American College of Clinical Pharmacy

Last Chance Webinar 2012:

Cardiology

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Conflict of Interest Disclosures

I have no conflicts of interest to disclose

Objectives

Given multiple patient cases, the pharmacist should be able to:

- Formulate evidence-based treatment plans for patients with a variety of cardiovascular disease subsets.
- Distinguish between the acute presentations of acute coronary syndromes, decompensated heart failure, and other acute cardiovascular diagnoses.
- Develop pharmacotherapy treatment plans for patients with stable angina, chronic heart failure, hypertension, and dyslipidemia.
- Assess key mortality reducing strategies for a patient with cardiovascular disease.

Case #1

- PD is a 59-year-old Hispanic man who was referred to your hypertension clinic. He has obesity, hypertension, Type 2 diabetes, hyperlipidemia, and benign prostatic hypertrophy. He does not smoke or drink alcohol and admits compliance to a diet and exercise program. He has no evidence of left ventricular hypertrophy. His medications include doxazosin 2 mg/day, enalapril 10 mg twice daily, and glyburide. His prostate symptoms are under good control. His blood pressure on three separate visits to your clinic has consistently averaged 138/88 mg Hg. Other labs include a serum creatinine of 1.7 mg/dl. K=4.9.

Of the following, which is the most appropriate next step for hypertension management in this man?

- Test Taking Rule #1. Assess the stem of the question!

Of the following, which is the most appropriate next step for hypertension management in this man?

A. Switch doxasozin to atenolol 50 mg daily
B. Add amlodipine 5 mg daily
C. Increase enalapril to 20 mg twice daily
D. Add losartan 50 mg

Hypertension cases

- Step #1
  - Define HTN
- Step #2
  - Define treatment goals
    - Determine TLC or 1 or 2 drug therapy
- Step #3
  - Address Lifestyle Modifications
- Step #4
  - Determine therapy
    - Comorbidities will suggest certain first line therapies

Step #1: Classification of BP

Classification	Systolic (mmHg)	Diastolic (mmHg)
Normal	<120	and <80
Prehypertension	120–139	or 80–89
Stage 1 Hypertension	140–159	or 90–99
Stage 2 Hypertension	≥160	or ≥100

Based upon the average of 2 or more values on 2 or more visits.

JNC=The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure.

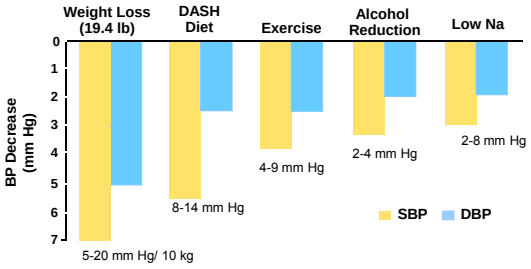
Chobanian AV et al. *Hypertension.* 2003;42:1206–1252. *JAMA* 2003;289(19):2560-72.

Step #2: Goal BP Recommendations

Patient Population	Goal BP
General Prevention*	<140/90 mm Hg
Diabetes*	<130/80 mm Hg
Significant chronic kidney disease[a]*	<130/80 mm Hg
Known CAD (MI, stable angina, UA)[#]	<130/80 mm Hg
Noncoronary atherosclerotic disease (ischemic stroke, TIA, PAD, AAA) or Framingham risk score ≥ 10%[#]	<130/80 mm Hg
Left ventricular dysfunction (systolic heart failure)[#]	<120/80 mm Hg

[a]Significant chronic kidney disease is considered moderate to severe chronic kidney disease, defined as estimated glomerular filtration rate less than 60 mL/min/1.73m2 (correlating to a SCr greater than 1.3 mg/dL in women or greater than 1.5 mg/dL in men); or albuminuria (greater than 300 mg/day or greater than 200 Alb/g creatinine).
*JNC7 supported goal. JAMA. 2003;289:2560–2572.
[#]AHA supported goal. Circulation 2007; 115:2761-2788.

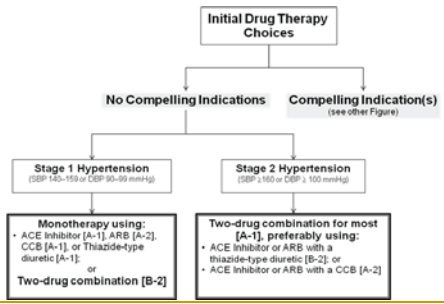
Step #3: Address lifestyle issues



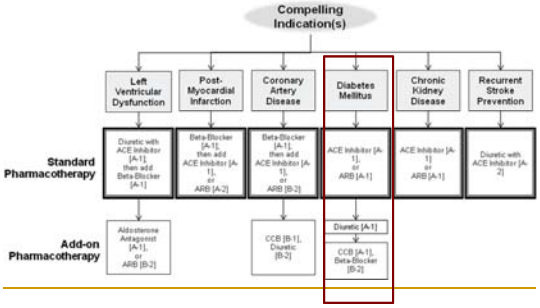
DBP = diastolic blood pressure; SBP = systolic blood pressure.

JAMA 2003;289:2560-2572.

Step #4: Determine Therapy



Step #4: Determine Therapy



Of the following, which is the most appropriate next step for hypertension management in this man?

A. Switch doxasozin to atenolol 50 mg daily
   A. BPH symptoms under control
B. Add amlodipine 5 mg daily
C. Increase enalapril to 20 mg twice daily
   A. Doubling of dose will not double BP lowering
   B. Watch K and Scr
D. Add losartan 50 mg
   A. No reason to add another RAS inhibitor

Case #2

- G.G. is a mildly overweight 55-year-old woman with a 4-year history of HTN, CAD, and a 20 pack-year smoking history. She was recently admitted to the hospital for community-acquired pneumonia. Her medical history is significant for hyperlipidemia and chronic angina. Her father had a MI when he was 63 years old. Before admission G.G. was treated with HCTZ 25 mg/day and metoprolol tartrate 75 mg twice daily. Her recent blood pressure readings have been 163-167/99-108 mm Hg and her pulse rate has been 58-62 bpm.

Which of the following is the best treatment recommendation for G.G.?

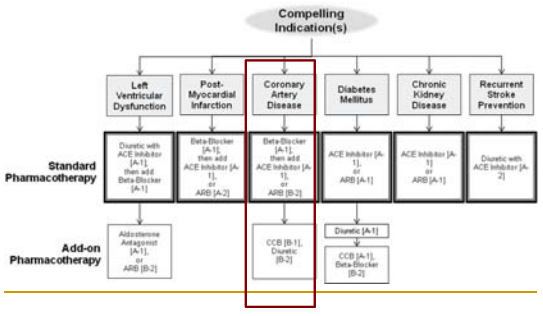
A. Increase HCTZ to 50 mg/day and maintain metoprolol.
B. Increase metoprolol tartrate to 100 mg twice daily and maintain HCTZ.
C. Discontinue metoprolol and initiate lisinopril 10 mg daily.
D. Add lisinopril 10 mg and maintain both HCTZ and metoprolol.

Test Taking Tip #2: Try to eliminate 2 of the responses. All 4 could be plausible, but, look for contraindications or options that don't make the best sense given the details of the case.

Which of the following is the best treatment recommendation for G.G.?

- A. Increase HCTZ to 50 mg/day and maintain metoprolol.
  - Doubling the dose of HCTZ will not double BP ↓
- B. Increase metoprolol tartrate to 100 mg twice daily and maintain HCTZ.
  - HR may limit BB titration
- C. Discontinue metoprolol and initiate lisinopril 10 mg daily.
  - Compelling indication: Needs BB for CAD and angina
- D. Add lisinopril 10 mg and maintain both HCTZ and metoprolol.
  - ACEI are recommended

Step #4: Determine Therapy



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C. Discontinue metoprolol and initiate lisinopril 10 mg daily.
D. Add lisinopril 10 mg and maintain both HCTZ and metoprolol.

Case #3

- C.K. is an obese 55-year-old with recent onset diabetes and coronary artery disease. He is being seen in lipid clinic. He was started two months ago on glipizide 10 mg twice daily, lisinopril 10 mg daily, and aspirin 81 mg daily. He is not on a specific diet and reports occasional exercise. He smokes ½ ppd tobacco. His fasting lipid profile reveals: TC= 192 mg/dl; LDL= 115 mg/dL; HDL=34 mg/dL; TG=215 mg/dL; glucose= 180 mg/dL; Hg A1C= 9.2%; WC= 42 inches; and SCr=1 mg/dL.

Which is the most appropriate lipid goal for A.K.?

A. Non-HDL cholesterol < 160 mg/dL
B. Non-HDL choldesterol < 130 mg/dL
C. LDL cholesterol < 100 mg/dL
D. LDL cholesterol < 70 mg/dL

NCEP–ATP III Guidelines

Risk Category	LDL Goal (mg/dL)	LDL Level to Consider Drug Therapy
***High Risk*: CHD or CHD Risk Equivalents (10-year risk >20%)**	**< 100 (optional < 70)***	**≥ 100 (<100: drug optional)**
***Moderately High Risk*: 2+ Risk Factors (10-year risk 10-20%)**	**< 130 (optional < 100)**	**≥ 130 (≥ 100: drug optional)**
***Moderate Risk*: 2+ Risk Factors (10-yr risk < 10%)**	**< 130**	**≥ 160**
***Lower Risk*: 0–1 Risk Factor**	**< 160**	**≥ 190 (≥ 160: drug optional)**

* Consider goal < 70 in everyone with stable CHD or very high risk

Optional Goal <70 mg/dL

- Established CAD *PLUS* (one of the following):
  1. Diabetes
  2. ACS
  3. High risk uncontrolled risk factors (like smoking)
  4. Metabolic syndrome

Which is the most appropriate lipid goal for A.K.?

A. Non-HDL cholesterol < 160 mg/dL
B. Non-HDL choldesterol < 130 mg/dL
C. LDL cholesterol < 100 mg/dL
D. LDL cholesterol < 70 mg/dL

Test Taking #2: Can you eliminate two choices?

Non-HDL

Risk Category	LDL Goal	Non-HDL
CHD and CHD risk equivalents (10-year risk > 20%)	< 100	< 130
Multiple (2+) risk factors (10-year risk ≤ 20%)	< 130	< 160
0 or 1 risk factor	< 160	< 190

Case #4

- P.C. is a 40 year old man referred to lipid clinic after his fasting lipid profile revealed a TG level of 1046 mg/dL. The patient has a history of gout for which he takes colchicine 0.6 mg/day. He states that he is adherent with a low fat diet and an exercise regimen for the last 3 months. His family history is significant for coronary artery disease and diabetes. He was started recently on fenofibrate 145 mg/day. He returns to clinic today with the following lab values: TC=277 mg/dL; LDL=132 mg/dL; HDL 32 mg/dL; TG 505 mg/dL; and glucose 70 mg/dL.

Which of the following is the most appropriate step in the management of dyslipidemia?

A. Switch to gemfibrozil 600 mg twice daily
B. Add immediate release niacin 1.5 grams daily
C. Titrate fish oil up to 2 grams twice daily
D. Add colestipol 30 grams daily

Which of the following is the most appropriate step in the management of dyslipidemia?

A. Switch to gemfibrozil 600 mg twice daily
   - Will not give you advantage over fenofibrate
B. Add immediate release niacin 1.5 grams daily
   - Dose titration; plus gout
C. Titrate fish oil up to 2 grams twice daily
D. Add colestipol 30 grams daily
   - Can increase TG

TG Lowering Effects

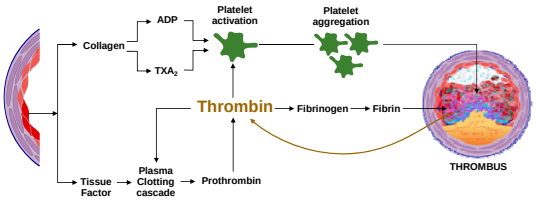
Drug	LDL	HDL	TG
Statins	↓ 22-60%	↑ 5-15%	↓ 7-40%
Niacin	↓ 15-26%	↑ 15-26%	↓ 20-50%
Ezetimibe	↓ 18-20%	↑ 1-5%	↓ 7-17%
Fibrates	↓ 5-20% (nl TG) ↑ up to 45% (↑↑ TG)	↑ 18-22%	↓ 30-55%
BAS	↓ 15-26%	↑ 3-6%	↑ up to10%
O3FA	May ↑ when TG very high	↑ 11-14%	↓ 26-45%

Case #5

- A 60 kg patient with a creatinine clearance of 60 ml/min with NSTEMI is taken to the cath lab for possible PCI. In addition to antiplatelet agents, which of the initial anticoagulation regimens would be the most appropriate for this patient?
  A. Enoxaparin 30 mg IVB, then 1 mg/kg SQ q12 hours
  B. Bivalirudin 0.75 mg/kg IV; then 1.75 mg/kg/hour
  C. UFH 80 units/kg bolus, titrated to aPTT of 50-70 sec
  D. Fondaparinux 2.5 mg SQ daily

Combatting Thrombus Formation

- Antiplatelets: Aspirin, P2Y12 antagonists, and GPIs



- Anticoagulants: UFH, LMWH, Fondaparinux, Bivalirudin

Anticoagulant Dosing in ACS

	UFH	Enoxaparin	Fondaparinux	Bivalirudin
Class		LMWH	Factor Xa inhibitor	DTI
UA/NSTEMI	60 unit/kg IVB (max 4000 units), 12 u/kg/hr IV (max 1000 units/hr)	1 mg/kg SQ BID	2.5 mg SQ QD	0.75 mg/kg IVB, 1.75 mg/kg/hr
STEMI	If GPI, 50-70 U/kg IVB If no GPI, 70-100 U/kg	30 mg IVB; then 1mg/kg SQ BID (Max: 100 mg x 2)	2.5 mg IVB; then 2.5 mg SQ QD	0.75 mg/kg IVB, 1.75 mg/kg/hr
PCI	Supplemental - target to ACT	Supplemental -dependent upon timing	Should not be used as sole AC in PCI	0.75 mg/kg IVB, 1.75 mg/kg/hr
Dose adjustments/cautions	Avoid in HIT or HIT history	If CrCl < 30 ml/min, 1 mg/kg QD	Avoid if CrCl< 30 ml/min	If CrCl < 30 ml/min, 1 mg/kg/hr

Case #5

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  - B. Bivalirudin 0.75 mg/kg IV; then 1.75 mg/kg/hour
  - C. UFH 80 units/kg bolus, titrated to aPTT of 50-70 sec
  - D. ~~Fondaparinux 2.5 mg SQ~~ daily

Case #6

- L.W., a 48 yo male with a PMH significant for DM and CAD, presents to the ED with complaints of worsening chest pain for the past several days, which has been somewhat relieved with SLNTG and rest. He underwent a percutaneous coronary intervention with two stents placed in his RCA and circumflex 9 months ago. He reports compliance with his Plavix prescription. Vital signs include a BP 98/58; HR 58 bpm. Troponins are negative yet ECG is positive for ST segment changes. He is taken to the cath lab where he underwent PCI with a new DES placed in his RCA.

Which of the following antiplatelet regimens should be most successful in maintaining stent patency in this man?

A. Clopidogrel 300 mg load, then 75 mg daily with aspirin 325 mg
B. Clopidogrel 600 mg load, then 75 mg daily with aspirin 81 mg
C. Prasugrel 60 mg load, then 10 mg daily with aspirin 81 mg
D. Ticagrelor 180 mg load, then 90 mg twice daily with aspirin 325

$P2Y_{12}$ Antagonists

Parameter	Clopidogrel (I, LOE A)	Prasugrel (I, LOE B)	Ticagrelor (I, LOE B)
FDA Indication	ACS managed medically or with PCI	ACS with PCI (no data before PCI)	ACS managed medically or with PCI
Dosing	LD: 300-600; may given second 300 mg load at time of PCI if 300 mg given prior MD 75 mg daily	LD: 60 mg, MD 10 mg daily (5 mg if <60 kg; BBW ≥75 y) CI: TIA/stroke	LD: 180 mg, MD 90 mg twice daily CI: ICH, severe hepatic dz
Peak Platelet Inhb	300 mg load ~ 6 hrs 600 mg load ~2 hrs	60 mg load ~1-1.5 hrs	180 mg load < 1 hr
Metabolism	Prodrug; converted by 2-step process involving 2C19 and 3A4	Prodrug; converted to active metabolite via multiple P450 pathways	Not prodrug; Reversible, noncompetitive binding; 3A4 (primary), 3A5, Pgp
T1/2	8 hrs metabolite	3.7 hours metabolite (range 2-15 hours)	7 hours (parent), 9 hours (active metabolite)
Non-responders	Exposure to active drug affected by CYP2C19 and CYP3A4 and PGP polymorphisms	No known issues	No known issues
Drug/Disease Interactions	PPI's inhibit 2C19, (concomitant use with omeprazole is discouraged per PI); enhanced bleeding with NSAIDS, VKA, O3FA, etc	Less prone but data are limited; enhanced bleeding with NSAIDS, VKA, etc	Careful with asthma, bradycardia: enhanced bleeding with NSAIDS, VKA; limit ASA to <100 mg
CABG hold time	5 days	7 days	5 days
Study	CREDO, CURE, PCI-CURE, CLARITY, COMMIT	TRITON-TIMI 38	PLATO

Choice of $P2Y_{12}$ Antagonist

2012 UA/NSTEMI Focused Update

- New Guideline does not recommend one agent over another
  - All receive Class I recommendation
  - Higher bleeding with newer antiplatelets
  - Efficacy vs. risk may best guide decisions re:choice
- Data come solely from 2 trials
  - TRITON-TIMI 38 and PLATO
  - Use in clinical practice should follow trial design
    - Prasugrel when proceeding to PCI
    - Ticagrelor was "all-comer" ACS

P2Y12 inhibitor choice:

- ACS with PCI planned:
  - BMS/DES for ACS-options are clopidogrel, prasugrel, or ticagrelor
- ACS medical management:
  - Options are clopidogrel or ticagrelor
- Clopidogrel *still* preferred:
  - BMS/DES after lytic therapy, STEMI 2009 and 2011 PCI
  - BMS/DES for non-ACS, 2011 PCI guidelines
- Contraindication/Considerations (avoid all with active bleeding):
  - History of TIA/Stroke- avoid prasugrel
    - Relative contraindications – weight <60 kg, age >75
  - Severe liver disease and H/O ICH- avoid ticagrelor
  - Genetic polymorphisms- avoid clopidogrel
- Cost considerations
  - Plavix - $208.88 (2012)- *generic pricing???*
  - Effient- $230.08 (2012)
  - Brilinta-$250.72 (2012) #60

Which of the following antiplatelet regimens should be most successful in maintaining stent patency in this man?

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B. Clopidogrel 600 mg load, then 75 mg daily with aspirin 81 mg
C. Prasugrel 60 mg load, then 10 mg daily with aspirin 81 mg
D. Ticagrelor 180 mg load, then 90 mg twice daily with aspirin 325

Long Term Antiplatelet Therapy

2012 UA/NSTEMI Focused Update

- Aspirin *plus* $P2Y_{12}$ antagonist
- Recommended for ***at least 12 months after ACS ± PCI***

Medical Management

- Class I:
  - Aspirin indefinitely PLUS clopidogrel 75 mg daily or ticagrelor 90 mg twice daily for up to 12 months

With PCI

- Class I:
  - Aspirin indefinitely PLUS clopidogrel 75 mg daily or prasugrel 10 mg daily or ticagrelor 90 mg twice daily for at least 12 months after DES or up to 12 months after BMS

Class IIa: *After PCI, it is reasonable to use 81 mg per day of aspirin in preference to higher maintenance doses.*

GPIs in ACS

	STEMI w/ PCI	UA/NSTEMI w/ or w/o PCI	Renal Adjustment
Abciximab (ReoPro)	0.25 mg/kg IVB, 0.125 mcg/kg/min x 12h	--	Not necessary
Eptifibatide (Integrilin)	180 mcg/kg IVB x 2 (10 mins apart), 2 mcg/kg/min x 12-18h	180 mcg/kg IVB, 2 mcg/kg/min x 12-72h	If CrCl <50, ↓ infusion 50% If dialysis, contraindicated
Tirofiban (Aggrastat)	25 mcg/kg IVB, 0.1 mcg/kg/min x 18h	0.4 mcg/kg/min x 30 min, 0.1 mcg/kg/min x 18-72h	If CrCl <30, ↓ infusion 50%

GPIs in high risk patients with UFH

2011 PCI Guideline

In UA/NSTEMI patients with high-risk features (e.g., elevated troponin level) not treated with bivalirudin and not adequately pretreated with clopidogrel, it is useful at the time of PCI to administer a GP IIb/IIIa inhibitor (abciximab, double-bolus eptifibatide, or high-bolus dose tirofiban) in patients treated with UFH.

In patients pretreated with clopidogrel, LOE B

2011 ACCF/AHA/SCAI PCI Guideline JACC 2011;58(24):e44-122.

Case #7

- YD is a 66 year old male presents to clinic with complaints of dyspnea. He has a history of ischemic cardiomyopathy, diabetes, and hypertension. His past surgical history includes PCI 10 years ago, and a CABG 5 years ago. His most recent ejection fraction is 30%. His BP is 125/80 mm Hg and HR is 82 bpm. His weight is 86 kg, K= 4.9 mEq/L, and SCr= 2.6 mg/dL. His medication regimen includes lisinopril 10 mg daily, carvedilol 12.5 mg twice daily, furosemide 40 mg daily, and potassium chloride 10 mEq daily. No volume overload is noted on physical exam, although the patient reports a 1-month history of dyspnea on exertion and episodes of paroxysmal nocturnal dyspnea. A cardiac catheterization is performed, showing disease not amenable to percutaneous coronary intervention.

Which of the following interventions would most likely benefit this patient?

A. Initiate spironolactone 25 mg daily
B. Change furosemide 40 mg IV BID
C. Initiate digoxin 0.125 mg daily
D. Up-titrate carvedilol to 25 mg twice daily

Which of the following interventions would most likely benefit this patient?

A. Initiate spironolactone 25 mg daily
   - Spironolactone ↓ mortality by 30% and ↓ hospitalizations for HF by 35% in Class III and IV
   - Eplerenone ↓ CV death or hopsitalization by 46% (Class II NYHA)
   - Aldosterone blockade should be considered after MI, with HF symptoms or history of DM, and an EF <40%
   - Avoid use if SCr is > 2.5 mg/dL in men, CrCl < 30 ml/min, or K is > than 5.0 mEq/L

Which of the following interventions would most likely benefit this patient?

A. Initiate spironolactone 25 mg daily
B. Change furosemide 40 mg IV BID
   - Symptom control
   - Fluid overload

Which of the following interventions would most likely benefit this patient?

A. Initiate spironolactone 25 mg daily
B. Change furosemide 40 mg IV BID
C. Initiate digoxin 0.125 mg daily
   - Benefits include improved symptoms, improved exercise tolerance, decreased hospitalizations when level is <1.0 ng/mL
   - Risk of toxicity increases with age and renal function
   - Drug is cleared more than 90% renally

Which of the following interventions would most likely benefit this patient?

A. Initiate spironolactone 25 mg daily
B. Change furosemide 40 mg IV BID
C. Initiate digoxin 0.125 mg daily
D. Up-titrate carvedilol to 25 mg twice daily
   A. Should be used in all stable patients
   B. Aim to achieve target dose in 8-12 weeks
   C. Target dose 25 mg BID; or 50 mg BID in > 85 kg
   D. Benefits with high over low doses

Case #8

- AN is a 58 year old Caucasian woman with a history of ischemic cardiomyopathy. Her most recent ejection fraction was 35%. She is currently receiving enalapril 10 mg twice daily, furosemide 80 mg twice daily, digoxin 0.125 mg daily, and simvastatin 40 mg daily. Two weeks ago, carvedilol was initiated at 3.125 mg twice daily. Today, she presents to clinic complaining of dizziness. Her average sitting BP is 115/70 mm Hg and standing is 98/60 mm Hg. Her heart rate is 85 bpm. Her K is 4.8 mEq/L.

Which of the following changes is best to address this patient's current symptoms?

A. Discontinue carvedilol
B. Decrease furosemide
C. Decrease enalapril
D. Increase enalapril to target dose

HFSA Guidelines

Under ACEIs- Background

- The major side effects of ACE inhibitors in patients with HF are hypotension and azotemia.
- Both are usually well tolerated and do not indicate the need to lower the dose or discontinue the ACE inhibitor.
- The azotemia commonly is related to a relative volume-depleted state caused by diuretic therapy and may be improved by a reduction in diuretic dose.
- Moderate renal insufficiency should not be considered a contraindication to the use of ACE-inhibitors, although careful attention to serum potassium and creatinine levels is imperative.

http://www.heartfailureguideline.org/ace_inhibitors/73

HFSA 2010 Practice Guideline-Beta Blocker Overview

General considerations	**Initiate at low doses**
	Up-titrate gradually, generally no sooner than at 2 week intervals
	Use target doses shown to be effective in clinical trials
	Aim to achieve target dose in 8-12 weeks
	Maintain at maximum tolerated dose
If symptoms worsen or other side effects appear	**Adjust dose of diuretic or concomitant vasoactive med.**
	Continue titration to target after symptoms return to baseline
If up-titration continues to be difficult	**Prolong titration interval**
	Reduce target dose
	Consider referral to a HF specialist

http://www.heartfailureguideline.org

Which of the following changes is best to address this patient's current symptoms?

A. Discontinue carvedilol
B. Decrease furosemide
C. Decrease enalapril
D. Increase enalapril to target dose

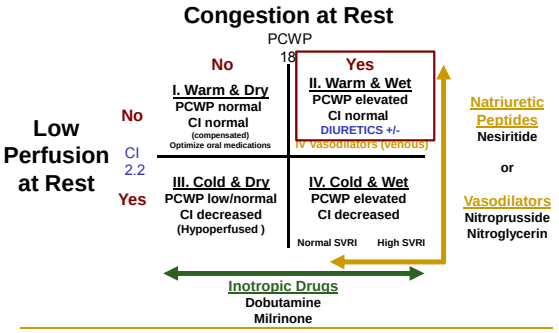
Case # 9

- D. K. is a 75-year-old man who presents to the emergency department with complains of progressive dyspnea on exertion (now 10 feet, previously 30 feet) and orthopnea (now 4 pillows, previously 2 pillows), increasing bilateral lower extremity edema (3+), and a 14 kg weight gain in the last month. His O2 sat is 96%. He is not compliant with his low sodium diet. He has a history of idiopathic dilated cardiomyopathy (EF 25%), atrial fibrillation, and hyperlipidemia. His labs include a BNP or 2300 pg/mL, K=4.9 mEq/L, BUN 22, SCr=1.0 mg/dL. BP is 110/60 mm Hg and HR=82 bpm. His home medications include carvedilol 12.5 mg twice daily, lisinopril 40 mg daily, furosemide 80 mg twice daily, spironolactone 25 mg daily, and digoxin 0.125 mg daily.

Which of the following is the best option for treatment of his heart failure exacerbation?

A. Carvedilol 25 mg twice daily
B. Milrinone 0.5 mcg/kg/min
C. Nesiritide 2 mcg/kg bolus, then 0.01 mcg/kg/min
D. Furosemide 120 mg IV twice daily

ADHF Quadrants and Treatment



Adapted from Fonarow GC. *Rev Cardiovasc Med.* 2001;2(suppl 2):S7–S12.

Which of the following is the best option for treatment of his heart failure exacerbation?

A. Carvedilol 25 mg twice daily
B. Milrinone 0.5 mcg/kg/min
C. Nesiritide 2 mcg/kg bolus, then 0.01 mcg/kg/min
D. Furosemide 120 mg IV twice daily

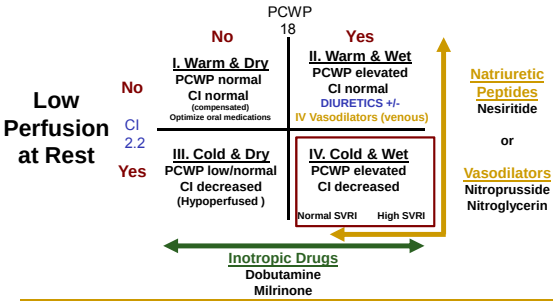
Case #10

- After an initial treatment response, D.K.'s urine output diminishes again. SCr rises to 4.4 mg/dL. He is drowsy and confused. His extremities are cool and clammy, his BP=100/58 mm Hg, HR=99 bpm. It is felt that he is no longer responding to current treatment. He is started on nitroglycerin 50 mcg/min with poor symptomatic response. According to hemodynamic measurements, his CI=1.5 L/min/m2, SVR 2650 dynes/cm5, PCWP 30 mm Hg.

Which of the following is the most appropriate medication based on his current symptoms?

A. Nesiritide 2 mcg/kg bolus, then 0.01 mcg/kg/min
B. Milrinone 0.20 mcg/kg/min
C. Dobutamine 5 mcg/kg/min
D. Sodium nitroprusside 0.3 mcg/kg/min

ADHF Quadrants and Treatment



Adapted from Fonarow GC. *Rev Cardiovasc Med.* 2001;2(suppl 2):S7–S12.

Which of the following is the most appropriate medication based on his current symptoms?

A. Nesiritide 2 mcg/kg bolus, then 0.01 mcg/kg/min
   A. Switching vasodilators at this point is not helpful
B. Milrinone 0.20 mcg/kg/min
   A. Can BP tolerate? Renal adjustment?
C. Dobutamine 5 mcg/kg/min
   A. Potential choice but on carvedilol
D. Sodium nitroprusside 0.3 mcg/kg/min
   A. Not first choice in renal impairment

Case #11

- A.P. is a 68 year old woman with a 4-5 day history of dizziness and palpitations. She has diabetes, hypertension, dyslipidemia, and chronic kidney disease. Her current drugs include glipizide XL 10 mg daily, lisinopril 10 mg daily, aspirin 81 mg daily, and simvastatin 40 mg daily. Her blood pressure is 155/75 mm Hg with HR of 125 bpm. Her ECG shows atrial fibrillation with rapid ventricular response. Her most recent echocardiogram showed a LVEF of 55% with no valvular defects. Her creatinine clearance is 26 ml/min.

Which of the following is the most appropriate to prevent thromboembolic events in A.P.?

A. aspirin 81 mg daily
B. aspirin 81 mg plus clopidogrel 75 mg daily
C. warfarin titrated to INR of 2.5
D. dabigatran 150 mg twice daily

Risk Stratification for OAC

Step 1: Determine the patients risk factors for stroke

■ACC/AHA

High: prior stroke, TIA, or embolus; Mitral valve disease; prosthetic valve
Moderate: HTN, HF, LVD (EF <35%, Age >75, DM
Weak: Age 65-75, Female, CAD, Thyrotoxicosis

■ $CHADS_2/CHA_2DS_2$-VASc

Letter	Condition	Points
C	CHF	1
H	HTN	1
A_2	Age ≥ 75	1 (or 2)
D	DM	1
S_2	CVA/TIA	2
V	Vascular Disease	1
A	Age 65-74	1
Sc	Sex Characteristic (Female)	1
		Max 6-9 Points

2011 ACCF/AHA/HRS AF Focused Update. Circulation 2011;123:1144-1150.
2012 Oral Antithrombotic Science Advisory. Stroke; 2012;43. DOI:10.1161/STR.0b013e318266722a

Choice of Antithrombotic Therapy

Step 2: Given patient risk, determine appropriate OAC

Risk Category	Oral Antithrombotic
No Risk Factors	ASA 81-325 mg daily or none
One Moderate Risk Factor	ASA 81-325 mg daily or OAC
Any High Risk or More than 1 Moderate RF	Warfarin (Class I LOE A) to INR 2-3 Dabigatran (Class I LOE B) Apixaban (Class I LOE B) Rivaroxaban (Class IIa, LOE B)
For high-risk patients deemed unsuitable for OAC	ASA + Clopidogrel (Class IIb, LOE B)

Agent selection should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics including TTR

2011 ACCF/AHA/HRS AF Focused Update. Circulation 2011;123:1144-1150.
2012 Oral Antithrombotic Science Advisory. Stroke; 2012;43. DOI:10.1161/STR.0b013e318266722a

Anticoagulant Considerations for AF

	Dabigatran (RE-LY), Oct 19, 2010	Rivaroxaban (ROCKET AF) Nov 4, 2011	Apixaban (AVERROES and ARISTOTLE)
MOA	DTI	Direct Factor Xa inihibitor	Direct and Competitive Factor Xa inihibitor
Dose	150 mg PO twice daily; 75 mg twice daily when CrCl 15-30 ml/min;	CrCl >50 ml/min: 20 mg PO daily (Class IIa, LOE B); CrCl 15-50 ml/min: 15 mg daily (Class IIb, LOE C)	5 mg twice daily (Class I LOE B); 2.5 mg twice daily (Class IIb LOE C) if : Age ≥ 80, weight ≤ 60 kg, or SCr ≥ 1.5 mg/dL
T ½	12-17 hours 80% renally eliminated	5-9 hours; renal (~36%) and fecal (~7%) clearance	8-15 hours
Metabolism/Drug interactions	Avoid PgP inducers (rifampin)	3A4/5 and PgP; avoid with strong inhibitors and inducers	3A4
Other considerations	No data- CrCl <15 ml/min Do not open capsules 4 month bottle expiration	Avoid: CrCl < 15 ml/min; Avoid in moderate and severe liver disease	CI: CrCl < 25 ml/min; Superiority over aspirin and warfarin

2011 ACCF/AHA/HRS AF Focused Update. Circulation 2011;123:1144-1150.
2012 Oral Antithrombotic Science Advisory. Stroke; 2012;43. DOI:10.1161/STR.0b013e318266722a

Dabigatran- Pradaxa™

Positives

- In the RE-LY trial, 150 mg dabigatran was superior to warfarin in preventing embolic strokes due to nonvalvular AF
- Prevents about five more strokes per 1000 patients per year than warfarin
- Less likely to cause ICH than warfarin
- Less drug interactions than warfarin; No dietary restrictions
- No need for INR monitoring

Downsides:

- Costs more than warfarin (~$260 per month; ~$5 per day)
- Twice daily dosing
- More likely to cause GI bleeding than warfarin
- More likely to cause dyspepsia than warfarin
- Special storage requirements
- No antidote for reversing the effect of dabigatran
- Renal elimination

Rivaroxaban-Xarelto®

Positives

- Non-inferior to warfarin for preventing stroke or systemic embolism in patients with relatively high stroke risk
- Lower rate of hemorrhagic stroke
- Predictable pharmacokinetics
- Once daily administration
- No required monitoring
- No dietary restrictions

Downsides

- Some data suggest once daily dosing insufficient, but BID dosing untested
- Higher rate of major GI bleed
- Cost- ~$6 per day
- Renal elimination
- Drug interactions
- No reliable reversal agent

Warfarin

Positives

- Still a viable option, especially in patients already on warfarin who are comfortable with INR monitoring and in centers with good INR control (i.e. >60%)
- Once daily dosing
- Best OAC in patients with CKD whose CrCl <30 ml/min
- Most likely best choice in patients who require triple therapy (with DAT)
- Cost considerations still make warfarin attractive

Downsides

- Inter-patient variability
- Significant drug interactions
- Narrow therapeutic window
- Routine monitoring
- Dietary restrictions
- Prolonged onset and offset of action
- Bleeding risk

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B. aspirin 81 mg plus clopidogrel 75 mg daily
C. warfarin titrated to INR of 2.5
D. dabigatran 150 mg twice daily

Case #12

- A 67 year old woman presents with fatigue and recent palpitations. She complains that she has not felt well for the past 2 days, with intermittent palpitations and dyspnea lasting 2 to 3 hours with each episode. She states that she is not able to do what she wants to do throughout the day. She has a history of atrial fibrillation, diabetes, dyslipidemia, and hypertension. Her echo reveals a large left atrial diameter with an estimated ejection fraction of 35%. BP=125/85 mm Hg. HR= 65 bpm. INR=2.3. SCr=1.2. CrCl ~ 53.86 ml/min. Her current medications include warfarin 5mg, metformin 500 mg BID, metoprolol succinate 150 QD, ramipril 10 mg QD, HCTZ 25 mg QD, and rosuvastatin 10 mg QD.

Which treatment plan is the best option for this patient at this time?

- Amiodarone load, then 200 mg daily
- Dofetilide 250 mcg Q12 hours
- Sotalol 160 mg BID
- Diltiazem 120 mg QD

Rate Vs. Rhythm Control

Pro	Con
Easier and less side effects; option for older patients	Electrical and structural remodeling; not best for younger patients

Rate Control

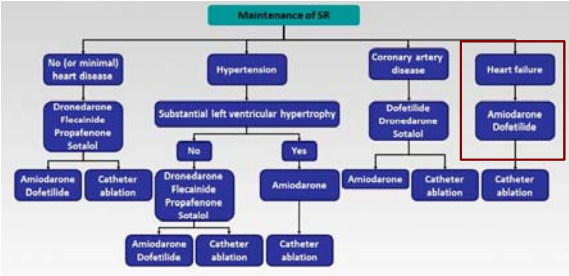
No Mortality Advantage

Rhythm Control

Pro	Con
Good for patients with symptoms; acceptable for all ages	Adverse drug effects, cost of meds and monitoring; high recurrence

2011 ACCF/AHA/HRS Guidelines

Choice of Pharmacotherapy for Maintenance of Sinus Rhythm



Adapted from Circulation 2011;123:104-23.

Which treatment plan is the best option for this patient at this time?

- Amiodarone load, then 200 mg daily
- Dofetilide 250 mcg q12 hours
  - Watch renal dosing and QT- risk for torsades
  - Patient will need to be admitted for initiation of tx
  - Watch drug-drug interactions
    - CI with thiazide diuretics
- Sotalol 160 mg BID
- Diltiazem 120 mg daily

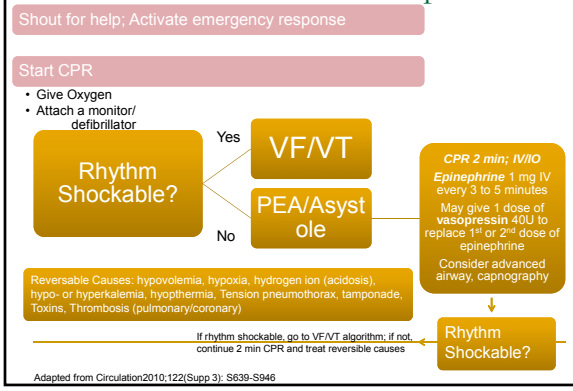
Case #13

- S.J. is a 81 year old female who was admitted to the hospital for treatment of community-acquired pneumonia. She has a history of type 2 diabetes, hypertension, and chronic kidney disease. While eating her breakfast, she buzzes the nurses station and complains of dizziness. When the nurse arrives, she has lost consciousness. Cardiopulmonary resuscitation is begun immediately. Once a monitor is in place, it shows that S.J. is in asystole.

Which treatment intervention is most appropriate at this time?

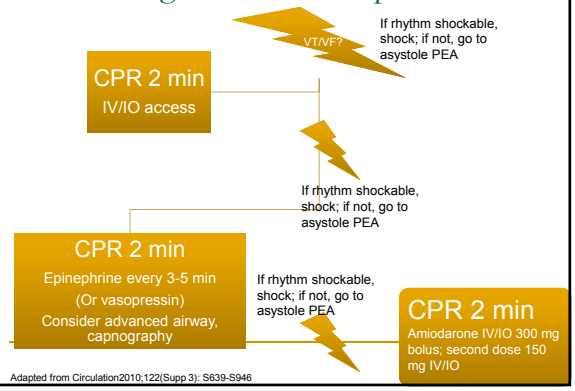
A. Transcutaneous pacing
B. Vasopressin 40 IU once, then 1 mg epinephrine every 3-5 minutes
C. Defibrillation with 200 joules (Biphasic device)
D. Atropine 1 mg every 3-5 minutes

Adult Cardiac Arrest 2010 Update



Adapted from Circulation2010;122(Supp 3): S639-S946

VT/VF Algorithm 2010 Update



Adapted from Circulation2010;122(Supp 3): S639-S946

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D. Atropine 1 mg every 3-5 minutes

Test Taking Tips

- Read the question stem!
- Try to eliminate 2 responses
- Look for drug-drug interactions or CI
- Do your homework
- Sleep and eat a good meal

Questions?

Questions are guaranteed in life; answers are not.

- a good mom