of cardiovascular death.

Type 1 myocardial infarction is a spontaneous MI related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries leading to decreased myocardial blood flow or distal platelet emboli with ensuing myocyte necrosis.

Type 2 myocardial infarction is myocardial infarction secondary to an ischemic imbalance. In instances of myocardial injury with necrosis, where a condition other than coronary artery disease contributes to an imbalance between myocardial oxygen supply and/or demand, the term 'MI type 2' is used. In critically ill patients, or in patients undergoing major (non-cardiac) surgery, elevated values of cardiac biomarkers may appear.

Type 3 myocardial infarction is death due to myocardial infarction. This is patients with symptoms or clinical features of myocardial ischemia prior to death.

Type 4a myocardial infarction is myocardial infarction related to percutaneous coronary intervention (PCI). Myocardial infarction associated with PCI is arbitrarily defined by elevation of cardiac troponin values >5 x 99th percentile upper reference limit in patients with normal baseline values or a rise of cardiac troponin values >20% if the baseline values are elevated and are stable or falling.

Type 4b myocardial infarction is associated with stent thrombosis detected by coronary angiography or at autopsy. Type 5 myocardial infarction is associated with coronary artery bypass grafting and is arbitrarily defined by elevation of cardiac biomarker values >10 x 99th percentile upper reference limit in patients with normal baseline cardiac troponin values (≤99th percentile upper reference limit).

3. What three things do we look at to differentiate between the three types of acute coronary syndromes?
the triad of chest discomfort, ECG abnormalities, and elevated blood biomarkers (troponin) of myonecrosis

UA	sx		
NSTEMI	sx	troponin	
STEMI	sx	troponin	EKG ST-elevation

<u>Aspirin</u>
4. What dose of aspirin is recommended for patients with an acute coronary syndrome?
ASA325 x1 then ASA81 daily

5. How long is aspirin recommended? Does this vary depending on STEMI vs. NSTEMI? (See review article, and p. 1093 of the ACC/AHA DAPT Guidelines; compare recommendation in STEMI and NSTEMI guidelines)
ASA81 daily (range 75-100mg)

PLATO: ticag with higher asa more ischemic events
clopidogrel: LD 600 except 300 maybe older or if on prev clopidogrel therapy

<u>P2Y12 Inhibitors</u>
6. What P2Y12 inhibitors are used in patients with an acute coronary syndrome? What are some of the differences between these options (contraindications, reversibility, platelet binding, etc)?

ticagrelor: 30min onset to 50% platelet inhibition, 88% max inhibition, 3-5d offset, reversible, CI ICH; use in ACS or hx MI
prasugrel: 60min onset to 50% platelet inhibition, 79% max inhibition, 7-10d offset, irreversible, CI ICH or hx TIA/stroke; use in ACS undergoing PCI
clopidogrel: 2-6h onset to 50% platelet inhibition, 35% max inhibition, 5-10d offset, irreversible; use in ischemic stroke, stable CAD, PAD, ACS, PCI
cangrelor: decr rate of thrombotic CV events (including stent thrombosis) in <u>patients not treated with an oral P2Y12 inhibitor or GP IIa/IIIb inhibitor</u> undergoing PCI

	clopidogrel	**prasugrel**	**ticagrelor**	**cangrelor**
Loading Dose	600mg PO	60mg PO	180mg PO	30 mcg/kg IV
Maintenance Dose	75 mg PO qday	10mg PO qday	90mg PO bid	4 mcg/kg/min for >2hrs or duration of PCI then 0.75 mcg/kg/min
Time to 50% plt inhibition*	2-6 hrs	1 hr	30 min	2 min
Max platelet inhibition	35%	79%	88%	>95%
Offset of action	5–10 d	7–10 d	3–5 d	**60 min**
Half-life	Parent 6 h, Active 30 min	Active 7 h	Parent 7 h, Active 9 h	3-6 min
Excretion	Renal 50%, Fecal 46%	Renal 68%, Fecal 27%	Renal 26%, Fecal 58%	Renal 58%, Fecal 35%
Receptor blockade	Irreversible	Irreversible	Reversible *Noncomp*	Reversible
Prodrug	Yes	Yes	No	No
CYP drug interaction	2C19	No (3A4, 3B6)	3A4	No (plasma)
Approved settings	ACS, stable CAD, PCI, PAD, ischemic stroke	ACS undergoing PCI	ACS or history of MI	PCI w or w/o ACS

Limitations ICH = intracranial hemorrhage	- modest inhibition - delayed onset - genetics (2C19, polymorphisms) - in DM, obese not as responsive - d/c 5 days prior to CABG	- higher efficacy, worse bleed risk* - CI: ICH, Hx TIA/stroke - in 75yo, use if DM + STEMI - precautions <60kg, bleeding - d/c 7 days prior to CABG	- higher efficacy, equal bleed risk - CI ICH - use ASA less than 100mg - SE: bradycardia, dyspnea - simva/lova max 40mg - d/c 5 days prior to CABG	
Switching	C→P 60mg LD irrespective of time C→T 180mg LD irrespective of time	P→C 600mg LD 24hrs after last P P→T 180mg LD 24hrs after last P	T→C 600mg LD 24hrs after last T T→P 60mg LD 24hrs after last T	

stopping 25%, mortality 50% if ischemic sx

7. Which P2Y12 inhibitor is preferred in patients with an acute coronary syndrome? What are reasons you might choose one of the other two options? Does it make a difference how the acute coronary syndrome is treated which agent you select?

reasonable to choose ticagrelor over clopidogrel in ACS patients with an early invasive strategy or PCI (stents, balloon angioplastides)
reasonable to choose prasugrel over clopidogrel in ACS patients who under go PCI who are not at high risk of bleeding (stroke, TIA, intracranial hemorrhage)
reasonable to choose ticagrelor over clopidogrel in ACS patients who are managed without intervention, only medical therapy (no stent, no PCI, no prasugrel)

ticagrelor is preferred – fastest onset and highest platelet inhibition

8. How long is a P2Y12 inhibitor recommended? Does this vary depending on STEMI vs. NSTEMI? Describe the difference between Stable Ischemic Heart Disease (SIHD) and Acute Coronary Syndrome (See DAPT Guidelines)

First question is is this an ACS – is it unstable angina, NSTEMI, or STEMI? Or are they SIHD?

ACS, BMS	minimum of 1 month; ideally 12 months	clopidogrel, prasugrel, ticagrelor
ACS, DES	minimum of 6 months; ideally 12 months	clopidogrel, prasugrel, ticagrelor
SIHD, BMS	minimum of 1 month; consider 12 months	clopidogrel
SIHD, DES	minimum of 3-6 months; consider 12 months	clopidogrel
Med Mgmt	ideally 12 months	clopidogrel, ticagrelor

clopidogrel, prasugrel, ticagrelor – LD given at time of PCI (percutaneous coronary intervention); followed by maintenance dose for at least 1 year

SIHD treated with PCI
In patients with SIHD treated with DAPT after BMS (bare metal stent) implantation, P2Y12 inhibitor therapy (clopidogrel) should be given for a minimum of 1 month.
In patients with SIHD treated with DAPT after DES (drug-eluting stent) implantation, P2Y12 inhibitor therapy (clopidogrel) should be given for at least 6 months.
In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.

ACS treated with PCI
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after BMS or DES implantation, P2Y12 inhibitor (clopidogrel, prasugrel, ticagrelor) should be given for at least 12 months.
In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation, it's reasonable to use ticagrelor in preference to clopidogrel for maintenance P2Y12 inh.
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIA, it is reasonable to choose prasugrel over clopidogrel for maintenance P2Y12 inhibitor therapy

9. How do we switch between P2Y12 inhibitors? What impact does the timing of the switch have on those recommendations? (See the Switching P2Y12 doc)
ticagrelor → clopidogrel - C 600mg LD 24 hours after last T dose
ticagrelor → prasugrel - P 60mg LD 24 hours after last T dose
clopidogrel → either - LD irrespective of timing and dosing

C→P 60mg LD irrespective of time C→T 180mg LD irrespective of time	P→C 600mg LD 24hrs after last P P→T 180mg LD 24hrs after last P	T→C 600mg LD 24hrs after last T T→P 60mg LD 24hrs after last T

<u>Other agents</u>
9. What do beta-blockers do for patients with an acute myocardial infarction? (see Table 2 of the AMI review article)
- reduce the incidence of tachyarrhythmias
- beta-blocker should be started in the first 24hr if there is no heart failure, low-output state, risk for shock, or other contraindication

Decrease myocardial oxygen demand by slowing the conduction through the AV node-> decreasing heart rate, decreasing contractility, decreasing blood pressure, as well as improve morbidity and mortality and reduce the incidence of tachyarrhythmias.

Which patients should not receive a beta-blocker?
Beta-blockers should be avoided for patients who have uncompensated heart failure, SA or AV node disease without pacemaker (eg. severe sinus bradycardia, heart block), or cardiogenic shock.

10. What do ACEI/ARB do for patients with an acute myocardial infarction? What patients benefit from an ACEI/ARB? (see Table 2 of the AMI article)
- LVEF <0.40, HTN, DM, CKD

ACE inhibitors should be started in all patients with LVEF of <0.40 and in those with hypertension, diabetes mellitus, or stable chronic kidney disease; ACE inhibitors may also be reasonable in all other patients with cardiac or other vascular disease.
- an ACE inhibitor (preferably) or ARB should be started in all patients after acute MI
- especially those with HF, LVEF <40%, CKD, DM, or other cardiac/vascular disease
- mortality benefits; prevent stroke, MI, death; decreases remodeling and progression to HF

11. What patients should be started on an aldosterone antagonist after and NSTEMI or STEMI? (see the NSTEMI and STEMI guidelines)
- decrease remodeling and progression to HF
- consider especially EF <40% (and DM)

NSTEMI
According to the 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation Acute Coronary Syndromes, aldosterone blockade is recommended for post-MI patients who are without significant renal dysfunction (creatinine > 2.5 mg/dL in men of > 2.0 mg/dL in women) or hyperkalemia (K+ > 5.0mEq/L) who are receiving therapeutic doses of ACEi and beta blocker and have a **LVEF 40% or less, diabetes, or heart failure.**
STEMI
Should be given to patients with STEMI and no contraindications who are already receiving an ACE-I and beta blocker and who have an EF $\leq$ 40% and either symptomatic HF or DM
Data for this comes from the EPHESUS study, which established the benefit of eplerenone added to optimal medical therapy in eligible patients. Early initiation (<7d) significantly reduced the rates of all-cause mortality, sudden cardiac death, and CV mortality/hospitalization

The big thing you will notice is that the NSTEMI guidelines used the word therapeutic doses of an ACEi and beta-blocker, but the STEMI guidelines do not. There is no definition of what therapeutic dose is either.

12. What statin therapy is recommended for a patient with an acute coronary syndrome?
- high-intensity <75yo unless not tolerated
- pleiotropic effects – antioxidant, plaque stabilizing, antiinflammatory
(obtain a fasting lipid profile, preferably within 24h)

Other
- PPIs should be used in patients with a history of prior GI bleeding treated with DAPT (Class I).
- increased risk of GI bleeding, including advanced age and concomitant use of warfarin, steroids, or NSAIDs, use of PPIs is reasonable (Class IIa).

Lipids

guidelines-misc.doc
Kelly Bartsch

Low-intensity (<30%)	simva 10	prava 10-20	lova 20 fluva 20-40	
Moderate-intensity (30-49%)	simva 20-40	atorva 10 (20)	rosuva 10 (5)	prava 40 (80) lova 40 (80)fluva 80
High-intensity (>50%)		atorva 40 (80)	rosuva 20 (40)	

Focus on:

1. Basics of cholesterol – which kinds are atherogenic? What component makes it atherogenic?
2. Risk assessment [see table below]

Population		Statin Intensity	LDL threshold for intensification	Preferred non-statin agent
Secondary Prevention	Not very high risk, <75yo	high	70	ezetimibe
	Not very high risk, >75yo	mod-high, continue high	------	------
	Very high risk	high or maximal	LDL >70 on max tolerated statin	ezetimibe
			LDL >70 or nonHDL >100 on max LDL lowering therapy	PCSK9i
Severe hypercholesterolemia	20-75 yo	high	LDL >____ or <50% reduction	
			<50% reduction with TRG <300	_____, then _____
	30-75 yo		LDL >____ on statin + ezetimibe	
	40 – 75 yo and baseline LDL >220 mg/dL		LDL >____ on statin + ezetimibe	
Diabetes	20-39yo with DM risk factors	low	------	------
	40-75yo	mod	------	------
	Multiple ASCVD risk factors		------	------
	10yr ASCVD risk >20%	high	>50% reduction of LDL	
	>75yo		------	------
Primary Prevention, ages 40-75, not in categories above	Low risk	lifestyle	------	------
	Borderline risk, with risk enhancers	mod	------	------
	Intermediate risk	mod	------	------
	High risk	high	------	------

<u>Antihyperlipidemics – Primary Literature</u>

For each study, focus on:

1. Basic study information [see table below]
2. Role of the medication in treating hyperlipidemia and/or patients with a history of ACS

Trial (year)	Question	Population	Results / Conclusions	Notes
HD-ROWS (2012)	rosuva80 qweek comparable to atorva10 qday	18-65yo, LDL>100, TGs <200	changes in HDL, TGs, hsCRP nonsignificant	
IMPROVE-IT (2015)	simva40-eze vs simva vs placebo CV death, nonfatal MI, UA hosp, coronary revasc, nonfatal stroke	post ACS LDL 50-100/125	eze lower LDL, improved CV outcomes	
REDUCE-IT (2018)	icosapent ethyl 2g bid with TGs <500		elevated TGs despite statin use, risk of ischemic events, CV death, sign lower	
EVOPACS (2019)	evolocumab PCSK9i post-ACS safety	very high-risk ACS, most not on statins	PCSK9i added to high-intensity statin, substantial LDL lowering; >95% pt target levels	

Know your CRAP and treat it PACK
Contractility
Rate
Afterload –(L)SVR – (R)PVR
Preload –CVP/RAP –LAP/PADP –PAP

Preload
Afterload
Rate
Contractility

Chronic Heart Failure

Here are the readings for our Chronic Heart topic discussion next week.

I would suggest starting with the HF drug review (Lancet 2019) and Metra (Lancet 2017). Then follow by reading the TRED –HF study. The last article is a reference for you which covers drugs which may exacerbate HF, some drugs may surprise you. I don't expect you to read it for Tuesday's discussion , but something you should keep for your files.

This will be an discussion not a lecture so please come prepared to the teach each other the following items
Issues to cover :

1. Types of Heart failure- common etiologies
2. What can cause an HF exacerbation
3. Non drug options all patients should be aware of
4. Guideline directed medical therapy – we will break this down by class- please know MOA, side effects and how to initiate therapy
5. Withdrawing drug therapy

https://www.uptodate.com/contents/heart-failure-clinical-manifestations-and-diagnosis-in-adults
https://www.uptodate.com/contents/overview-of-the-management-of-heart-failure-with-reduced-ejection-fraction-in-adults
https://www.uptodate.com/contents/initial-pharmacologic-therapy-of-heart-failure-with-reduced-ejection-fraction-in-adults
https://www.uptodate.com/contents/pathophysiology-of-heart-failure-with-reduced-ejection-fraction-hemodynamic-alterations-and-remodeling

Chronic Heart Failure Topic Discussion

- Clinical syndrome characterized by fatigue and dyspnea, induced by left ventricular dysfunction, often w/ signs of congestion
- NYHA classification – symptom severity

HFpEF 2/2 HTN Southeast; big heart muscle rule out amyloid
HFrEF 2/2 CAD

Types of HF – Common Etiologies

- HFrEF reduced EF (< 40%)
  - Etiology: CAD, peripartum, valvular heart disease (mitral regurg, tricuspid regurg)
  - risk factors lead to cardiac injury → development of myocardial dysfunction → worsening sx until end stage HF
  - Cardiac chamber enlargement due to cardiac remodeling, weak contraction (deficient inotropism), elevated filling pressures (preload), and increased peripheral resistance (afterload)
  - Inability to provide adequate CO at rest or w/ exercise
  - Myocardial interstitial fibrosis stiffens the heart and creates basis for arrhythmias
- HFpEF – preserved EF (> 50%) https://www.uptodate.com/contents/pathophysiology-of-heart-failure-with-preserved-ejection-fraction
  - Etiology: HTN, amyloid
  - s/sx of HF but preserved EF
  - patients tend to be older and have more comorbidities (e.g., HTN, DM, Afib, anemia, COPD)
  - tx = management of sx and comorbidities
  - no GDMT >>> diuretics for congestion, control ventricular rate, consider spirono (TOPCAT trial), treat HTN
- HfmrEF https://www.uptodate.com/contents/treatment-and-prognosis-of-heart-failure-with-mid-range-ejection-fraction

Causes of HF Exacerbation

F – Failure to comply with fluid/sodium restriction, food, fever
A – Arrhythmia (atrial fibrillation, esp. if LA > 5cm), Apnea (sleep), ACS, adherence
I – Ischemia (MI), infection
L – Levothyroxine – hyper/hypothyroidism
U – Uncontrolled HTN, Uremia
R – Renal Failure
E – Embolus (pulmonary), Electrolyte disturbance
D – Drugs: associated with worsening HF
– NSAIDs – Corticosteroids – Thiazolidinediones – NonDHP CCBs
– Probenecid, Bile Acid Sequestrants – New initiation/titration of BB
– Anti-arrhythmics that are negative inotropes, decrease CO further (Class I - quinidine, propafenone; Class III - dronedarone)

HF predisposed to Vfib

Non-Drug Options Patients Should be Aware of

- Decrease alcohol consumption
- Sodium restriction → 2-3g
- Exercise
- Weigh at same time every day → 2-3 lbs/day or 5lbs/wk → call doctor
- 2 L fluid restriction (EVERYTHING liquid)

GDMT

Drug	MOA	Side Effects	Initiation
RAAS inhibitors **ACE** – lisinopril, enalapril, captopril **ARB** – losartan, candesartan, valsartan ARNI – sacubitril/valsartan	ACE - Decrease preload by inhibiting RAAS, decrease afterload by inhibiting angiotensin II (vasoconstrictor) ARB – NI – inhibit breakdown of BNP → increased secretion of sodium and water	Hyperkalemia	
β-blockers (carvedilol, metoprolol succinate, bisoprolol)		Hypotension, fatigue, bradycardia	
MRA – spironolactone, eplerenone		Hyperkalemia, SCr	
Diuretics – furosemide (IV 100% bioavailable), torsemide, bumetanide	Reduce preload	Hypokalemia, high uric acid (gout)	

Withdrawing Drug Therapy
"In conclusion, in this pilot study, withdrawal of pharmacological heart failure treatment in patients with recovered dilated cardiomyopathy was associated with relapse in 40% of cases. This finding suggests that complete withdrawal of treatment should not usually be attempted in such patients"

- The three major determinants of the left ventricular (LV) performance (reflected as stroke volume) are the preload (venous return and end-diastolic volume), myocardial contractility (the force generated at any given end-diastolic volume), and the afterload (aortic impedance and wall stress).
- Remodeling is defined as an alteration in the structure of the heart in response to hemodynamic load and/or neurohormonal activation. Pathologic remodeling may occur with pressure overload (eg, aortic stenosis, hypertension), volume overload (eg, valvular regurgitation), or following cardiac injury (eg, myocardial infarction [MI]). In each of these settings, remodeling may transition from an apparently compensatory process to a maladaptive one.
- The hypothesis that remodeling is pathogenically important in HF is supported by the observation that certain therapies (eg, angiotensin converting enzyme inhibitors) that improve survival in patients with HF can slow or reverse certain parameters of cardiac remodeling.

- Reducing afterload in patients with HF via the administration of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or direct vasodilators (eg, hydralazine) has the dual advantage of increasing cardiac output and, over the long term, slowing the rate of loss of myocardial function.

Arrythmias

https://www.cvphysiology.com/Arrhythmias/A006
https://www.cvphysiology.com/Arrhythmias/A004

Chapter 12 - Clinical Aspects of Cardiac Arrhythmias
BRADYARRHYTHMIAS
Sinoatrial Node
Escape Rhythms
Atrioventricular Conduction System

TACHYARRHYTHMIAS
Supraventricular Arrhythmias
Ventricular Arrhythmias

Alt impulse formation:
- SA not firing; breakdown of normal (SA stops) normal SA 60-100bpm, conduct thru AV node J point right after QRS QRS <100 PR <200
- automaticity: ↑ rate of firing
- triggered activity
- ectopy

Alt impulse conduction:
- reentry
- heart blocks

Slow
- bradycardia: sinus
- SSS
- pauses
- escape:
  - junctional escape rhythm; AV takes over 40-60bpm; no P-wave or within QRS and flipped upside down if >60bpm, accelerated junctional rhythm
  - idioventricular: (IVR) rate <40bpm - if >40bpm, accelerated IVR

AVBlocks

tiny block 40ms; big block 200ms

DAD- DIG leads to hyperCa
EAD- QT TdP

Tachy- QRS wide or narrow 100ms
- wide: VT, VF, PVCs, SVT with aberrency - PVCs, Vtach, polymorphic, monomorphic
- narrow: reg vs. irreg R-R interval
  - irreg: AF (starts LA, unstable junction from pulm vein to mycardium)
  - reg: Aflutter typical: can do CTI (cavotricuspid isthmus) scarring in RA atypical: in LA, post AF ablation - see Afib guidelines for Aflutter pics

5-10yrs more data coming out: stroke prediction; arrythmia burden to stroke risk (devices/monitors)

Anti-Arrhythmias

antiarrythmias.docx

To make the topic interactive, I am assigning each of you a drug to review. Please be prepared to share the following on Tuesday:

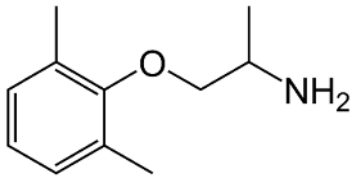
1. Mechanism of action
2. Dose- include any issues related to dosage forms (ER vs IR, etc), when adjustments are needed (renal dysfxn, hepatic dysfxn, special populations, etc.)
3. Adverse effects- include specific proarrhythmic effects if applicable
4. Drug interactions- focus on very serious and very common ones
5. Monitoring- consider baseline during initiation and long-term

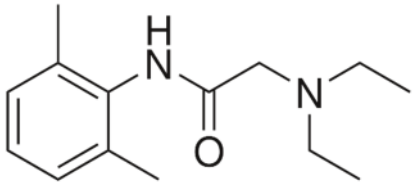
· Amiodarone- Hou
· Dofetilide - Chiou
· Flecainide- Chu
· Mexiletine- Murphy
· Sotalol- Hasan

We will focus on these 5 meds- the most commonly used ones. You will have about 10 minutes to share your findings. I will fill in the gaps with the other meds. Also, I have attached a good guidance document from Europe to help you.

Ib: lidocaine, mexiletine, phenytoin

mexiletine





Mechanism of Action

Class IB antiarrhythmic, structurally related to lidocaine, which inhibits inward sodium current, decreases rate of rise of phase 0, increases effective refractory period/action potential duration ratio

Dosing

Capsule, Oral, as hydrochloride: 150 mg, 200 mg, 250 mg

Administration: Administer around-the-clock rather than 3 times daily to promote less variation in peak and trough serum levels; administer with food or antacid
- 10 mg/mL oral suspension may be with made with capsules and either distilled water or sorbitol

Ventricular arrhythmias: Management of life-threatening ventricular arrhythmias
- Initial: 150 to 200 mg every 8 to 12 hours (may load with 400 mg if necessary); adjust dose as needed in 50 or 100 mg increments no more frequently than every 2 to 3 days up to 300 mg every 8 to 12 hours; usual dose: 150 to 300 mg every 8 to 12 hours; maximum dose: 1.2 g/day.

Ventricular premature beat (symptomatic) suppression (off-label use):
- Initial: 100 to 150 mg every 8 to 12 hours; adjust dose as needed in 50 or 100 mg increments no more frequently than every 2 to 3 days up to 300 mg every 8 to 12 hours; usual dose: 150 to 300 mg every 8 to 12 hours; maximum dose: 1.2 g/day.

"suppression and prevention of haemodynamically stable VT as well as for prevention of recurrent ventricular fibrillation"
"idiopathic VT successfully treated by catheter ablation after failed beta-blocker therapy; mexiletine, sotalol, flecainide, amio, propaf alternatives"
"Mexiletine, flecainide, and ranolazine are effective for shortening QTc interval in LQT3 syndrome"

"that mexiletine may be considered for those with long QT syndrome type 3 who present with torsades de pointes" (AHA/ACC/ Heart Rhythm Society HRS)

Switching from IV lidocaine: Initiate 200 mg dose of mexiletine when lidocaine infusion is stopped.
Switching from oral procainamide: Initiate a 200 mg dose of mexiletine 3 to 6 hours after the last dose of procainamide.
Switching from other oral antiarrhythmics (eg, disopyramide, quinidine): Initiate 200 mg dose of mexiletine 6 to 12 hours after the last dose of the former agent.

Renal: No dosage adjustment necessary.
Hepatic: Patients with hepatic impairment or hepatic congestion secondary to heart failure may require dose reduction; half-life is approximately doubled in patients with hepatic impairment.

"Mexiletine and disopyramide should also be avoided in post-myocardial infarction patient"

Adverse Effects

Cardiovascular: Exacerbation of cardiac arrhythmia (10% to 15%; patients with malignant arrhythmia)
- Palpitations (4% to 8%), chest pain (3% to 8%), angina pectoris (2%), ventricular premature contractions (1% to 2%)

CNS: Dizziness (11% to 25%), Tremor (13%), ataxia (10% to 20%), nervousness (5% to 10%), unsteady gait

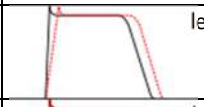
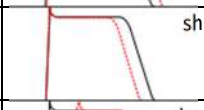
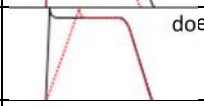
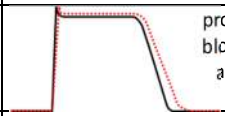
Gastrointestinal: Gastrointestinal distress (41%), nausea (≤40%), vomiting (≤40%)

Drug Interactions
Substrate of CYP1A2 (major), CYP2D6 (major)
Inhibits CYP1A2 (moderate)- tizanidine
Amio increases mexiletine levels
Mexiletine also enhances the effects of warfarin

"Mexiletine 50–70% protein bound; t1/2 10–12 h; ~10% excreted unchanged in urine"
Onset of action: 30 to 120 minutes (with loading regimen)
Absorption: Well absorbed
Distribution: V_d: 5 to 7 L/kg
Protein binding: 50% to 60%
Metabolism: Hepatic via CYP2D6 metabolism to inactive metabolites (~90%) and major metabolites p-hydroxymexiletine, hydroxy-methylmexiletine, and N-hydroxy-mexiletine (minimal antiarrhythmic activity); low first-pass effect
Bioavailability: 90%
Half-life elimination: ~10 to 12 hours; ~ 15 hours in severe renal impairment (CrCl < 10 ml/min); ~ 25 hours in moderate to severe hepatic impairment
Time to peak, serum: 2 to 3 hours
Excretion: Urine (10% as unchanged drug); urinary acidification increases excretion, alkalinization decreases excretion

Test interactions: Abnormal liver function test, positive ANA, thrombocytopenia

Monitoring
Liver function tests, ECG
Therapeutic range: 0.5 to 2 mcg/mL; potentially toxic: >2 mcg/mL
Monitor cardiac status. Assess for CNS changes (trembling, unsteady gait, ataxia, lightheadedness, dizziness, or nervousness). Mexiletine has a low toxic:therapeutic ratio and overdose may easily produce severe and life-threatening reactions.

Class	Drugs	Block	ECG	Conduction Velocity (Na^+ or SNS)	Refractory Period (K^+ or Ca^{2+})	[a](high rates and ischemia)
Ia	procainamide quinidine disopyramide	Na^+/K^+	QRS QT	↓	↑	 lengthens AP (right shift)
Ib	lidocaine tocainide mexiletine	Na^+ fast on-off	-	↓[a]	-	 shortens AP (left shift)
Ic	flecainide propafenone moricizine	Na^+ slow on-off	QRS	↓↓	-	 does not affect AP (no shift)
II	β-blockers	SAN AVN	PR	↓ SAN AVN	↑ SAN AVN	s
III	amiodarone dofetilide sotalol	K^+	QT	-	↑	 prolong repolarization due to blocking K-channels. affects phase 3, affect QT interval prolong
IV	diltiazem verapamil	Ca^{2+}	PR	↓ SAN AVN	-	
V	adenosine magnesium dixogin					

due to K-blocking, affects QT
other III: ibutilide, dronedarone, vernakalant, bretylium
amiodarone: blocks K Na Ca HR; rest are specific for K-blocking
doesn't change automaticity (other classes do)
sotalol: β-blocker and K-blocker; use for ventricular arrythmias and Afib (w/o LV dysf)
risk of QT, blocking K-channel prolonging QT, cause proarrhythmias

Class Ic (flecainide, propafenone)
- strongest negative inotropic (watch HFrEF)
- low risk of QT-prolongation
- absorption lower with food
- 2D6, HL 20hr (higher in renal failure)
- everyone gets 100mg q12h initial
- for atrial arrhythmias
- CI structural heart disease, cardiogenic shock; BBW proarrhythmia*: Afib→Aflutter
- use-dependent Ic (amio is reverse use-dependent)

Class III
sotalol
- beta-blocker (L-isomer), K-blocker (D-isomer)
- >160mg/d
- increase QT and JT
- all renal elim, HL 12hrs (renal dysf way higher)
- AF/AFL: 120 q12h initial better than 80 q12h.
- VT/VF:
- baseline QT <450
- QT vs. QTc debate
- if QRS long, JT = QT-QRS = <330 to initiate therapy
- OPTIC trial
- QT direct relation to dose; if QT high, hold/reduce dose, washout, recheck QT

dofetilide
- can cardioversion with 2-3 days 500mcg, sotalol does not
- renal adjustments
- if QTc <440; or <500 if IVCD intraventicular conduction delay
- indicated AF with HFrEF

amiodarone
- III (K), I (Na), BB, CCB, alpha
- Load IV 150/1mg/min 0.5mg/min →total load 7-10g over days-weeks (6-7g atrial, 8-10g ventricular)
- Laoad PO 100-400mg/dose bid-tid max 600 single dose (nausea)
- HL 40-55d; load won't get to steady state faster but will get to therapeutic range quicker
- ADE: brady/QT (low rate of TdP bc homogenous polarization); corneal microdeposits, thyroidism, NV, pulm fibrosis, hep, skin blue, gait disturb, periph neuropat
- DDIs: warf don't empirically reduce just monitor more freq; cyclosporine; simva/atorva

https://www.uptodate.com/contents/amiodarone-drug-information

ibutilide only IV only to cardiovert ppl

Atrial Fibrillation

Focus on the 2021 review article. 2014 AF guideline executive summary reference; 2019 focused update that primarily updates some of the anticoagulation recs
AFFIRM trial

Left Atrium
-irregular R-R intervals; no P wave (SA node bystander); sometimes narrow/wide QRS

Afib with RVR (sx palp, sob, fatigue, syncope, angina, stroke, no sx)

Rate
- bb: consider not in CHF acute, bad airway
- dilt 0.25-0.35 mg/kg or 10-20mg x1 CIV = 5-15mg/hr; works in minutes
- dig bad press; mortality higher levels—slow 6hrs, narrow ther range (0.5-0.8), renal, doeesn't work exercise-induced good CHF and hypotensive
- amio: could cardiovert you increase stroke risk (6-12bpm slow rate)
- ablation of AV node and place pacemaker (repeated admission for afib or CRT device with HF)

Stroke Risk
Virchow's triad
LAA left atrial appendage 90% clots form there (slower rate than rest of LA)
Acute Stroke <48hrs AC if plan to cardiovert >48hrs do OAC >3wk or do TEE
Once DCCV: 4 weeks then do C2V
C2V: ≥2M or 3F
DOAC
- dabig and apix superior to warfarin at ischemic stroke; rest are non-inferior
- rivarox/apix maybe less renal consideration and no contraindication <15ml
- renal: apix HD if no >80yo and <60kg 5bid
- cost issues with medicare mostly
- mech valves- dabig vs. warfarin worse outcomes and bleed risk
  - def of nonvalv afib (mostly mitral valve) RIVER trial TAVR
Watchman-if can't anticoagulate
- in the LAA: left atrial appendage occlusion devices; prevent stasis in LAA
- should be on AC 45d after so endothelial goes over; ECHO too check for flow behindit
- PROTECT-AF noninferior to warfarin
C2V best way to predict stroke?
Afib burden (percent time in afib) may be better predictor of stroke

Rhythm
RFA: radiofrequency ablation superior to amio (amio efficacy 1yr 60%)
Diff ablation types
- Afib ablation 4-5hrs: making all the dots in circles in the LA efficacy: 70% first, 80% second
- AV node ablation (Rate): get rid of AV node and you're paced; 10min
- flutter ablation: target an anomotical issues 45min
- MAZE surgery
AADs – see figure based on safety (amio is most effective at maintaining NSR at 1 yr)
- post-MI (CAD) best sotalol

Cardioversion
shock on QRS shock on T wave →vfib
brevital last 7-10min

important to AC post-DCCV 75% strokes occur <48hrs, 100% within a week

Afib ECG: irregularly irregular; A 400-600bpm, V 120-180bpm
mech: reenry – disorganized, "functional"; continual AVN stimulation, rapid Vrate
treatment: control Vresponse: AV node block (adenosine); restore sinus rhythm: DCC

Atrial fibrillation
Mechanism: Disorganized "functional" reentry; Continual AV node stimulation and irregular, often rapid, ventricular rate
Acute therapy: 1. Control ventricular response: AV node block 2. Restore sinus rhythm: DC cardioversion
Chronic therapy: 1. Control ventricular response: AV nodal block 2. Maintain normal rhythm: K+ block, Na+ block, Na+ channel block with τrecovery >1 sec

Atrial fibrillation – irregularly irregular ventricular response (rate and rhythm)

	Atrial Flutter		Atrial Fibrillation
Atrial Rate (bpm)	250-350	300:150 is 2:1	400-600
Ventricular Response (bpm)	100-300 regular rhythm - sawtooth flutter waves, frequent P waves		120-180 irregular rhythm
Characteristics	less common usually resolves or degenerates to fib		more common acute, chronic (>1yr), paroxysmal (mins-hrs)

Atrial Fibrillation Risk Prediction Framingham Heart Study (10 yr AF risk)
- Age - SBP - BMI - Antihypertensives - PR interval (indicative of how big atria is; and AV node) - Age @ Dx significant cardiac murmur (valvular disorder) - Age @ Dx HF

RF: age, CAD, M, Euro, HTN, obesity, smoking, DM, OSA, FH
New dx 19% after acute event such as pneumonia or surgery (most common); also MI, PE, thyrotoxicosis, alc tox

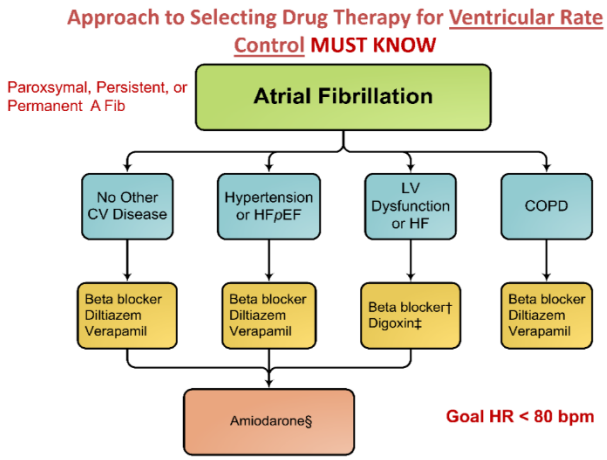
paroxysmal	recurrent episodes that stop on their own or with intervention that last <7days (comes and goes)
persistent	recurrent episodes that last >7 days
permanent	an ongoing long-term episode; clinician/patient decision
nonvalvular	absence of rheumatic mitral valve disease/repair or a prosthetic heart valve

Mechanisms of AF
Causes of AF: PIRATES
• Pulmonary embolism, Pulmonary disease, Post-operative, Pericarditis
• Ischemic heart disease, Idiopathic (lone afib), Intravenous central line (right atrium)
• Rheumatic valvular disease (MR or MS)
• Anemia, Alcohol, Age, Autonomic tone (vagal mediated AF)
• Thyroid Disease (hyperthyroidism)
• Elevated BP (HTN)
• Sleep Apnea, Sepsis

AF Symptom Presentation
– Mild (Rate Control/±Anticoagulation/±Restoration of Sinus Rhythm [DCC or Pharmacologic]/ Chronic Rate Control)
• Palpitations • Anxiety • General fatigue • Weakness • SOB
– Moderate-Severe (Rate Control/Anticoagulation/Restoration of Sinus Rhythm [DCC]/ Chronic Rate/Rhythm Control)
• Pre-syncopal • Syncope (Low SBP) • Heart Failure Sx [Severe SOB/Fatigue]/Pulmonary Edema/+S3 • Angina • Low Urine Output to Anuria

https://www.uptodate.com/contents/rhythm-control-versus-rate-control-in-atrial-fibrillation
https://www.uptodate.com/contents/the-management-of-atrial-fibrillation-in-patients-with-heart-failure

Therapeutic Goals for AF
AF #1
- Control ventricular rate/Eliminate Symptoms (digoxin, non-DHP CCBs, beta-blockers, amiodarone)
- Beta-blockers (first line) if no contraindications (metoprolol/esmolol [oral/IV])
  - Monitor orthostatic BP, HR, ECG
- Rate-limiting CCBs (second line); (diltiazem: oral/iv, verapamil oral/iv); do not use DHPs
  - Monitor orthostatic BP, HR, ECG
- Digoxin: hypotensive patients only! Do not use chronically due to inability to control rate with sympathetic stimulation (I.e. exercise);
  Oral/iv - must load (1mg: 0.5mg first dose, 0.25mg 6hrs later, then 0.25mg 6 hours later);
- Amiodarone: HFrEF and AF (additional rhythm control)



Approach to Drug Therapy for Ventricular Rate Control (paroxysmal, persistent, or permanent)
Single: beta-blocker, CCB (diltiazem, verapamil) -> amiodarone
HTN: beta-blocker, CCB -> amiodarone

HFpEF: beta-blocker, CCB -> amiodarone
HFrEF: beta-blocker, digoxin -> amiodarone
COPD: beta-blocker, CCB (no amiodarone)

AF #2

- Prevent thromboembolic complications (warfarin, DTI, DOACs, occasionally aspirin)

- <48 hours: may chose not to anticoagulate
- >48 hours or unknown: do 3 weeks prior to AAD then for 4 weeks
- TEE evidence of thrombus: Yes anticoagulate prior to conversion
- VTE event Hx: Yes anticoagulate prior to conversion
- CHA_2DS_2-VASc score >1: Yes anticoagulate

CHA_2DS_2-VASc

Clinical Prediction for Risk of Stroke

0-ASA 1-ASA/OC 2+ Oral Anticoagulant

	Condition	Pts
C	CHF (LF Sys Dys)	1
H	HTN (BP >140/90 or on meds)	1
A_2	Age ≥75	2
D	DM	1
S_2	Prior CVA/TIA or VTE event	2
V	Vascular Dx (PAD, AMI, plaque)	1
A	Age 65-74	1
Sc	Female Gender	1

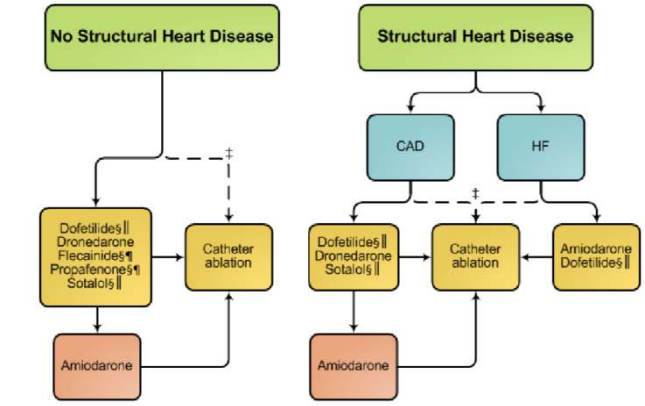
AF #3

- Convert to Normal Sinus Rhythm (AAD's, direct current cardioversion)

- Sedate with Versed (or barbituates) first, then:a
- DCC: emergencies and hemodynamically instability
  - Greater effectiveness than AAD's
  - Determine TE risk first
- Pharmacological conversion
  - Antiarrhythmic agents:
    - If AF <7 days: dofetilide, flecainide (no HFı
    - If AF >7 days: dofetilide or amiodarone

- **Maintain sinus rhythm** (Rate control agents or AAD's)
  - amiodarone for maintenance rhythm control (AFIRM study)

Strategies for Rhythm Control in Patients with Paroxysmal* and persistent AF MUST KNOW



Monitoring for Long-Term Rhythm Control Agents

- ECG – QT prolongation, PR prolongation, heart block, HR
- Ischemia – angina, increase SL NTG use, reduction in exercise
- Labs – basic metabolic panel, potassium, magnesium (too higl

Rate vs. Rhythm? in patients without mod-severe arrhythmia symptom:

- Control ventricular rate, don't worry about atrial rhythm, and provide stroke prophylaxis
- Try to achieve/maintain sinus rhythm, control ventricular rate during possible recurrence, and provide stroke prophylaxis

Negative predictors for staying in normal rhythm after cardioversion: >12mo AF, >4.5cm atrial size, multiple episodes

AFIRM: no benefit in mortality or stroke risk to treating AF with AADs (rhythm control)

Cardioversion

Transthoracic defibrillation, which rapidly delivers a stored charge to the heart across two surface pads or paddle electrodes, is used emergently for life-threatening tachycardias. Cardioversion, which refers to shock delivery synchronized with the QRS complex, is advised in patients with either supraventricular arrhythmias (Chapter 58) or ventricular tachycardia (VT) (Chapter 59) because a nonsynchronized shock coincident with the vulnerable period of the T wave may precipitate ventricular fibrillation (VF). The resulting shock extinguishes re-entrant arrhythmias by simultaneously depolarizing large portions of the atria and/or ventricles. Defibrillation is used for disorganized rhythms in which synchronization to the QRS complex is not appropriate, such as VF or rapid polymorphic VT. In these emergent situations, attempts to synchronize may delay delivery of the shock.

Cerebrovascular Disease

Casey will be working fromhome for this topic discussion and will be co-leading it with Angad. I have removed the room and we will use teams. Please be somewhere you can participate and have microphone. I have attached a few trials you will want to familiarize yourself with. Each one of you have been assigned to an article to be able to explain briefly to the rest of the group. I have also attached the acute ischemic stroke guidelines so you can familiarize yourself with terminology and some of the scoring systems or rating scales that are used in the trials you are looking at.

CHANCE – Casey and Alex https://www.wikijournalclub.org/wiki/CHANCE
POINT – Kushal and Ryan https://www.wikijournalclub.org/wiki/POINT
Compress – Brilliana/Sarah/Rachel

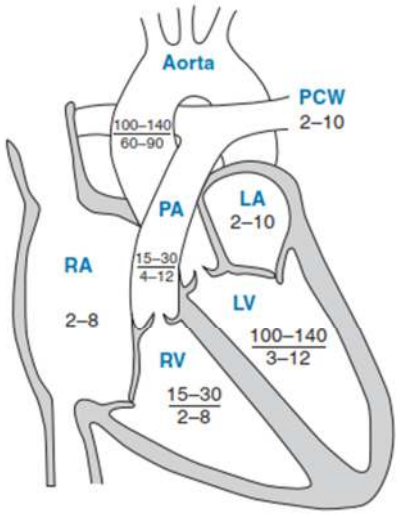
CHANCE: Clopidogrel in High-risk patients with Acute Nondisabling Cerebrovascular Events (2013)
Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

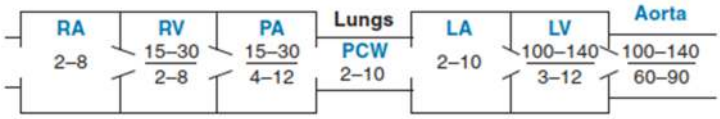
Clinical Question: Among patients with acute TIA or minor ischemic stroke, does the early administration of aspirin/clopidogrel reduce rates of subsequent strokes when compared to aspirin monotherapy?
Bottom Line: Among patients with acute TIA or minor ischemic stroke, starting aspirin/clopidogrel within 24h of symptom onset reduces the 90-day stroke incidence without increasing bleeding rates, when compared to aspirin monotherapy.

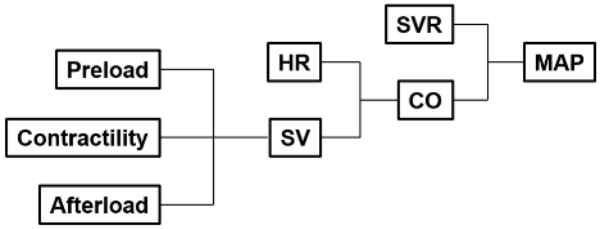
https://www.rxfiles.ca/rxfiles/uploads/documents/DAPT%20and%20Triple%20Therapy%20Newsletter%20and%20Chart.pdf

Hemodynamics

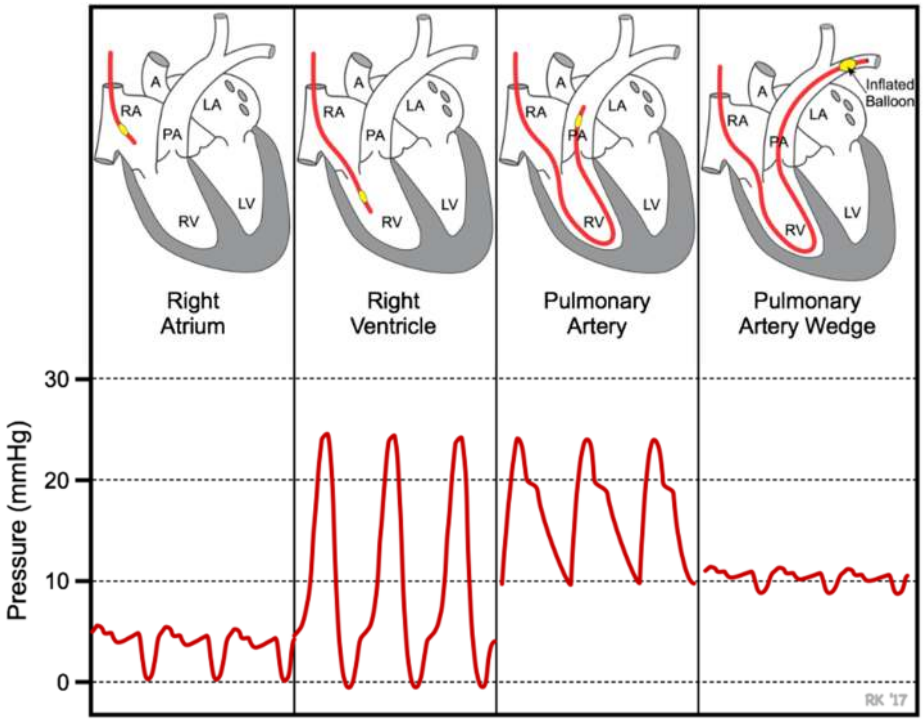
MAP	Mean Arterial Pressure (mean BP) MAP = (1/3 SBP) + (2/3 DBP)	70-10 mmHg
SV	Stroke Volume (from LV per beat) SV = CO/HR (mL/beat)	60-130
SI	Stroke Volume Index (mL/m^2/beat)	30-65
CO	Cardiac Output CO = SV*HR	4-8 L/min
CI	Cardiac Index CI = CO/BSA	2.8-4.2 L/min/m^2
CVP	Central Venous Pressure (Preload R)	2-8 mmHg
PCWP	Pulmonary Capillary Wedge Pressure (Preload L)	6-12 mmHg
RAP	Right Arterial Pressure	2-6 mmHg
RVP	Right Ventricle Pressure	15-25 mmHg
PAP	Pulmonary Artery Pressure	10-22 mmHg
SVR	Systemic Vascular Resistance (Afterload L, pressure LV has to pump against) SVR = 80*(MAP-CVP)/CO SVR ≅ MAP/CO	900-1400 dyn*s/cm^5
PVR	Pulmonary Vascular Resistance (Afterload R, pressure RV has to pump against) PVR = 80*(mPAP-PCWP)/CO	150-250 dyn*s/cm^5
PaO_2	partial pressure O_2	90 mmHg
SaO_2	arterial oxygen saturation	98%
pCO_2	partial pressure CO_2	40 mmHg (arterial)
$ScVO_2$	mixed venous oxygen saturation	60%–80%
$ScvO_2$	central venous oxygen saturation	







MAP = CO*SVR product of cardiac output and systemic vascular resistance
SVR afterload L, pressure LV has to pump against
CO = HR*SV product of HR and volume ejected by the heart
HR (chronotropy)
SV is impacted by preload, contractility, afterload
Preload volume in ventricles at end of diastole prior to systole; an increase in preload = increase contractility (except HF)
CVP preload right side volume status; PCWP preload left side volume status
Contractility (inotropy) ↑inotropy via ↑sympathetic activation, ↑catecholamines, ↑parasymp (vagal) inhibition, ↑afterload, ↑HR
Afterload resistance LV has to overcome to eject blood volume into aorta; controlled by vasoconstriction/vasodilation



Chapter 3 Cardiac Catheterization
Chapter 9 Physiology
https://www.cvphysiology.com/Heart%20Failure/HF008

CVC cath thru juglar from SVC into RA; only gets RA=CVP
RHC/Swan/PA-cath goes thru RA RV then sits in pulmonary artery (balloon)
Use waveforms to determine where the cath tip is with balloon inflated; notch in PA is when Pulm valve closing

RA=CVP = 0-5 *Preload R
RV = 25/5
PA = 25/10 = Mean 15 (Pulm HTN = mean PA >20)
PCWP = 10 *Preload L - it's an estimate of LVEDP from the right side RHC if LHC = LAP = LVEDP directly measured; in theory should be equal

Cardiac Output (CO) dependent on preload afterload contractility
Calculate via Swan (in Pulm valve) or CVC (RA)
- Fick Method relies on oxygen consumption: SvO2 leaves LV at 100%, comes back to RA SvO2 70% (lose 30% oxygen)
  - assumes oxygen demand unchanged, only variable change is how much oxygen body needs
  - calculates difference between LV 100% - RA 70% return (can see HF pt with 30-40%)
  - CO 4-6 L/min - CI = CO/BSA = >2.2 L/min/m2
- Thermodilution (TDCO, heat change) saline injected into RA via Swan, temp measured at RA and along catheter; graph 1-T / distance → get AUC
  - lower CO = greater AUC - more reliable but takes time/effort

SVR = MAP-CVP/CO normal 900-1200 *Afterload L A at LV goes to body = MAP a at RA from body = CVP(RAP)
  e.g. 90-5/5 = 17woods units *80 dynes = 1360
PVR = mPAP-PCWP/CO normal 1 woods *Afterload R
  e.g. 15-10/5 = 1 woods

PVR in Woods
SVR in dynes

CO-warm /cold -perfusion
CVP/PCWP -wet/dry -volume status

Preload SV vs. PCWP High preload give diuretics PCWP elevates, equivalent to preLV/LA and in pulmonary vessels where you get edema in lungs
Afterload SV vs. SVR
- HF pt: Hydral increase afterload without decreasing BP; as long as SBP >85s

<u>HYDRALAZINE</u>

BP	= SVR	*	CO	
↓↓	= ↓↓↓		↑	normal pt
--	= ↓↓↓		↑↑↑	HF

<u>Riley</u>
Systolic dysfunction >>> higher preload to maintain SV
- Body activates RAAS and catecholamines to increase preload
- Further remodeling
- Too much preload = sx of HF
- Narrow window b/w adequate CO and congestive sx of HF
- Frank-Starling curve

Systolic dysfunction >>> increased afterload causes more significant decrease in SV
- Vasodilators to decrease afterload – no net change in BP
- Higher RAAS and catecholamine activity

Right atrial pressure (CVP) – 5
Tricuspid open and pulmonic closed – RV preload = CVP

RV – 25/5
PA – 25/10 (mean 15)
PCWP (end of diastole, valve open, estimate LV end diastolic pressure) – 8-12

Fick estimates CO by looking at oxygen saturation (flow through the system changes, all else constant)
- More blood flow = less oxygen extraction
- Normal 4-6 L/min
- CI (CO/BSA) = 2.5 (HF want > 2)

GOAL for HF = lowest SVR possible w/o manifesting hypotension

PAP elevation: left HF, parenchymal lung disease, (chronic bronch, emphysema), pulmonary vascular (PE, PH, ADRS)

Mean right atrial pressure is reduced when there's intravascular volume depletion
Mean right atrial pressure is elevated in right ventric failure, right-sided valvular disease, cardiac tamponade (chambers surr'd by high-pressure pericardial fluid)

Preload: The ventricular wall tension at the end of diastole. In clinical terms, it is the stretch on the ventricular fi bers just before contraction, often approximated by the end-diastolic volume or end-diastolic pressure.
Afterload: The ventricular wall tension during contraction; the resistance that must be overcome for the ventricle to eject its content. Often approximated by the systolic ventricular (or arterial) pressure.
Contractility (inotropic state): Property of heart muscle that accounts for changes in the strength of contraction, independent of the preload and afterload. Reflects chemical or hormonal infl uences (e.g., catecholamines) on the force of contraction.
Stroke volume (SV): Volume of blood ejected from the ventricle during systole. SV = End-diastolic volume = End-systolic volume.
Ejection fraction (EF): The fraction of end-diastolic volume ejected from the ventricle during each systolic contraction (normal range is 55% to 75%). EF = Stroke volume = End-diastolic volume.
Cardiac output (CO): Volume of blood ejected from the ventricle per minute. CO ——————————————————————————————
SV Heart rate.
Compliance: Intrinsic property of a chamber that describes its pressure–volume relationship during fi lling. Refl ects the ease or diffi culty with which the chamber can be filled. Strict definition: Compliance = Δ Volume/Δ Pressure.

Pulmonary Embolism

see Riley SUNSET PE

I have also attached our updated version of our EBM guideline. There are other helpful resources on our pharmacy intranet that the attached guideline links to like our PE checklist for systemic lytics, dosing for thrombolytics both CDT and systemic lytics, and a long-term anticoagulation table.

Pulmonary Embolism Response Team (PERT)

- Determine appropriate therapy based on clinical picture
  - Systemic thrombolytic therapy
  - Catheter directed thrombolytic therapy
  - Anticoagulation: Heparin, Bivalirudin
- Assist with dosing and timing of thrombolytics and anticoagulation

pulmonary embolism: heparin infusion with or without thrombolysis or embolectomy

1. Pathophysiology and Risk Factors - Section 3.2, 3.3 and Figure 2 of the ESC document

Strong risk factors (OR >10): - Fracture of lower limb - Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months) -Hip or knee replacement - Major trauma - Myocardial infarction (within previous 3 months) - Previous VTE - Spinal cord injury

Moderate (OR 2-9): chemo, CHF, ESAs, HRT, oral contraceptives, infection UTI HIV PNA, cancer, central venous lines, IV cath/leads, autoimmune, transfusions

RV failure due to acute pressure overload considered primary cause of death in severe PE

PAP increases if >30-50% is occluded

PE-induced vasoconstriction (TxA2 and 5HT) contriubtes to initial increase in PVR after PE; anatomical obstruction and hypoxic lung increase PVR

Figure

2. Workup including diagnosis and risk stratification Section 4 of the ESC document and the PERT Consortium Document (should be familiar with laboratory tests and diagnostic testing that can be ordered)

Clinical presentation: dyspnea, cp, syncope, hemoptysis

Assessment of clinical probability:

Avoiding overuse of tests

D-dimer: negative predictive value of D-dimer testing is high, and a normal D-dimer level renders acute PE or DVT unlikely

PERC (PE rule-out criteria): age>50, HR>100, O2 <95%, hx VTE, recent trauma/surgery <4wk, hemoptysis, unilateral leg swelling, estrogen

- if meets any of the PERC, PE not ruled out

Calculate Wells Criteria score: s/s DVT (3.0), PE likely dx-CXR (3.0), HR>100 (1.5), Immobilization >3d or surg <4wk (1.5), hx VTE (1.5), hemoptysis (1), malignancy (1)

≥4 PE likely: suggested empiric options: heparin, enoxaparin

<4 PE less likely: perform hs D-dimer to rule out PE → D-dimer positive? No, PE excluded Yes, CTPE study or V/Q scan

3. Review the hospital EBM guideline to find out how the PERC, Wells, and PESI Score are used, what is the definition of massive, intermediate, or low risk PE. They are also included in the PERT consortium document that is a good review.

massive: hemodynamically unstable → full-dose systemic lytics, anticoag treatment (→may include catheter-directed lytics, embolectomy, ECLS)

- defined as SBP <100 for >15min or req pressors, decrease in SBP 40 from baseline, cardiac arrest

submassive: PESI score >0 → normal BNP and hs-trop (53M, 35F) and no RV strain on TTE/CT → anticoag/DOAC, ICU/PCU if abnormal anticoag/DOAC, med

low risk: PESI = 0; anticoag/DOAC, outpatient

(PESI- age 80, hx cancer, hx chronic cardiopulm disease, HR >110, SBP<100, O2 <90%)

4. Treatment Options and Duration including Thrombolytics; Heparin and LMWH; Direct oral anticoagulants and warfarin. There is lots of primary literature here we can get into later, but for the best interest of time we will want to know what treatment options are available for patients with massive, submassive, and low risk PE. We will each take a section to cover:

Appendix A

Massive: UFH without lytics bolus 80u/kg followed by 18u/kg/hr after lytics: without a bolus-18u/kg/hr

Submassive: UFH bolus 80u/kg follwed by 18u/kg/hr

Low risk PE: DOAC, warfarin with bridge

alteplase contraindications: hx hemorhaggic stroke, active internal bleeding, recent bleeding/trauma/bleed within 3 weeks

Catheter Directed Lytics – explanation of what it is, what medications are used, dosing, and potential advantages and disadvantages to this strategy. Sunset PE trial is looking at EKOS vs non-EKOs CDT

-CDT involves slow infusion of lytic agent through standard multiple side hole catheters placed within clot

- tPA

SUNSET PE

Patients with sPE undergoing USAT did not have improved thrombus reduction in comparison with SCDT.

Both USAT and SCDT produced significant RV function improvement; however, the SCDT group demonstrated a superior RV/LV ratio reduction.

There were no significant safety differences.

USAT does not appear to confer greater benefit than SCDT in the treatment of submassive PE.

In patients with submassive PE, USAT does not appear to demonstrate better clinical efficacy than SCDT.
Given the 10-fold higher cost and lack of clinical superiority of USAT, there is no compelling reason to use USAT over SCDT for treatment of sPE in a clinical setting.
Further research is warranted to evaluate the potential benefit of USAT in shortening the dose/duration of thrombolytic therapy.

Thrombolytics – Dosing (cardiac arrest vs non-cardiac arrest), anticoagulant use with thrombolytics, contraindication/precautions). The document PE-systemic lytics review should be a helpful summary of the studies looking at this.

Long-term treatment for pulmonary embolism and on oral anticoagulants for acute and long-term therapy for pulmonary embolism.

PAH

For the article attached: Section 1 – Look at figures/tables Section 2 – Read Section 3 – Ignore

PH dx: RHC- **PVR >3** (normal 1), **PCWP <15** (normal 10), **PA_{mean} mPAP >20** (normal 15)
PH 1: = PAH; idiopathic, genetic, HIV →treatment with drugs that vasodilate the PA
PH 1°: PVOD (never treated with PAH drugs), hard to diagnose, PVOD where PV backs up and get pulm edema
PH 2: left heart dx except PCWP >15, high filling pressures. Number one cause of PH →treatment treat LHD
PH 3: lung disease (any that cause chronic hypoxia like COPD) →treat underlying lung disease and Tyvaso for ILD 2021 inhaled
PH 4: CTEFH- chronic thromboembolic pulmonary hypertension; TE starts distal comes back proximal; riociguat for CTEFH
PH 5: multifactorial/systemic diseases

Group 1 PH (PAH)
RHC- vasoreactivity challenge (inhaled NO or epoprostenol); if positive then → CCB trial (only 5% have positive vasoreactivity)
if negative vasoreactivity → risk assessment→REVEAL risk score: >9 high risk
High risk: 1 year mortality >10% → infused IV prostacyclins (epoprostenol or treprostinil) mortality beneft
Low/Mod risk: dual therapy (ERA+NO)

NO Pathway
- sildenafil: PDE5i; tid, 20/mo, NVD GI flushing
- tadalafil: PDE5i; qd, 100s/mo, NVD GI flushing
- riociguat: soluble guanylate cyclase (sGC) stimulator; tid, 15k/mo; 3A4 substrate, REMS (teratogenic, females); hypotension, NVD GI flushing

ERA: Endothelin receptor antagonists: ETR_A bad causes vasoconstriction; ETR_B not that bad (scavenger)
- ambrisentan: A, qd, 15k/mo (300-500/dose); peripheral edema highest incidence; REMS (teratogenicity)
- bosentan: A/B, bid, 10k/mo off-patent; hepatotoxicity; REMS monitor LFTs monthly; REMS (teratogenicity)
- macitentan: A, qd, 15k/mo (300-500/dose); anemia (predictble 1-3 drop Hgb); REMS (teratogenicity)

Prostacyclin pathway IP receptor agonists
- epo half life short
- tre longer

if nonadherent even for a short time or day can land in ER or die; will lead to RV failure
SE: headache 90%, GI NVD, if titrate too fast or bolus or flush a line then systemic hypotension

oral/inhaled: 1) moderate risk who were treated with dual therapy and remain in mod risk to goal bring you low risk. 2) high risk can't tolerate (oral triple therapy)
goal of therapy: low risk profile

Characteristics of medications used in the treatment of pulmonary hypertension

Drug	Route of administration	Dose range (adult)	Half-life
Prostacyclin pathway agonists			
Epoprostenol	Continuous IV infusion via central venous catheter	1 to 12 nanograms/kg/minute initially Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs	3 to 5 minutes (single dose) 15 minutes (continuous infusion)
Treprostinil	Continuous IV infusion via central venous catheter or continuous subcutaneous infusion	0.625 to 1.25 nanograms/kg/minute initially Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs	4 hours
	Inhaled	One to three inhalations (ie, 6 to 18 micrograms), four times daily initially Maintenance dose may be gradually titrated up to nine inhalations (ie, 54 micrograms), four times daily	4 hours
Iloprost	Inhaled	2.5 to 5 micrograms, six to nine times daily	20 to 30 minutes (half-life of pulmonary vasodilating effect)
Selexipag	Oral Intravenous formulation is available for temporary use when unable to take oral therapy	200 to 1600 micrograms twice daily Dose titrated up every one to two weeks until therapeutic response or dose limiting toxicity occurs For intravenous formulation, see labeling for dosing	0.8 to 2.5 hours (selexipag) 6.2 to 13.5 hours (active metabolite)
Endothelin receptor antagonists			
Bosentan	Oral	62.5 to 125 mg, two times daily; Dose is adjusted for low body weight or drug interactions*	5 hours
Ambrisentan	Oral	5 to 10 mg daily	9 hours
Macitentan	Oral	10 mg per day	14 to 18 hours (parent drug)
Nitric oxide-cyclic guanosine monophosphate enhancers			
Soluble guanylate cyclase stimulant			
Riociguat	Oral	Initial dose 0.5 to 1 mg three times daily, titrated up by 0.5 mg three times per day every two weeks until therapeutic response or dose limiting toxicity occurs (maximum dose 2.5 mg three times daily)	12 hours
Phosphodiesterase type 5 inhibitors			
Sildenafil	Oral	20 mg, three times daily	4 hours
	IV	10 mg, three times daily; Dose is adjusted for drug interactions*	4 hours
Tadalafil	Oral	40 mg daily; Dose is adjusted for drug interactions*	35 hours
Calcium channel blockers¶			
Nifedipine	Oral	Start 30 mg per day. Increase to the maximum tolerated dose over days to weeks.	7 hours
Diltiazem extended-release	Oral	Start 120 mg per day. Increase to the maximum tolerated dose over days to weeks.	6 to 9 hours
Amlodipine	Oral	Start 2.5 mg per day. Increase to the maximum tolerated dose over days to weeks.	30 to 50 hours

Orientation Links

Module	Materials
Scoring and Documentation	Scoring Presentation Scoring and Documentation Handout Patient Scoring Responsibilities
Pharmacokinetics	Pharmacokinetics Orientation Pre-test and homework problems (emailed)
Vancomycin AUC & ASP	Vancomycin AUC-Based Monitoring Presentation Vanco AUC Handout Vanco AUC Tipsheet Introduction to Antimicrobial Stewardship Program (ASP)
Anticoagulation	Anticoagulation Resident Orientation Anticoagulation IM Lecture
Renal	Chronic Kidney and End Stage Renal Disease IM Lecture CRRT Review
Hepatic	Powerpoint (emailed)
Monitored Meds Review and Expectations	Link
Medication History Review	Med Rec Video
Code Blue	ACLS Pharmacology Pharmacy Code Blue Training: Case-Based learning
STEMI-Alert	STEMI-Alert