



## 2012 Updates in Therapeutics:

### The Pharmacotherapy Preparatory Review & Recertification Course

#### Cardiology I.

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## Conflict of Interest Disclosures

Sheryl L. Chow

No conflicts of interest to disclose

## Learning Objectives and/or Agenda

1. Formulate evidence-based treatment strategies for patients with acute decompensated heart failure.
2. Describe an appropriate treatment strategy for atrial and ventricular arrhythmias using evidence-based medicine.
3. Prepare a treatment strategy for a patient newly given a diagnosis of idiopathic pulmonary arterial hypertension.
4. Select appropriate pharmacologic therapy and develop a monitoring plan for antihypertensive drug therapy for managing hypertensive crises

Page Number (2-166)

## Acute Decompensated Heart Failure

Hunt SA, Abraham WT, Chin MH, et al. 2009 Focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults. *J Am Coll Cardiol* 2009; 53:1343–82.

Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 comprehensive heart failure practice guideline. *J Card Fail* 2010; 16:e1–194.

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## Hemodynamic Parameters

Parameter	Normal	ADHF
CO	4-7	2-4
CI	2.8-3.6	1.3-2
PCWP	8-12 (15-18)	18-30
SVR	800-1200	1500-3000

- $BP = CO \times SVR$
- $CO = SV \times HR$
- Stroke volume depends several factors
  - inotropy, afterload, preload

Page 2-168 – Table 1

## ADHF Signs and Symptoms

### ■ Congestion

- DOE or at rest
- Orthopnea, PND
- Peripheral edema
- Rales
- Early satiety, N/V
- Ascites
- Jugular venous distension
- Hepatojugular reflux

### ■ Hypoperfusion

- Fatigue
- Altered mental status or sleepiness
- Cool extremities
- Worsening renal function
- Narrow pulse pressure
- Hypotension
- Hyponatremia

Page 2-168 – Table 2

## Hemodynamic Classification

### Forrester's Hemodynamic Subset

CI 2.2	Subset I. Normal Warm and Dry	Subset II. Congestion Warm and Wet
	Subset III. Hypoperfused Cold and Dry	Subset IV. Congestion + Hypoperfusion Cold and Wet

18  
PCWP

Page 2-169

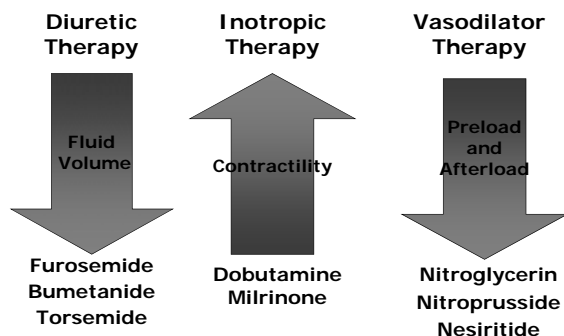
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IV - Cold and Wet (Congestion and Hypoperfusion)	PCWP > 18 mmHg CI < 2.2 L/min/m <sup>2</sup>	If MAP <50, IV dopamine If MAP ≥50, IV inotrope -or- IV vasodilator (venous/arterial)*

\*Compelling reason for inotrope = SBP < 90, symptomatic hypotension, or worsening renal function.

Page 2-169 – Table 3

## ADHF Drug Therapy



Page 2-170 – Table 4

## ADHF Case #1 Q1

1. DD is a 72 YOM admitted for ADHF

### HPI:

- Dyspnea on exertion (30 ft → 10 ft)
- Orthopnea (2 pillows → 4 pillows)
- Bilateral lower extremity edema (3+)
- Weight gain 13 kg = 30 lbs in 3 weeks
- Dietary nonadherence

### PMH:

- ICDM, LVEF 25%
- Paroxysmal atrial fibrillation
- Hyperlipidemia

Page 2-173 – Q#1 (Answer Page 2-191)

## ADHF Case #1 Q1

### Pertinent Labs:

- BNP 2300 (0-50), K<sup>+</sup> 4.9
- BUN 32, SCr 2 (baseline?)
- AST 40, ALT 42, INR 1.3, PTT 42

### BP 108/62 mmHg, HR 82 BPM (O<sub>2</sub> sat?)

### Home Medications:

- carvedilol 12.5 mg 2 times/day
- lisinopril 40 mg/day
- furosemide 80 mg two times/day
- spironolactone 25 mg/day
- digoxin 0.125 mg/day

Page 2-173 – Q#1 (Answer Page 2-191)

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Page 2-169 – Q#1 (Answer Page 2-191)

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\*Compelling reason for inotrope = SBP < 90, symptomatic hypotension, or worsening renal function.

Page 2-169 – Table 3

### ADHF Patient Case # 1 Q1

1. Which of the following is the best option for treating his ADHF?

-  A. Carvedilol 25 mg BID
-  B. Nesiritide 2 mcg/kg IVB, 0.01 mcg/kg/min
-  C. Furosemide 120 mg IV BID
-  D. Milrinone 0.5 mcg/kg/min

Handout Page 2-173; Answer Page 2-191

### ADHF Guidelines: *Diuretic Therapy*

- Recommended as an IV loop diuretic for patient admitted with fluid overload
- When response to diuretics is minimal, the following should be considered:
  - Fluid & sodium restriction,
  - Initiation of increased doses or continuous infusion of loop diuretic,
  - Addition of a second type of diuretic (metolazone or chlorothiazide), or
  - Ultrafiltration

Page 2-170 – Table 4

### ADHF Guidelines: *Vasodilator Therapy*

- May be considered in addition to IV loop diuretics to rapidly improve symptoms in patients without symptomatic hypotension
- May be considered if persistent symptoms despite maximal loop diuretics and oral drug therapy
- **When adjunctive therapy is required, IV vasodilators should be considered over inotropic drugs**

Page 2-170- Table 4

### ADHF Guidelines: *Inotropic Therapy*

- May be considered in patients with *diminished peripheral perfusion or end-organ dysfunction*, particularly if:
  - Marginal systolic blood pressure (< 90 mmHg),
  - Symptomatic hypotension exists despite adequate filling pressures, or
  - Unresponsive to, or intolerant of, IV vasodilators
- May be considered in similar patients with fluid overload if they respond poorly to IV diuretics or have worsening renal function.

Page 2-170 – Table 4

### ADHF Guidelines: *Invasive Monitoring*

- Routine use of hemodynamic monitoring with invasive IV lines (e.g. pulmonary artery catheter) is not recommended
- Should be considered:
  - Unclear volume status
  - Hypotension (SBP < 80)
  - Worsening renal function during therapy
  - Refractory to initial treatment

Page 210 – Table 4





## Diuretic Therapy

- Increase dose before increasing frequency of loop diuretic
  - (Note: Ceiling effect at  $\approx 160$ – $200$  mg IV furosemide)
- Add a second diuretic with a different mechanism of action
  - PO: HCTZ 12.5–25 mg/day, metolazone 2.5–5 mg/day
  - IV: CTZ 250–500 mg/day
    - gastrointestinal edema
    - expensive generic - reserve for NPO or refractory to PO
- Continuous infusion loop diuretic
  - Furosemide 0.1 mg/kg/hour IV doubled every 4–8 hours, maximum 0.4 mg/kg/hour

Page 2-171 – Table 5

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Handout Page 2-173; Answer Page 2-191





## ADHF Case #2 Q2

2. DD is started on IV loop diuretics with minimal urine output (SCr 2.7,  $K^+$  5.4). He is transferred to the CICU for diuretic-refractory ADHF.
- $O_2$  sat 87% on 4-L NC
  - BP 110/75, HR 75 beats/min

Page 215 – Q#2 (Answer Page 232)

## ADHF Patient Case # 2 Q2

2. In addition to a one-time dose of IV CTZ, how else should DD's ADHF be treated?

-  A. Nitroglycerin 20 mcg/minute
-  B. Sodium nitroprusside 0.3 mcg/kg/minute
-  C. Dobutamine 5 mcg/kg/minute
-  D. Milrinone 0.5 mcg/kg/minute

Handout Page 2-173; Answer Page 2-191

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Page 2-169 – Table 3

## Vasodilator Therapy

	NTP	Nesiritide	NTG
Clinical effects	Vasodilator (venous and arterial)	Vasodilator (venous and arterial)	Vasodilator (venous > arterial)
Indication	Warm & wet, Cold & wet alternate to inotropes, HTN Crises	Warm & wet, Cold & wet alternate to inotropes	Warm & wet, ACS, HTN Crises
Half-life	< 10 minutes	20 minutes	1-4 minutes
Elimination	Cyanide (hepatic), thiocyanate (renal)	NP receptor C (no renal/hepatic adjustment)	Inactive metabolites in urine

Page 2-172 – Table 7

## ADHF Case #3 Q3

3. A swan-ganz hemodynamic catheter is placed

- Cardiac index (CI)
  - 1.5 (2.8-3.6 L/min/m<sup>2</sup>)
- Systemic vascular resistance (SVR)
  - 2650 (800-1200 dynes/sec/cm<sup>5</sup>)
- Pulmonary capillary wedge pressure (PCWP)
  - 30 (8-12 mmHg, 15-18 mmHg in HF)

Page 2-173– Q#3 (Answer Page 2-191)

## Hemodynamic Classification

Forrester's Hemodynamic Subset

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	18	
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Page 2-169 - (Answer Page 2-191)

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\*Compelling reason for inotrope = SBP < 90, symptomatic hypotension, or worsening renal function.

Page 2-169 – Table 3

## ADHF Patient Case # 3 Q3

Which one of the following is the most appropriate medication now?

- A. Milrinone 0.2 mcg/kg/min
- B. Dobutamine 5 mcg/kg/min
- C. Nitroglycerin 20 mcg/min
- D. Phenylephrine 20 mcg/min

Handout Page 2-173; Answer Page 2-191

## Inotropic Therapy

	Dobutamine	Milrinone
Mechanism of action	β-agonist, slight peripheral vasodilation	PDE inhibitor, moderate peripheral vasodilation
Typical dose	5 mcg/kg/min	No bolus, 0.1-0.375 mcg/kg/min
Indication	ADHF Cold & Wet –or– Cold & Dry (if PCWP > 15)	
Half-life	2 minutes	1 hour, 2-3 hours if HF or CrCl < 50 ml/min
Other comments	Consider if hypotensive.	Consider if receiving a β-blocker.

Page 2-171 – Table 6

## Arrhythmias

**ACCF/AHA/HRS 2011 Focused update on the management of patients with atrial fibrillation (updating the 2006 guideline). *Circulation* 2011; 123:104–23.**

**AHA 2010 guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010; 122:S729-S767.**

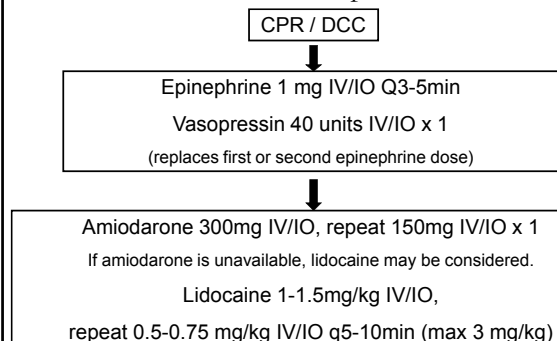
Page 2-190

## Antiarrhythmic Drug Classes

Class I Na <sup>+</sup> channel blockers	IA: Quinidine, procainamide, disopyramide IB: Lidocaine, mexiletine (phenytoin) IC: Propafenone, flecainide, moricizine	Slows depolarization
Class II β-blockers	Metoprolol, esmolol, atenolol	Slows AVN conduction (↓ HR)
Class III K <sup>+</sup> channel blockers	Amiodarone, sotalol, dofetilide, dronedarone, ibutilide	Slows repolarization (↑ QT)
Class IV Ca <sup>2+</sup> channel blockers	Diltiazem, verapamil	Slows AVN conduction (↓ HR)

Page 215 – Table 8

## Adult Cardiac Arrest –pulseless VT, VF



Page 2-178 – Table 10

## Symptomatic Brady/Tachycardia

- Symptomatic bradycardia
  - If unstable, atropine 0.5 mg every 3-5 minutes
  - If atropine fails, pacing, dopamine, or epinephrine
- Symptomatic tachycardia
  - If unstable, DCC
  - If stable and narrow complex (QRS < 120 msec)
    - Regular rhythm = supraventricular tachycardia
    - Irregular rhythm = atrial fibrillation
  - If stable and wide complex (QRS > 120 msec)
    - VT or TdP

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## Supraventricular Tachycardia

- Vagal maneuvers and/or adenosine 6 mg IVP (with 20-mL saline flush), then 12 mg IVP (may repeat x 1)
  - If converts, likely AT, PSVT, or WPW
  - If PSVT (not WPW) and temporary conversion, consider diltiazem or verapamil
  - If WPW, avoid diltiazem, verapamil, and digoxin
- Do not give adenosine for unstable or irregular or polymorphic wide complex tachycardia

Page 2-178

## Atrial Fibrillation

Rate Control	
General presentation	β-blockers, nondihydropyridine CCBs
Heart failure	Digoxin, amiodarone
Accessory pathway	Amiodarone
Rhythm Control	
Unstable, < 48 hours	DCC, UFH immediately beforehand
Unstable, unknown or > 48 hrs	DCC, TEE+UFH immediately beforehand and AC 4 wks after DCC
Stable, unknown or > 48 hrs	Rate control+AC 3-4 wks before and AC 4 wks after DCC - Elective DCC or CC (class I or III agents)

Page 2-179– Table 11

## Class IA Antiarrhythmics

- Quinidine
  - N/V/D (30%), TdP
  - DI with warfarin, digoxin
- Procainamide
  - Lupus-like syndrome, TdP, ADHF
  - Adjust dose in renal/hepatic dysfunction
- Disopyramide
  - Anticholinergic effects, TdP, ADHF

Page 2-175 – Table 9

### Class IC Antiarrhythmics

- Only use if no structural heart disease
  - HF, CAD, LVH, valvular disease
- Propafenone
  - ADHF, bronchospasm (beta-blocking properties)
  - Digoxin ↑ 70%, warfarin ↑ 50%
- Flecainide
  - ADHF
  - Digoxin ↑ 25%

Page 2-176 – Table 9

### Class III Antiarrhythmics

- Sotalol\*
  - AF and VT maintenance alone (not conversion)
  - CI in ClCr < 40ml/min, QT > 440 msec
- Dofetilide\*
  - AF conversion & maintenance (not VT)
  - CI in ClCr < 20ml/min, QTc > 440 msec
  - Metabolized by CYP450-3A4, secreted by kidney
- Ibutilide
  - AF conversion alone
  - CI LVEF < 30%, QTc > 440 msec
  - Metabolized by CYP450-3A4

\*Hospitalization for QTc monitoring 2-3 hrs after first five doses. Discontinue agents if QTc > 500 msec!

Page 2-176 and 177 – Table 9

### Class III Antiarrhythmics

- Amiodarone
  - Multiple AEs - PFTs, TFTs, LFTs, skin, eyes
  - Multiple DIs - warfarin, digoxin, statins (CYP3A4)
- Dronedarone
  - AEs – worsening HF, QT prolongation
  - CI in QTc ≥ 500 msec, NYHA class IV HF or recent ADHF, severe hepatic disease, AVB or HR < 50
  - DIs with CYP3A4 inhibitors, QT prolonging drugs

Page 2-176 and 177 – Table 9

### Ventricular Tachycardia

- Consider adenosine only if regular and monomorphic
- Procainamide, sotalol, amiodarone
  - Lidocaine (second line)
- Avoid procainamide and sotalol if prolonged QT

General presentation	Procainamide
Associated with AMI	Lidocaine
Associated with CAD	Amiodarone, β-blockers, Procainamide

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### Torsades de pointes

- Primarily when QTc > 500 msec
- Withdrawl of QT-prolonging medications and correction of low Mg<sup>2+</sup> and K<sup>+</sup>
  - Class I (IA and IC) and III agents
  - Assess for drug interactions
  - Assess for QT prolonging drugs
    - www.torsades.org
- If unstable, DCC
- If stable, IV magnesium

Page 2-179

### Special Populations

- Heart Failure
  - Avoid IA and IC agents
  - Atrial arrhythmias – amiodarone, dofetilide
  - Ventricular arrhythmias - amiodarone
- Acute MI
  - Avoid IA and IC agents
  - Dofetilide – neutral effect on mortality in LV dysfunction post -MI

Page 2-180

## Arrhythmias Case #1 Q4

4. CD is a 68 YOM admitted for syncope

- HPI: presyncopal syndrome
  - Seeing black spots & dizziness, passing out
- In hospital on telemetry:
  - Sustained ventricular tachycardia (VT)
- Vital signs: BP 120/75, HR 80 BPM
- Labs: BUN 30 mg/dl, SCr 2.2 mg/dl (~ CrCl 30 mL/min)

Page 2-181 – Q#4 (Answer Page 2-191)

## Arrhythmias Case #1 Q4

### Past Medical History

- HF NYHA class III
  - LVEF 30%
- MI x2
- HTN x20 yrs
  - Left ventricular hypertrophy
- Diabetes
  - Nephropathy

### Medications

- Lisinopril 5 mg QD
- Furosemide 20 mg BID
- Metoprolol 25 mg BID
- Digoxin 0.125 mg QD
- Glyburide 5 mg QD
- Aspirin 325 mg QD

Page 2-181 – Q#4 (Answer Page 2-191)

## Arrhythmia Patient Case # 1 Q4

4. Which is the best drug therapy to initiate for treatment of sustained VT?

- A. Amiodarone 150mg IV over 10min, 1mg/min x6 hrs, then 0.5mg/min
- B. Sotalol 80mg BID, titrated to QTc ~ 450 msec
- C. Dofetilide 500mcg BID, titrated to QTc ~ 450 msec
- D. Procainamide 20mg/min, max 17mg/kg

Handout Page 2-181 Q#4; Answer Page 2-191

## Pulmonary Arterial Hypertension

**Medical therapy for pulmonary arterial hypertension: updated ACCP evidence-based clinical practice guidelines. *Chest* 2007; 131:1917-28.**

**ACF/AHA 2009 expert consensus document on pulmonary hypertension. *J Am Coll Cardiol* 2009; 53:1573-619.**

Page 2-190

## Pulmonary Arterial Hypertension

- **Diagnosis**
  - mPAP >25 mmHg
  - PCWP ≤ 15 mmHg
  - PVR > 3 Woods units
- **WHO classification**
  - Functional class I-IV
- **Treatment goals**
  - Relieve acute dyspnea
  - Improve exercise capacity
  - Prevent death
- **Acute vasodilator response testing**
  - ↓ mPAP 10-40 mmHg
  - Predicts response to CCB or vasodilator

mPAP=mean pulmonary artery pressure

Page 2-182 – Table 13 and 14

## PAH Initial Algorithm

Supportive Care	
Oxygen, diuretic if needed, warfarin, immunizations	
Initial Therapy	
Acute vasoreactivity testing positive, initiate CCB	
If sustained response, continue CCB	
Negative Response to Acute Vasoreactivity Testing	
<b>Lower Risk</b> First line: ERA s or PDEI s (oral) Alternatives: epoprostenol or treprostinil (IV ) Iloprost (inhaled), treprostinil (SC)	<b>Higher Risk</b> Epoprostenol or treprostinil (IV ) Iloprost (inhaled) ERA s or PDEI s (oral) Treprostinil (SC)
Reassess: consider combination therapy, investigational protocols, atrial septostomy, lung transplantation	

Page 2-183 – Table 15

## PAH Treatment Options

Drug	Adverse Effects	Considerations
<b>Calcium Channel Blockers (Class II PAH)</b>		
Various agents	Hypotension, peripheral edema, cardiac conduction delay (diltiazem)	Should not be used without positive response testing! Selection based upon HR.
<b>Prostacyclin Analogs (Class II-IV* / III-IV PAH)</b>		
Epoprostenol (Flolan)	IV related AEs, rebound if discontinued	Medical emergency if infusion interrupted
Treprostinil* (Remodulin)	SQ related AEs (>80%) limit use	Local treatments, rotate SQ site q3 days
Inhaled iloprost (Ventavis)	Mild transient cough, less systemic AEs	6-9 inhalations daily (15 mins/nebulization)

Page 2-184 – Table 16

## PAH Treatment Options

Drug	Adverse Effects	Considerations
<b>Endothelin Receptor Antagonists (Class II-III* / III-IV PAH)</b>		
Bosentan (Tracleer)	Edema, hypotension, liver disease, induction/ inhibition via 2C8/9, 3A4	Monitor LFTs & Hgb, use two contraceptive methods
Ambrisentan* (Letairis)	Higher rate edema, lower rate hypotension, liver disease	Monitor LFTs, use two contraceptive methods
<b>Phosphodiesterase Inhibitors (Class II-IV PAH)</b>		
Sildenafil (Revatio)	Headache, facial flushing	Augments other therapies, CI if nitrates Caution with 3A4 DDIs
Tadalafil (Adcirca)	Same as above	Same as above

Page 2-183 and 184 – Table 16

## PAH Case #1 Q7

7. RW is a 38-year old obese woman

- Increasing fatigue & SOB
- Walks 10-20 feet at baseline → SOB at rest
- ABG: pH 7.31/pCO<sub>2</sub> 65/pO<sub>2</sub> 53/ 85%
- PE: 3 pillow orthopnea, 3+ pitting edema
- PMH: atrial fibrillation
- CT angiography: enlarged pulmonary artery, mean pressure 56 mmHg

Page 2-186 – Q#7 (Answer Page 2-192)

## PAH Patient Case #1 Q7

7.ECHO: Right atrial & ventricular hypertrophy

- Labs: BUN 21, Scr 1.2, AST 145, ALT 90, INR 2.1, PTT 52
- Vitals: BP 108/62, HR 62
- Home Meds: warfarin 2.5mg QD  
ipratropium 2puffs Q6h  
salmeterol 2 puffs BID  
diltiazem 480mg CD QD

Page 2-189 – Q#7 (Answer Page 2-192)

## PAH Patient Case #1 Q7

7. Which one is the best evidence-based management strategy for idiopathic pulmonary arterial hypertension?

- A. Increase diltiazem to 600mg/day
- B. Start sildenafil 20mg TID
- C. Start epoprostenol 2 ng/kg/min
- D. Start bosentan 62.5mg BID

Handout Page 2-189 (Q #7); Answer Page 2-192

## Hypertensive Crises

Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 1. *Am J Health Syst Pharm* 2009;66:1343–52.

Rhoney D, Peacock WF. Intravenous therapy for hypertensive emergencies, part 2. *Am J Health Syst Pharm* 2009;66:1448–57.

Page 2-190

## Hypertensive Crises

- Hypertensive Urgency
  - Acutely elevated BP, DBP > 120-130 mmHg, and no TOD
- Hypertensive Emergency
  - Acutely elevated BP, DBP > 120-130 mmHg
  - Target organ damage (TOD) present
    - Brain: HTN encephalopathy, stroke
    - Heart: ACS, HF, aortic dissection
    - Eyes: papilledema, retinopathy
    - Kidney: decreased UOP, ARF

Page 2-186

## Hypertensive Crises

- Treatment goals:
  - Urgency
    - MAP reduction to goal range in 24 hrs
  - Emergency
    - 25% MAP reduction within 30-60 min
- Drugs:
  - IV used for emergency
  - IV or PO used for urgency
  - Selected based on comorbidities and TOD

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## Hypertensive Emergency - IV

Drug	Adverse Effect
Nitroprusside*	Cyanide/thiocyanate toxicity CI: Renal/hepatic failure
Esmolol and Labetalol	Bronchospasm, HF exacerbation, bradycardia/heart block
Nicardipine*	Reflex tachycardia, N/V Caution: Angina/MI, acute HF, ↑ ICP
Nitroglycerin*	Headache, nausea, tachyphylaxis
Hydralazine*	Reflex tachycardia, HA, variable duration
Enalaprilat	Renal insufficiency/failure, hyperkalemia CI: Pregnancy, renal artery stenosis
Fenoldopam	Headache, flushing, cerebral ischemia
Clevidipine	Caution in elderly (renal/hepatic function), HF, β-blocker use, etc.

\*Caution: ↑ ICP

Page 2-187 – Table 17

## Hypertensive Urgency – oral drugs

Drug	Adverse Effect
Captopril	Renal insufficiency/failure, hyperkalemia CI: Pregnancy, renal artery stenosis
Clonidine	Sedation, dizziness CI: Severe carotid artery stenosis
Minoxidil	Tachycardia, edema CI: Angina, HF
Nifedipine	Flushing, headache, edema CI: Severe aortic stenosis, coronary artery or cerebrovascular disease
Labetalol	Bronchospasm, HF exacerbation, bradycardia/heart block

Page 2-188 – Table 18

## Hypertensive Crises Patient Case#1 Q9

9. AW is a 68-year old man
- PMH: ESRD on HD, HTN, CAD s/p MI, moderately depressed LVEF, GERD
  - Presents with acute-onset SOB and CP
  - After HD, had large BBQ meal with salt & smoked cocaine-laced marijuana
  - Medication nonadherence for 2 days and 2 kg weight gain within 24hrs
  - Worsening orthopnea, acute chest tightness, nausea, pain 7/10

Page 2-189 – Q#9 (Answer Page 2-194)

## Hypertensive Crisis Patient case #1 Q9

9. AW went to the emergency dept.
- BP: 250/120mmHg
  - PE: crackles ½ way up lungs
  - CXR: bilateral fluffy infiltrates, cephalization
  - ECG: sinus tachycardia, HR 122, ST depressions in leads II, III, AVF
  - Labs: BUN 48, SCr 11.4; BNP 2350, TpT 1.5, CK 227, and MB 22
  - Admitted for hypertensive emergency

Page 2-189 – Q#9 (Answer Page 194)

### Hypertensive Crisis Patient Case#1 Q9

9. Which one of the following is the best medication to manage AW's HTN emergency?

- A. IV NTG 5mcg/min, titrated to 25% reduction in MAP
- B. Labetolol 2mcg/min, titrated to 50% reduction in MAP
- C. Sodium nitroprusside 0.25mcg/kg/min, titrated to 25% reduction in MAP
- D. Clonidine 0.1mg PO every 2 hrs PRN, titrated to 50% reduction in MAP

Handout Page 2-189-Q#9; Answer Page 2-194



### Updates in Therapeutics® 2012:

#### The Pharmacotherapy Preparatory Review & Recertification Course

##### Cardiology II

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### Conflict of Interest Disclosures

**I have no conflicts of interest to disclose**

### Agenda

- Acute coronary syndromes
- Peripheral Arterial Disease
- Dyslipidemia

### Acute Coronary Syndromes

Rooke TW, Hirsch AT, Misra S, et al. 2011 ACCF/AHA focused update of the Guideline for the Management of Patients with Peripheral Artery Disease (Updating the 2005 Guidelines): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2011;58:2020-45.

Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: Executive Summary. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation* 2011;124:2129-38.

Kushner FG, Hand M, Smith SC, Jr et al. 2009 focused update of the ACC/AHA for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update): a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2009; 54:2205-41.

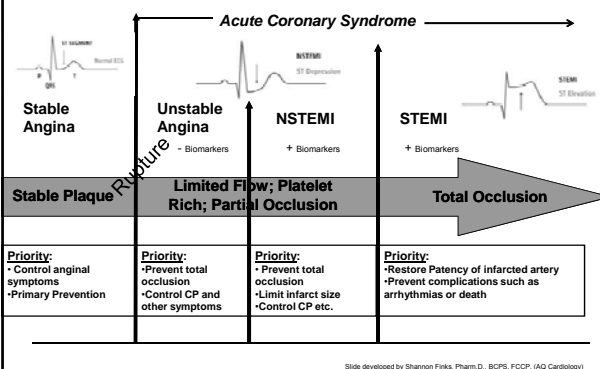
Grundy SM, Cleeman JI, Baird Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Panel III Guidelines. *Circulation* 2004;110:227-239.

## Coronary Artery Disease

- Causes 1 out of every 6 deaths in the U.S
- 785,000 Americans suffer a new coronary event, 470,000 will suffer a recurrent attack
- A coronary event occurs approximately every 25 seconds
- Claims 1 life every 39 seconds

• AHA Heart and Stroke Statistics 2012

## ACS Pathophysiology and Characteristics



## ACS Defined

### Unstable angina (UA)

- Chest pain that often occurs at rest, can occur suddenly, may worsen suddenly, or may be stuttering in nature recurring over days to weeks.
- Diagnosis: ST-segment depression, T-wave inversion, or no ECG changes may occur, but no positive biomarkers for cardiac necrosis present

### Non-ST-elevation MI (NSTEMI)

- Symptoms similar to Unstable Angina but differentiated based on markers and EKG
- Diagnosis: Positive cardiac enzyme biomarkers of necrosis (troponin I or T elevation, CKMB fraction > 5%–10% of total CK), EKG- ST depression, T wave inversions, or transient ST-elevation

### STEMI

- Classic symptoms include worsening of chest pain lasting more than five minutes, accompanied by shortness of breath, nausea, or weakness. Other symptoms may include chest discomfort with or without radiation to other areas such as the arms, back, neck, jaw, or abdomen, and diaphoresis.
- Diagnosis: ST-elevation of > 1 mm above baseline on ECG, positive biomarkers

Page 2-200

## Goals of Therapy

### ■ UA/NSTEMI goals

- Prevent total occlusion
  - Antiplatelets (ASA, P2Y<sub>12</sub>, +/- GPIs) and antithrombotics
  - PCI – PTCA or stent implantation
- Control CP and associated symptoms

### ■ STEMI goals

- Restore patency and minimize infarct size (PCI or lytics)
  - Door-to-needle < 30 mins (lytics), Door-to-balloon < 90 mins (PCI)
  - If > 90 mins to PCI, fibrinolysis unless contraindicated
- Prevent complications
- Control CP and associated symptoms

Page 2-200

## Invasive vs Conservative Strategy

UA/NSTEMI	TIMI Scoring
History	Age >65 More than 3 cardiac risk factors* History of CAD >50% stenosis
Presentation	Severe angina, ASA within 7 days, elevated markers, ST-segment deviation >0.5 mm

\* HTN, DM, HLD, smoking, family history

Score = 0-1 mortality 7%, Score = 2 mortality 8%,  
Score = 3 mortality 13%, Score = 4 mortality 20%,  
Score = 5 mortality 26%, Score = 6-7 mortality 41%

Page 2-201, Table 2

## Invasive vs. Conservative Strategy

Invasive	Conservative
Recurrent angina/ischemia at rest Elevated biomarkers New/presumably new ST depression S/S of HF or new/worsening mitral regurgitation High risk findings from noninvasive testing Hemodynamic instability Sustained VT PCI w/ 6 months Prior CABG High-risk score (e.g., TIMI, GRACE) Reduced LVEF (<40%)	Low risk score (TIMI, GRACE) Patient/Physician preference in the absence of high risk features

Page 2-201, Table 3

## UA/NSTEMI & STEMI Initial Management

<b>M</b> = Morphine	Morphine 1 to 5 mg IV if symptoms not relieved by NTG or recur
<b>O</b> = Oxygen	Oxygen if O <sub>2</sub> saturation < 90% or high-risk features for hypoxemia
<b>N</b> = Nitroglycerin	NTG spray or SL tablet 0.4 mg x 3 doses (if pain unrelieved after one dose, call 911) NTG IV 5 mcg/min, titrate to CP relief or 200 mcg/minute
<b>A</b> = Aspirin*	ASA chew and swallow non-enteric coated 162–325 mg x 1 dose
<b>B</b> = Beta blocker* * = mortality reducing	PO/IV beta blocker, oral preferred Page 2-202, Table 4

## UA/NSTEMI Algorithm

Strategy	Early Invasive	Delayed PCI	Early Conservative
Anticoagulant therapy	ENOXAPARIN UFH FONDAPARINUX (+UFH@PCI) BIVALRUDIN	ENOXAPARIN UFH FONDAPARINUX (+UFH@PCI) BIVALRUDIN	ENOXAPARIN FONDAPARINUX UFH
Antiplatelet therapy (ASA +)	CLO or PRA or TIC +ABCIX or EPTI @PCI if receiving +UFH/ENOX/ FONDAPARINUX	CLO or PRA or TIC If high/mod risk, +EPTI/TIRO before angio/PCI or @PCI	CLO or TIC If +stress test, ABCIX/EPTI w/ UFH/ENOX, or BIVAL @PCI

Page 2-203, Table 5

## STEMI Algorithm

Symptoms ≤ 12 hours	
Primary PCI	Fibrinolysis
CLOPIDOGREL or PRASUGREL or TICAGRELOR	CLOPIDOGREL
UFH with ABCIXIMAB (alternatively EPTIFIBATIDE or TIROFIBAN) or BIVALRUDIN alone	IV UFH x at least 48 hours or IV/SC ENOXAPARIN for hospitalization, up to 8 days (preferred, selected pts) or IV/SC FONDAPARINUX for hospitalization, up to 8 days

Page 2-203, Table 6

## Antiplatelet Agents

ASA	CLO / PRA/TIC
<b>Initial therapy</b> – ASA 162–325 mg nonenteric orally or chewed x 1 <b>Pre-PCI</b> – ASA 81–325 mg before PCI <b>No stent</b> – ASA 81 mg/day indefinitely <b>Post-stent</b> –BMS/DES: 81 mg daily –TIC: 325 mg initially, then 75-100 mg daily	<b>Initial therapy</b> – STEMI Pre-PCI after lytics– CLO 300 if with 24 hrs of event – CLO 600 mg if > 24 hrs after event <b>Pre-PCI</b> – CLO 600 mg, PRA 60 mg, TIC 180 mg <b>No stent (STEMI + lytic)</b> – CLO 75 mg/d x 14 d, up to 1 yr <b>Post-stent</b> – CLO 75 mg/day/PRA 10 mg/day (5 mg/day if < 60 kg), TIC 90 mg BID x at least 12 months, up to 15 months (BMS or DES )

Page 2-204, Table 7

## P2Y<sub>12</sub> Antagonists

Parameter	Clopidogrel	Prasugrel	Ticagrelor
FDA Indication	ACS managed medically or with PCI	ACS with PCI	ACS managed medically or with PCI
Dosing	LD: 300-600, MD 75 mg daily	LD: 60 mg, MD 10 mg daily (5 mg if <80 kg; BBW ≥75 y) CI: TIA/stroke	LD: 180 mg, MD 90 mg twice daily CI: ICH, severe hepatic dz
Peak Platelet Inhib	300 mg load ~ 6 hrs 600 mg load ~2 hrs	60 mg load ~1-1.5 hrs	180 mg load
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
T <sub>1/2</sub>	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 PII); enhanced bleeding with NSAIDs, VKA, SSFA, 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

## Clopidogrel- Plavix®

Indication	Loading Dose	Maintenance Dose
UA/NSTEMI	300 mg (P.I.) -600 mg (with stenting- 2011 PCI guidelines)	75 mg daily
STEMI without fibrinolytic therapy	300 mg (P.I.) -600 mg (with stenting- 2011 PCI guidelines)	75 mg daily
STEMI with fibrinolytic therapy	300 mg if within 24 hours, and 600 mg if more than 24 hours since fibrinolysis	75 mg daily
Recent MI, Stroke, PAD	N/A	75 mg daily

## GP IIb/IIIa Inhibitors

	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%

Page 2-204 Table 8

## Anticoagulants Agents

	Unfractionated Heparin	Enoxaparin (Lovenox)	Fondaparinux (Arixtra)	Bivalirudin (Angiomax)
Classification	LMWH	Factor Xa inhibitor	DTI	
UA/NSTEMI	60-unit/kg IVB (max 4000 units), 12 units/kg/hour IV (maximum 1000 units/hour) for 48 hours or end of PCI, goal aPTT 1.5-2 × control	1 mg/kg SC BID for 24-48 hours (UA/NSTEMI) or until end of PCI or throughout hospitalization or up to 8 days (STEMI)	2.5 mg SC QD (If STEMI, give initial 2.5 mg IVB)	0.1-mg/kg IVB, then 0.25 mg/kg/hour IV
PCI	Supplemental doses to target ACT*	If last dose < 8 hours, none If last dose ≥ 8 hours, 0.3 mg/kg IVB if last dose 8-12 hours prior	Fondaparinux should not be used as a sole anticoagulant in PCI	UA/NSTEMI - 0.5-mg/kg IVB, 1.75 mg/kg/hour IV STEMI - 0.75-mg/kg IVB Discontinue at end of PCI or continue at 0.25 mg/kg/hour if needed (Hold UFH 30 minutes before administration)
STEMI primary PCI*	If GP IIb/IIIa, UFH 50-70 units/kg IVB If no GP IIb/IIIa, UFH 70-100 units/kg IVB Supplemental doses to target ACT*	If prior treatment with enoxaparin and last dose < 8 hours, nothing else needed If last doses given at least 8 to 12 hours earlier, administered 0.3 mg/kg IVB	2.5 mg IVB; then 2.5 mg SC QD	0.75 mg/kg, 1.75 mg/kg/hour IV
Dose adjustments/contraindications	Avoid if history of HIT	If CrCl < 30 mL/minute, 1 mg/kg SC QD Avoid if > 175 kg or CrCl < 15 mL/minute	Avoid if CrCl < 30 mL/minute	Adjust infusion dose in severe renal dysfunction (IVB dose same)

Page 2-205 Table 9

## Thrombolytics

	Dosing
Alteplase (rt-PA, Activase)	15 mg IV, then 0.75 mg/kg over 30 minutes (max 50 mg), then 0.5 mg/kg (max 35 mg) over 60 minutes
Reteplase (r-PA, Retavase)	10 units IV, repeat 10 units IV in 30 minutes
Tenecteplase (TNK-tPA, TNKase)	< 60 kg, 30 mg IV; 60-69 kg, 35 mg IV; 70-79 kg, 40 mg IV; 80-89 kg, 45 mg IV; > 90 kg, 50 mg IV (about 0.5 mg/kg)

r-PA = Reteplase; TNK = tenecteplase; rt-PA = alteplase

Page 2-206 Table 10

## Contraindications to Thrombolytics

Relative Contraindications	Absolute Contraindications
BP > 180/110 mm Hg on presentation History of TIA or CVA < 3 months prior History of chronic poorly controlled HTN INR 2-3 on warfarin Recent trauma, major surgery, CPR, internal bleeding in 2-4 weeks Streptokinase exposure > 5 days earlier or prior allergic reaction (if given streptokinase again) Active peptic ulcer Age > 75 years Pregnancy Known intracranial pathology (dementia)	ANY prior hemorrhagic stroke Ischemic stroke within 3 months (except in past 3 hours) Intracranial neoplasm or arteriovenous malformation Active internal bleeding Aortic dissection Considerable facial trauma or closed-head trauma in past 3 months

Page 2-206 Table 11

### UA/NSTEMI Case #1

- JD is a 66-year old woman
  - PMH: prior MI, HTN, HLD, DM
  - Presents with sudden-onset diaphoresis, N/V, dyspnea, band-like chest pain (8/10), radiating to left arm
  - HPI: 1 month prior, typical angina frequency with less exertion
  - ECG: ST depressions in leads II, III, AVF, and hyperdynamic T waves
  - Cardiac enzymes positive

Page 2-207 (Ans 2-229)

Q#1

### UA/NSTEMI Case #1

- Home Meds: aspirin 81mg daily  
simvastatin 40 mg every night  
metoprolol 50 mg twice daily  
metformin 1 gm twice daily
- Diagnosis: NSTEMI
- TIMI Risk=6
  - 41% risk at 14 days of: all-cause mortality, new or recurrent MI, or severe recurrent ischemia requiring urgent revascularization.

Page 2-207 (Ans 2-229)

Q#1

### NSTEMI Case #1

1. Which is the best NSTEMI strategy for JD?
- ❑ A. Aspirin and clopidogrel, UFH + eptifibatide, at time of PCI if indicated
  - ❑ B. Aspirin, enoxaparin, plus cardiac catheterization for possible PCI
  - ❑ C. Medical management with abciximab plus enoxaparin, aspirin, & clopidogrel
  - ❑ D. Medical management with aspirin, clopidogrel, UFH

Q#1

Page 2-207 (Ans 2-229)

### NSTEMI Case #2

2. JD received a PCI and paclitaxel-eluting stent in her RCA. Which one of the following best represents how long clopidogrel therapy should continue?
- ❑ A. 1 month
  - ❑ B. 3 months
  - ❑ C. 6 months
  - ❑ D. At least 12 months

Q#2

Page 2-207 Ans 2-229

### NSTEMI Case #3

3. Which one of the following is the optimal lifelong ASA dose once dual therapy with clopidogrel after PCI with stent implantation is completed?
- ❑ A. 25 mg
  - ❑ B. 81 mg
  - ❑ C. 325 mg
  - ❑ D. 650 mg

What if ticagrelor is chosen as the DAT strategy?

Q#3

Page 2-208 (Ans 2-299)

### Dual Antiplatelet Therapy after ACS

- Reduces the risk of stent thrombosis
- Aspirin *plus* P2Y<sub>12</sub> antagonist
  - ❑ Thienopyridines: ticlopidine, clopidogrel, and prasugrel
  - ❑ Cyclopentyltriazolopyrimidine (CPTP): ticagrelor
- Recommended for at least 12 months after PCI
  - ❑ BMS/DES for ACS-options are clopidogrel, prasugrel, or ticagrelor
  - ❑ BMS/DES for non-ACS, 2011 PCI guidelines prefer clopidogrel
  - ❑ For BMS for non-ACS, DAT recommended for 1 month, unless high bleeding risk (minimum of 2 weeks)
- Continuation beyond 12 months may be considered for DES
- After PCI, it is reasonable to use 81 mg aspirin in preference to higher doses
- Consequences of early cessation include stent thrombosis, MI, and death

2011 PCI Guidelines: *Circulation*. 2011; 124: e574-e651.

### Long-term Medications

- Beta-blockers
- ACE inhibitors
  - ❑ Within 1<sup>st</sup> 24 hrs if anterior MI, HF signs or LVEF < 40%
  - ❑ Avoid IV agents to prevent hypotension
- Aldosterone antagonists
  - ❑ MI & LVEF < 40% and either symptomatic HF or DM and on ACE inhibitor
- Statins
  - ❑ LDL goal < 100 mg/dL, < 70 mg/dL reasonable

Page 2-206

### STEMI Case #1

4. RV is a 52 YOM
- PMH: HTN, hypertriglyceridemia
  - HPI: presents to major university teaching hospital within 3 hours
    - ❑ Crushing 10/10 substernal chest pain radiating while eating (at rest)
    - ❑ Nausea, diaphoresis, SOB
    - ❑ Never experienced CP of this character/intensity

Q#4

Page 2-208 (Ans 2-229)

## STEMI Case #1

- Home Meds: lisinopril, gemfibrozil
- Vitals: HR 68, BP 178/94, wt 100kg
- ECG:
  - 3mm ST Elevation in V<sub>2</sub>-V<sub>4</sub>, I, aVL
- Labs:
  - Serum chemistry WNL
  - Positive myoglobin
  - Positive cardiac enzymes
    - CK 175, MB 17.4, Troponin T 0.8
- Diagnosis: STEMI

Q#4

Page 2-208 (Ans 2-229)

## STEMI Case #1

4. Which of the following should be done for STEMI treatment?
- A. Primary PCI with stent of artery, abciximab, clopidogrel, aspirin, UFH
  - B. Reteplase 10 U bolus x2, 30min apart + UFH 60 U/kg bolus & 12 U/kg/hr
  - C. Abciximab + enoxaparin 100mg SQ BID + tenecteplase 25mg IVP
  - D. Tirofiban + UFH infusion

Q#4

Page 2-208 (Ans 2-229)

## Peripheral Arterial Disease (PAD)

Alan T. Hirsch, Ziv J. Haskal, Norman R. Hertzler, Curtis W. Bakal, Mark A. Creager, et al. ACC/AHA 2005 Practice Guidelines for the Management of Patients with Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic): A Collaborative Report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Peripheral Arterial Disease). Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006;113:e463-e465.

Oline JW, Allie DE, Belkin M, Bonow RO, et al. ACCF/AHA/ACR/SCAI/SIR/SVM/SVS 2010 Performance Measures for Adults with Peripheral Arterial Disease: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures, the American College of Radiology, the Society for Cardiac Angiography and Interventions, the Society for Interventional Radiology, the Society for Vascular Medicine, the Society for Vascular Nursing, and the Society for Vascular Surgery (Writing Committee to Develop Clinical Performance Measures for Peripheral Arterial Disease. *Circulation* 2010; 122:2583-2618

## Peripheral Arterial Disease

### Definition

- A generic term that encompasses vascular insufficiencies due in non-coronary arteries secondary to atherosclerotic occlusions. The arteries affected supply blood flow to the brain, visceral organs, and limbs.
  - Affects approximately 27 million people affected by the disease.
  - The incidence increases with age with approximately 20% of patients over 70 years affected.

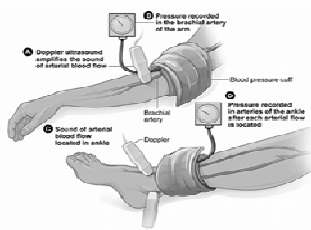
### Symptoms

- Leg or hip pain during walking
- Cold legs and feet
- Changes in skin color
- Pain that is reduced upon resting
- Numbness or tingling

Page 2-209

## Diagnosis

### Ankle Brachial Index



National Heart Lung and Blood Institute Diseases and Conditions Index, Available from: [http://www.nhlbi.nih.gov/health/dci/Diseases/pad/pad\\_diagnosis.html](http://www.nhlbi.nih.gov/health/dci/Diseases/pad/pad_diagnosis.html)

Page 2-209

## ABI Calculation

Calculation of ABI  
Right ABI= HRAP/HAP  
Left ABI= HLAP/HAP

### ABI Interpretation

Level	Interpretation
1 to 1.4	Normal ABI
0.91 – 0.99	Borderline
≤0.9	Abnormal

Values >1.40 indicate noncompressible arteries

Page 2-210

- Age greater than 50 years
- Cigarette Smoking
- Diabetes
- High Cholesterol
- Family History
- Hypertension
- Coronary disease
- Stroke

Page 2-210 – Table 13

```

graph TD
    A["PAD Population (50 years and older)"] --> B["Initial clinical presentation"]
    B --> C["Asymptomatic PAD  
20%, 60%"]
    B --> D["Asymptomatic PAD  
40%, 40%"]
    B --> E["Claudication  
10%, 10%"]
    C --> F["Progressive  
Ischemic Equivalents"]
    E --> G["Critical Isch Ischemia  
1%, 10%"]
    E --> H["3-year outcomes"]
    G --> I["Lower extremities"]
    I --> J["Minor extremities Isch  
10%"]
    I --> K["Ischemic  
10%"]
    I --> L["CV Mortality  
15%"]
    H --> M["Limb mortality"]
    H --> N["CV mortality & morbidity"]
    M --> O["Nonhealing Ischemic Equivalents  
10%, 10%"]
    M --> P["Wound healing  
10%, 10%"]
    M --> Q["Critical Isch Ischemia  
1%, 10%"]
    N --> R["Nonfatal cardiovascular event  
(MACE or nonfatal CV)"]
    N --> S["MACE  
10%, 10%"]
    R --> T["CV Mortality  
10%"]
    R --> U["Non-CV Mortality  
10%"]
    S --> T
    S --> U
  
```

Page 2-211

- Diet - Exercise
- Smoking Cessation – varenicline, bupropion, or nicotine replacement therapy
  - People who smoke are diagnosed with PAD as much as 10 years before a non-smoker
- Drug Therapy
  - Statins initiation – Goal LDL-C of less than 70 mg/dL for patients deemed very high risk
  - Fibric Acid agents – Utilized for patients with low HDL-C, normal LDL-C, and high triglycerides
  - Antihypertensives – Goal blood pressure of < 140/90 mmHg if non diabetic and < 130/80 mmHg if diabetic or chronic kidney disease
    - Beta Blockers- not contraindicated
    - Angiotensin Converting Enzyme Inhibitors
  - Diabetes Control including proper foot care – Goal HgA1C < 7%
  - Antiplatelet Agents
    - Recommended for all patients with lower extremity disease
    - Aspirin 75 to 325 mg PO daily is effective (34% ↓nonfatal stroke)
    - Clopidogrel 75 mg PO daily is an alternative to aspirin
    - Warfarin – Not recommended

Page 2-211

6. C.J. is a 56 year old male who presents to his primary care providers office for a follow-up visit following his evaluation for possible peripheral arterial disease. His past medical history is significant for hypertension and he is a smoker (2 packs per day x 20 years). His ABI comes back at 0.86. Based on these results, how would CJ's peripheral arterial disease be classified?

- A. Normal
- B. Borderline
- C. Abnormal
- D. Noncompressible

Page 2-212. (Ans. 2-230)

- CJ currently takes lisinopril 10 mg PO daily as his only medication. He has no known drug allergies. Based on his ABI results, which of the following medication regimens in addition to a statin and smoking cessation would be the most appropriate to initiate at this time?

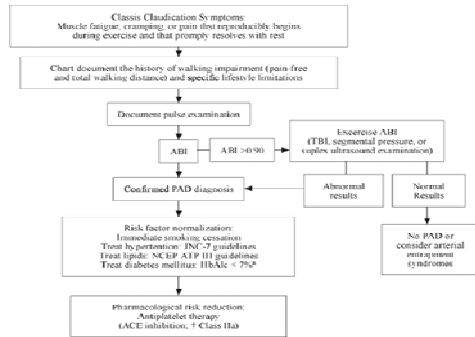
- A. Folic acid
- B. Warfarin
- C. Aspirin
- D. Clopidogrel

Page 2-212 (Ans 2-230)

- Cilostazol (Pletal)
  - Mechanism of Action – a phosphodiesterase type 3 inhibitor that causes an increase in cyclic adenosine monophosphate. It has both vasodilatory and antiplatelet effects.
  - Dose - 100 mg orally twice daily
  - **Class I: to improve symptoms and increase walking distance**
  - Avoid use in patients with heart failure
- Pentoxifylline (Trental)
  - Mechanism of Action – a methylxanthine derivative. Reduces blood and plasma viscosity, inhibit neutrophil adhesion and activation, increase erythrocyte and leukocyte deformability and lower plasma fibrinogen levels.
  - Dose- 400 mg PO three times daily
  - **Class lib: Second-line agent to improve walking distance**
  - Questionable Efficacy
- Additional Therapies *Not Helpful!*
  - Oral vasodilator prostaglandins
  - Vitamin E

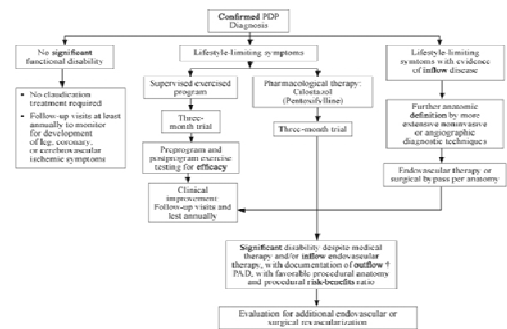
Page 2-212

## Treatment Algorithm



Page 2-213, Figure 3

## Treatment Algorithm Cont:



Page 2-214, Figure 4

## Dyslipidemia

## Lipid and Lipoprotein Classification

1.	<b>LDL (mg/dL)</b>	
	Less than 100	Optimal
	100–129	Near-optimal/above optimal
	130–159	Borderline high
	160–189	High
	190 or more	Very high
2.	<b>HDL (mg/dL)</b>	
	Less than 40	Low
	60 or more	High
3.	<b>TC (mg/dL)</b>	
	Less than 200	Desirable
	200–239	Borderline high
	240 or more	High
4.	<b>TG (mg/dL)</b>	
	Less than 150	Normal
	150–199	Borderline high
	200–499	High
	500 or more	Very high

Page 2-215

## Risk Assessment

- For patients with multiple (two or more) risk factors, perform Framingham 10-year CHD risk assessment.
- For patients with zero or one risk factor, 10-year risk assessment is not required.
- Ten-year CHD risk assessment is based on Framingham tables.
  - Gender
  - Age
  - Total cholesterol
  - Smoking
  - High-density lipoprotein
  - Systolic BP

Page 2-215

## Risk Factors

- Cigarette smoking
- Hypertension (blood pressure [BP] 140/90 mm Hg or higher or taking an antihypertensive drug)
- Low HDL (less than 40 mg/dL)
- Family history of premature CHD
- Coronary heart disease in male first-degree relative younger than 55 years
- Coronary heart disease in female first-degree relative younger than 65 years
- Age (men 45 years or older; women 55 years or older)

### Main **Negative** Risk Factor

- High HDL (more than 60 mg/dL) (subtract 1 from the total number of risk factors)

Page 2-215

## CAD and Risk Equivalents- *High Risk*

- Coronary heart disease (CHD): myocardial infarction, coronary artery bypass graft, percutaneous coronary intervention with or without stent, acute coronary syndrome
- Other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease)
- Diabetes mellitus
- Ten-year risk of CHD is more than 20% based on Framingham.

Page 2-215

## NCEP-ATP III Guidelines-2004

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

\* Consider goal < 70 in everyone with stable CHD or very high risk (ACS: CHD with multiple risk factors)

Page 2-216

## Patient Case 8

- M.M. is a 63-year-old woman who has just finished 6 months of diet and exercise for dyslipidemia. She has a history of gout, CHF, HTN, and asthma, and a 15 pack-year history of tobacco (but quit 3 years ago); she drinks 3 beers/day. She was adopted, so no family history records are available. Her current medications are albuterol MDI, lisinopril, furosemide, and Tums 2 tablets/day. Vital signs are BP 134/84 mmHg; HDL 54 mg/dL; LDL 193 mg/dL; TG 148 mg/dL; and total cholesterol 236 mg/dL.

Page 2-216

## Patient Case

- According to NCEP guidelines, which of the following is the goal LDL for M.M.?
  - Less than 100
  - Less than 130
  - Less than 160
  - Less than 190

Page 2-217

## Case #8

- According to NCEP guidelines, how many CHD risk factors are present?
  - Zero
  - One
  - Two
  - Three

Page 2-217 (Ans 2-230)

## NCEP-ATP III Guidelines-2004

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

\* Consider goal < 70 in everyone with stable CHD or very high risk (ACS: CHD with multiple risk factors)

Page 2-216, Table 14

## Approximate and Cumulative LDL Cholesterol Reduction Achievable By Dietary Modification

Dietary Component	Dietary Change	Approximate LDL Reduction
<b>Major</b>		
Saturated fat	<7% of calories	8-10%
Dietary cholesterol	<200 mg/day	3-5%
Weight reduction	Lose 10 lbs	5-8%
<b>Other LDL-lowering options</b>		
Viscous fiber	5-10 g/day	3-5%
Plant/sterol stanol esters	2g /day	6-15%
Cumulative estimate		20-30%

Source: Adapted from ATP III 2002, Page 2-217

## Determining What Lipid Therapy to Use

### Management of Low HDL

- If TG is 500 mg/dL or greater, TG is primary target.
- If TG is 200–499 mg/dL, non-HDL is secondary target of therapy.
- If TG is less than 200 mg/dL and HDL is low, consider niacin or fibrates; may add to statins after lowering LDL
- Niacin is safer in combination with statins than with fibrates (myopathy).
- Smoking Cessation, exercise

Page 2-218

## Determining What Lipid Therapy to Use

### Management of Very High TG Concentrations (500 mg/dL or more)

- Therapy goal: Prevent acute pancreatitis
- Very low-fat diets (15% or less of caloric intake), reduce or eliminate alcohol
- Triglyceride-lowering drug usually required
- Fibrate or niacin
- Reduce TG before LDL lowering
- After TG concentrations are reduced, lower LDL
- Achieve LDL goal before treating non-HDL
- Non-HDL cholesterol: secondary target
- Non-HDL = VLDL + LDL (VLDL = very low-density lipoprotein)
- Non-HDL = (TC – HDL)
- Non-HDL: secondary target of therapy when serum TG is 200 mg/dL or greater
- Non-HDL goal: LDL goal plus 30 mg/dL

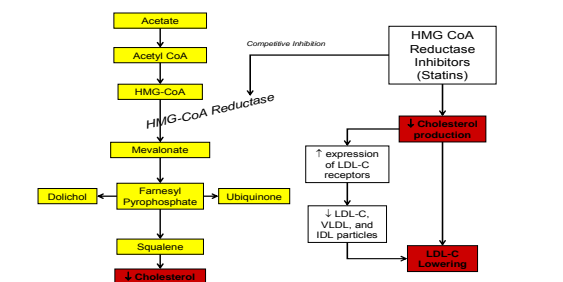
Page 2-218

## 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

Page 2-218, Table 16

## Pharmacotherapy



Page 2-220, Figure 5

## Statins

- Drugs of choice for high LDL and/or CHD or CHD risk
  - Reduce LDL 24%–60%.
  - Reduce TG 7%–40%.
  - Raise HDL 5%–15%.
- When selecting a statin, consider the percentage of LDL reduction needed.
  - $(\text{current LDL} - \text{goal LDL}) / \text{current LDL} \times 100$
  - Select an initial dose to achieve an LDL reduction of 30%–40% if possible.
- Outcomes data
  - Reduce major coronary events.
  - Reduce CHD mortality.
  - Reduce coronary procedures (percutaneous transluminal coronary angioplasty/coronary artery bypass graft).
  - Reduce stroke.
  - Reduce total mortality.

Page 2-221

## Statin Adverse Effects

### Statin Safety Assessment Task Force

- Definitions describing muscle findings in patients taking statins:
  - **Myalgia**
  - **Myopathy\***
    - Complaints of myalgia (muscle pain or soreness), weakness, and/or cramps, plus
    - Elevation in serum CK >10 x ULN
  - **Rhabdomyolysis**
    - CK 10,000 > IU/L, or
    - CK >10 x ULN plus an elevation in serum creatinine or medical intervention with IV hydration

*Am J Cardiol* 2006;97(suppl 8A):89C–94C.

## Factors That Increase the Risk of Statin-Induced Myopathy

Patient Characteristics	Statin Properties
Increasing age	High systemic exposure
Female sex	Lipophilicity
Renal insufficiency	High bioavailability
Hepatic dysfunction	Potential for drug-drug interactions metabolized by CYP pathways (particularly CYP450 3A4)
Hypothyroidism	
Diet (i.e. grapefruit juice)	
Polypharmacy	

*Adapted from: Rosenson RS. Am J Med. 2004;116:408-416*

FDA Consumer Health Information  
www.fda.gov/consumer

## FDA: Limit Use of 80 mg Simvastatin



- June 2011 – Due to increased risk of muscle injury, the FDA says this dose should only be used by patients who have been taking it for 12 months or longer without ill effect.
- If on Simvastatin 40mg and not at goal LDL, choose a different statin rather than raising the simvastatin dose to 80 mg

www.fda.gov March 4, 2012

## Statin Drug Interactions

Agent	Recommendations
Amiodarone	DNE Lova 40mg; Simva 20mg; consider limiting atorva/fluva
Azoles, Macrolides	Hold Lova/Simva during treatment; Limit 1 mg pitava
Amlodipine	DNE Simva 20mg *Caduet=Amlodipine + Atorvastatin
Diltiazem/Verapamil	DNE Simva 10mg with D/V; DNE Lova 20 with D/V Consider limiting atorvastatin dose
Cyclosporine	Avoid Simva/Lova/Pitava; DNE Atorva 10mg; Rosuva 5mg
Gemfibrozil	Rosuva 10mg; AVOID Simva and Lova; Consider limiting dose of atorva
Griseofulvin	Avoid Atorva; Simva; Lova

## Statin/Fibrate Combination Therapy: Pharmacokinetic Interactions

	GEMFIBROZIL	FENOFIBRATE
Atorvastatin	↑ in C <sub>max</sub> (expected)	No effect
Simvastatin	↑ in C <sub>max</sub> by 2-fold	No effect
Pravastatin	↑ in C <sub>max</sub> by 2-fold	No effect
Rosuvastatin	↑ in C <sub>max</sub> by 2-fold	No effect
Fluvastatin	No effect	No effect
Lovastatin	↑ in C <sub>max</sub> by 2.8-fold	Not available
Cerivastatin	↑ in C <sub>max</sub> by 2–3-fold	No effect

Tricor (package insert). Abbott Laboratories. 2004; Kytkund C et al. Clin Pharmacol Ther. 2001;69:340-345; Pan WJ et al. J Clin Pharmacol. 2000;40:316-323; Backman JT et al. Clin Pharmacol Ther. 2000;68:123-129; Backman JT et al. Clin Pharmacol Ther. 2002;72:685-691; Abbott Laboratories. Data on file. 2005; Davidson MH. Am J Cardiol. 2002;90:50K-60K; Prokaskartanoni T et al. Drug Metab Dispos. 2002;30:1285-1287; Martin PD et al. Clin Ther. 2003;25:409-471; Bergman AJ et al. J Clin Pharmacol. 2004;44:1054-1062

## Statins – Another FDA Warning

- No More Routine Periodic Monitoring of Liver Enzymes
  - LFT's should be performed before starting statin therapy, and as clinically indicated thereafter.
  - CI: Severe liver disease (AST/ALT > 3 x ULN)
  - Serious liver injury with statins is rare and unpredictable and routine periodic monitoring of LFT's does not appear to be effective in detecting or preventing this rare side effect.
  - Patients should notify their HCP immediately if they have symptoms of liver problems: unusual fatigue or weakness; loss of appetite; upper belly pain; dark-colored urine; yellowing of skin or whites of the eyes.
- Memory Loss and Confusion with Statins
  - These reports generally have not been serious and the patients' symptoms were reversed by stopping the statin.
  - Patients should still alert their health care professional if these symptoms occur.

www.fda.gov March 4, 2012

## Statins – FDA Warning

### ■ Hyperglycemia with statin use:

- The FDA is also aware of studies showing that patients being treated with statins may have a **small increased risk** of increased blood sugar levels and of being diagnosed with type 2 diabetes mellitus. The labels will now warn healthcare professionals and patients of this potential risk.

www.FDA.gov March 4, 2012

## Statin LDL - Lowering

Statin	Brand Name	Daily Dose (mg)	LDL Lowering (%)
Fluvastatin	Lescol	20 - 80	22 - 35
Pravastatin	Pravachol	10 - 40	24 - 45
Lovastatin	Mevacor	20 - 80	29 - 45
Simvastatin	Zocor	20 - 80	30 - 55

Page 2-222, Table 18

## Pharmacokinetics

Statin	Bioavail	T <sub>1/2</sub> (hours)	Metabolism	Pro-drug	Solubility
Pravastatin	17%	1.5-2	n/a	No	Hydrophilic
Fluvastatin	24%	1	2C9	No	Lipophilic
Lovastatin	<5%	2-3	3A4	Yes	Lipophilic
Simvastatin	<5%	2	3A4	Yes	Lipophilic
Atorvastatin	12%	14	3A4	No	Lipophilic
Rosuvastatin	20%	20	Limited 2C9	No	Hydrophilic
Pitavastatin	51%	12	2C9,2C8	Yes	Lipophilic

Page 2-223, Table 19

## Dosing of Statins in Renal Disease

Drug	GFR 30-59	GFR 15-29	GFR < 15 or HD
Atorvastatin	10-80 mg	10-80 mg	10-80 mg
Fluvastatin	10-80 mg	10-40 mg	10-40 mg
Lovastatin	20-80 mg	10-0 mg	10-20 mg
Pravastatin	20-40 mg	10 initial; 20-40 mg	20-40 mg
Rosuvastatin	5-40 mg	5 mg initial; 10 mg max	Levels in HD are 50% higher than in normal fnct
Simvastatin	20-80 mg	5 mg initial;	Page 2-224, Table 20

## Bile Acid Sequestrants

### Principal actions

- Reduce LDL 15%–26%.
- Raise HDL 3%–6%.
- May increase TG concentrations
- Reduce major coronary events.
- Reduce CHD mortality.
- Mechanism of action: bind to bile acids to disrupt enterohepatic recirculation of bile acids. Liver is stimulated to convert hepatocellular cholesterol to bile acids.
- Adverse effects: GI distress/constipation
- Decreased absorption of other drugs: warfarin, β-blockers, and thiazides, so administer drugs 1–2 hours before or 4 hours after bile acid
- Contraindications: dysbetalipoproteinemia, raised TG concentrations (especially greater than 400 mg/dL)

Pages 2-223

## Bile Acid Sequestrants

	Dose	% LDL-C Reduction
Colestipol	5 grams	-12%
	10 grams	-20%
	15 grams	-24%
Cholestyramine	4-8 grams	-9%
	8-12 grams	-13%
	12-16 grams	-17%
	16- 20 grams	-21%
	20-24 grams	-28%
Colesevelam	3.8 grams	-15%
	4.5 grams	-18%

Page 2-224, Table 22

## Niacin

### Main actions

- Lowers LDL 15%–26%
- Lowers TG 20%–50%
- Raises HDL 15%–26%
- Reduces major coronary events

Mechanism of action: inhibits mobilization of free fatty acids from peripheral adipose tissue to the liver, so reduces VLDL synthesis (LDL and TG)

Adverse effects: flushing, hyperglycemia, hyperuricemia, upper GI distress, hepatotoxicity; monitor LFTs at baseline, every 6–12 weeks, and then yearly

Sustained release appears to be more hepatotoxic than other preparations (e.g., OTCs).

- Available as "Slo-Niacin" or 2 times/day generic niacin OTC; this should be avoided.
- Extended release and sustained release are less likely to cause flushing.
- Contraindications: liver disease, severe gout, active peptic ulcer
- Flushing can be minimized by taking aspirin 30 minutes before niacin, taking at bedtime with food, and avoiding hot beverages, spicy foods, and hot showers around the time of administration.

Page 2-224

## Niacin Dose Effects

	TC	LDL-C	TG	HDL-C
■ Niaspan 500 mg	-2%	-3%	-6%	+10%
■ Niaspan 1000mg	-5%	-9%	-5%	+15%
■ Niaspan 1500mg	-11%	-14%	-28%	+22%
■ Niaspan 2000 mg	-12%	-17%	-35%	+26%

Page 2-225, Table 24

## Fibrates

### Main actions

- Lower LDL 5%–20% (with normal TG)
- May raise LDL up to 45% (with very high TG)
- Lower TG 30%–55%
- Raise HDL 18%–22%
- Reduce progression of coronary lesions
- Reduce major coronary events

Mechanism of action: reduces rate of lipogenesis in the liver

Adverse effects: dyspepsia, gallstones, myopathy, increased hepatic transaminases; monitor LFTs every 3 months during first year and then periodically

Page 2-225

## Fibrates

Drug*	Brand Name	Dose
Gemfibrozil	Lopid	600 mg 2 times/day
Fenofibrate	TriCor	48–145 mg/day without regard to meals
Fenofibrate	Lofibra micronized	67–200 mg/day with meals
Fenofibrate	Lofibra	54–160 mg/day with meals
Fenofibrate	Antara	43–130 mg/day without regard to meals
Fenofibrate	Fenoglide	40–120 mg/day with meals
Fenofibrate	Lipofen	50–150 mg/day with meals
Fenofibrate	Triglide	50–160 mg/day without regard to meals
Fenofibric Acid	Trilipix	45–135 mg daily without regard to meals

Page 2-225, Table 25

## Ezetimibe

Ezetimibe (Zetia) 10 mg/day

- Efficacy
- Lowers LDL 18%–20%
- May raise HDL 1%–5%
- Lowers TG 7%–17%

Mechanism of action: inhibition of cholesterol absorption

Adverse effects: headache, rash; no monitoring necessary, except LFTs when coadministered with statins

- Adjunctive therapy to statin
- No outcomes data
- In patients with familial hypercholesterolemia, combined therapy with ezetimibe and simvastatin did not result in significant changes in intima-media thickness compared with simvastatin alone, despite decreases in concentrations of LDL and C-reactive protein
- Possible increased cancer risk; but evidence is conflict

Page 2-226

## Ezetimibe

	Total C	LDL -C	Trig	HDL -C
Ezetimibe* Alone	-12%	-18%	-7%	+1%
Ezetimibe +*~ HMG-CoA	-17%	-25%	-14%	+3%
Ezetimibe+ Fenofibrate 160mg	-22%	-20%	-44%	+19%

Page 2-226

## Omega 3 Acid Ethyl Esters

Omega-3-Acid Ethyl Esters (Lovaza)

- Efficacy
- Lowers TG 26%–45%
- May raise LDL up to 45% when TG concentrations are very high
- Raises HDL 11%–14%

Mechanism of action: unknown. Possible inhibition of acyl CoA:1,2 diacylglycerol acyltransferase, increased hepatic  $\beta$ -oxidation, or reduction in TG hepatic synthesis

Adverse effects: GI (e.g., burping, taste perversion, dyspepsia); at more than 3 g/day: inhibition of platelet aggregation, bleeding

Dose: 4 g/day as a single daily dose or in two divided doses

Page 2-226

## Patient Case

- Which one of the following medications is best to recommend to treat M.M.'s lipids?

- Ezetimibe 10 mg/day
- Fenofibrate 145 mg/day
- Colesevelam 625 mg 6 tablets/day
- Atorvastatin 20 mg/day

HDL 54; LDL 193; TG 148; Goal LDL < 130

Page 2-226, (Ans 2-230)

## Effects of Lipid-Lowering Therapy on the Lipid Profile

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%

## Patient Case

- Which one of the following medications is best to recommend to treat M.M.'s lipids?

- Ezetimibe 10 mg/day
- Fenofibrate 145 mg/day
- Colesevelam 625 mg 6 tablets/day
- Atorvastatin 20 mg/day

HDL 54; LDL 193; TG 148; Goal LDL < 130

Page 2-226, (Ans 2-230)

## Questions?

*Questions are guaranteed in life; answers are not.*

- a good mom



**2011 Updates in Therapeutics:**  
**The Pharmacotherapy Preparatory Review & Recertification Course**  
Cardiology III

Robert L Page, Pharm.D., MSPH, BCPS (AQ cards), FAHA, FCCP, FASHP, FASCP, CGP  
University of Colorado School of Pharmacy and School of Medicine

## Conflict of Interest Disclosures

**I have no conflicts to disclose**

## Learning Objectives

1. Recommend patient-specific pharmacologic management of chronic heart failure, with an emphasis on mortality-reducing drugs and their target dosages.
2. Develop an appropriate pharmacologic and monitoring plan for patients with atrial fibrillation.
3. Given a patient with hypertension, outline the optimal pharmacologic management on the basis of practice guidelines and clinical trial evidence.
4. Create an evidence-based drug regimen for a patient with coronary artery disease in both the presence and absence of stable angina.

## Page Pointers

- Absolutely do not study this....



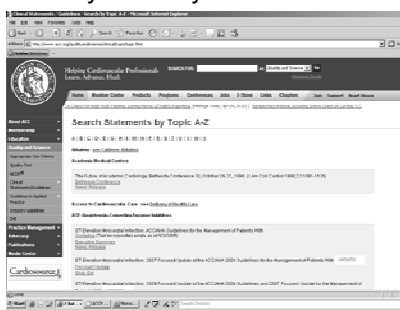
## Page Pointers

- Absolutely do study this....[www.cardiosource.org](http://www.cardiosource.org)



## Page Pointers

- Absolutely do study this....



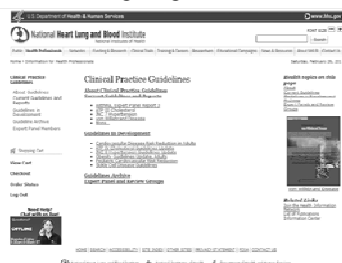
## Page Pointers

- And this....[www.americanheart.org](http://www.americanheart.org) (click Health/Research)



## Page Pointers

- And  
..www.nhlbi.nih.gov/guidelines/index.htm



## Topics Covered

- Chronic Heart Failure
- Atrial Fibrillation
- Hypertension
- Chronic CAD and Stable Angina

## Case #1

- 48 year old female
- ETOH-induced HF, EF is 20%
- NYHA class III (symptoms of dyspnea and fatigue)
- BP = 112/70 mmHg, HR = 68 beats/minute
- Medications:
  - lisinopril 20 mg daily
  - furosemide 40 mg BID
  - carvedilol 12.5 mg BID
  - spironolactone 25mg daily
  - digoxin 0.125 mg daily

### Labs:

140	105	12	
4.0	26	0.8	98

Ca 9.0 dig 0.7 ng/mL  
Mg 2.0  
Phos 2.8

Page Number 236-Case #1

## Case #1-Question??

Which of the following is the best approach to maximize the management of her heart failure?

- Increase carvedilol to 25mg 2 times/day
- Increase lisinopril to 40 mg/day
- Increase spironolactone to 50mg/day
- Increase digoxin to 0.25 mg/day

Page Number 236-Case #1

## Neurohormonal Blockade in HF

Medication	1° Neurohormone affected	Effect on mortality	Effect on hospitalizations
ACE Inhibitor	Angiotensin II	↓ 25%	↓ 30%
Beta Blocker	Norepinephrine	↓ 35%	↓ 25%
Aldosterone Blocker	Aldosterone	↓ 30%	↓ 35%
Digoxin	Central sympathetic outflow	0%	↓ 6%

## ACEI Dosing in HF

Drug	Starting Dosage	Target Dosage	Maximal Dosage
Captopril	6.25 mg TID	50 mg TID	50 mg TID
Enalapril	2.5 mg BID	10 mg BID	20 mg BID
Lisinopril	2.5-5 mg/day	20 mg/day	40 mg/day
Perindopril	2 mg/day	8 mg/day	16 mg/day
Ramipril	1.25-2.5 mg/day	5 mg BID	10 mg/day
Trandolapril	1 mg/day	4 mg/day	4 mg/day

Note: Fosinopril and quinapril may be used; however, they do not have the same magnitude of mortality-reducing data as the above-listed angiotensin-converting enzyme inhibitor.  
BID = 2 times/day; TID = 3 times/day.

Page Number 240-Table 5

## Beta Blocker Dosing in HF

Agent	Starting Dosage	Target Dosage
Bisoprolol	1.25 mg/day	10 mg/day
Carvedilol	3.125 mg BID	25 mg BID*
Metoprolol succinate XL <sup>b</sup> (metoprolol CR/XL)	12.5–25 mg/day	200 mg/day

\*50 mg 2 times/day if weight is more than 85 kg.

<sup>b</sup>Few or no data exist with metoprolol tartrate.

BID = 2 times/day; CR = controlled release; XL = extended release.

Page Number 242-Table 6

## Aldosterone Blockade and Digoxin Dosing in HF

- Spironolactone
  - 25 mg daily if SCr < 2.5, K < 5.0
  - Decrease to 12.5 mg daily or discontinue if K > 5.0
- Eplerenone
  - 25 mg daily if SCr < 2.5, K < 5.0
  - Increase to 50 mg daily if tolerated
- Digoxin
  - Goal serum level 0.5-0.8 ng/mL
  - Minimizes adverse effects and ventricular arrhythmias
  - Remember drug interactions
    - Amiodarone, dronedarone, macrolides
    - CT's, Azole antifungals

Page Number 242-243





## Other Considerations

- Vitals
  - BP = 112/70
  - HR = 68
- Titrated slowly
  - double dose Q2 weeks maximum
  - only 1% incidence of significant bradycardia
  - HR decreases an average of 12 bpm
  - No significant change in BP
- Assess for edema/fluid retention, fatigue, dizziness

Page Number 236

## Case #1-Question??

Which of the following is the best approach to maximize the management of her heart failure?

-  Increase carvedilol to 25mg 2 times/day
-  Increase lisinopril to 40 mg/day
-  Increase spironolactone to 50mg/day
-  Increase digoxin to 0.25 mg/day

Page Number xxx-Case #1

## Case #2

- 62 year old male
- CAD (MI 3 years ago)
- HF (EF = 25%)
  - NYHA Class II
- HTN
- Depression
- CRI (SCr = 2.8 mg/dL)
- PVD
- OA
- Hypothyroidism
- Medications
  - aspirin 81mg daily
  - simvastatin 40 mg QHS
  - enalapril 5 mg BID
  - metoprolol CR/XL 50 mg daily
  - furosemide 80 mg BID
  - cilostazol 100 mg BID
  - acetaminophen 650 mg QID
  - sertraline 100 mg daily
  - levothyroxine 0.1 mg daily

Page Number 236-Case #2

## Case #2

- 62 year old male
- CAD (MI 3 years ago)
- HF (EF = 25%)
  - NYHA Class II
- HTN
- Depression
- CRI (SCr = 2.8 mg/dL)
- PVD
- OA
- Hypothyroidism
- Medications
  - aspirin 81mg QD
  - simvastatin 40 mg QHS
  - enalapril 5 mg BID
  - metoprolol CR/XL 50 mg QD
  - furosemide 80 mg BID
  - cilostazol 100 mg BID
  - acetaminophen 650 mg QID
  - sertraline 100 mg QD
  - levothyroxine 0.1 mg QD

## Case #2

- 62 year old male
  - CAD (MI 3 years ago)
  - HF (EF = 25%)
    - NYHA Class II
  - HTN
  - Depression
  - CRI (SCr = 2.8 mg/dL)
  - PVD
  - OA
  - Hypothyroidism
- |             |   |
|-------------|---|
| Medications | <ul style="list-style-type: none"><li>aspirin 81mg QD</li><li>simvastatin 40 mg QHS</li><li>enalapril 5 mg BID</li><li>metoprolol CR/XL 50 mg QD</li><li>furosemide 80 mg BID</li><li>cilostazol 100 mg BID</li><li>acetaminophen 650 mg QID</li><li>sertraline 100 mg QD</li><li>levothyroxine 0.1 mg QD</li></ul> |
|-------------|---|

## Case #2

- 62 year old male
  - CAD (MI 3 years ago)
  - HF (EF = 25%)
  - NYHA Class II
  - HTN
  - Depression
  - CRI (SCr = 2.8 mg/dL)
  - PVD
  - OA
  - Hypothyroidism
- |             |   |
|-------------|---|
| Medications | <ul style="list-style-type: none"><li>aspirin 81mg QD</li><li>simvastatin 40 mg QHS</li><li>enalapril 5 mg BID</li><li>metoprolol CR/XL 50 mg QD</li><li>furosemide 80 mg BID</li><li>cilostazol 100 mg BID</li><li>acetaminophen 650 mg QID</li><li>sertraline 100 mg QD</li><li>levothyroxine 0.1 mg QD</li></ul> |
|-------------|---|

## Case #2

- 62 year old male
  - CAD (MI 3 years ago)
  - HF (EF = 25%)
  - NYHA Class II
  - HTN
  - Depression
  - CRI (SCr = 2.8 mg/dL)
  - PVD
  - OA
  - Hypothyroidism
- |             |   |
|-------------|---|
| Medications | <ul style="list-style-type: none"><li>aspirin 81mg QD</li><li>simvastatin 40 mg QHS</li><li>enalapril 5 mg BID</li><li>metoprolol CR/XL 50 mg QD</li><li>furosemide 80 mg BID</li><li>cilostazol 100 mg BID</li><li>acetaminophen 650 mg QID</li><li>sertraline 100 mg QD</li><li>levothyroxine 0.1 mg QD</li></ul> |
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|-------------|---|

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|-------------|---|

### Case #2

- BP = 120/70 mmHg
- HR = 72 beats/minute
- Labs WNL except for Cr = 2.8 mg/dL
- TSH = 2.6 mU/L
- HF considered stable

### Case #2-Question??

Which of the following is the best approach to maximize the management of his heart failure?

- ☐ Discontinue metoprolol and begin carvedilol 12.5 mg 2 times/day
- ☐ Increase enalapril 10mg 2 times/day
- ☐ Add spironolactone 25mg/day
- ☐ Increase digoxin to 0.125 mg/day

### Case #2

- Discontinue metoprolol and begin carvedilol 12.5 mg BID
  - No reason to change beta blockers
    - No data clearly places one beta blocker as better than another in HF so long as you are recommending a beta blocker with evidence
    - A reasonable option would be to increase the metoprolol from 50 mg to 100 mg daily

Page Number 236-Case #2

### Case #2

- Add spironolactone 25 mg QD
  - Not appropriate therapy in this patient
    - Based on EMPHASIS trial, possibly
    - BUT.....Cr = 2.8 mg/dL (K reportedly WNL)

### Case #2

- Add digoxin 0.125 mg daily
  - Could be considered
    - Useful in patients with symptomatic LV dysfunction despite optimal diuretic, ACEI, beta-blocker, and spironolactone (if appropriate) therapy
    - Dose of 0.125 mg daily may be too high in 62 year old male with creatinine = 2.8
    - No mortality benefit derived from digoxin therapy but the composite of hospitalization and mortality!

## Case #2

- **increase enalapril to 10 mg BID**
  - Should be strongly considered
    - current enalapril 5 mg BID is not at ACEI target dose associated with decreased morbidity and mortality.
  - BP = 120/70, should tolerate dosage increase without problem
  - Monitor creatinine and K (currently WNL) after dosage increase

## Hydralazine/Isosorbide dinitrate

- **MOA: Vasodilation and nitric oxide-dependent endothelium function**
  - Superior to placebo
  - Inferior to ACEI
- **Alternative to ACEI or ARB in truly intolerant or contraindication situation**
- **Added to standard therapy in class III-IV HF African-Americans**
  - Decreases mortality 39%
  - Decreases hospitalizations 33%
  - Hydralazine 40 mg + isosorbide dinitrate 75 mg TID

Page Number 244

## Case #3

- **Which one of the medications from the patient in case 2 may be adversely affecting his cardiac prognosis?**

- a. acetaminophen
- b. sertraline
- c. cilostazol
- d. levothyroxine

Page Number 245

## Harmful medications

- **Promote fluid retention**
  - NSAIDs
  - Corticosteroids
  - Minoxidil
  - Thiazolidinediones
- **Negative inotropic activity (cause neurohormonal activation)**
  - Class I and III antiarrhythmics (except dofetilide and amiodarone)
  - Diltiazem and Verapamil
  - Itraconazole
- **Exacerbate HF**
  - Dronedarone

Page Number 245-246

## Harmful medications

- **Positive inotropic activity/tachycardia**
  - Anagrelide
  - Amphetamines
- **Increase ventricular arrhythmias**
  - Class I and III antiarrhythmics (except dofetilide and amiodarone)
  - Amphetamines
  - Cilostazol

Page Number 245-246

## Case #3-Question??

Which one of the medications from the patient in case 2 may be adversely affecting his cardiac prognosis?

-  Acetaminophen
-  Sertraline
-  Cilostazol
-  Levothyroxine

## Case #4

- 52 year-old male

**CC:** Several weeks of a 'fluttering' feeling in his chest on occasion over the past several weeks.

- HTN-receiving metoprolol tartrate 50mg 2 times/day
- Labs-all WNL

Page Number 247-Case #4

## Case #4

- BP = 130/78 mmHg
- HR = 76 beats/minute



### EKG findings:

- irregularly irregular rhythm
- no p-waves

## Case #4-Question??

What is the most appropriate approach to manage his atrial fibrillation?

- Begin digoxin 0.25 mg/day
- Begin diltiazem 240 mg/day
- Begin warfarin (titrate to INR of 2.5)
- Begin dabigatran 150 mg 2 times/day

## UPDATE...UPDATE...MAKE A NOTE

# CHEST

Official publication of the American College of Chest Physicians



**Antithrombotic Therapy for Atrial Fibrillation : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines**

John J. You, Daniel E. Singer, Patricia A. Howard, Deirdre A. Lane, Mark H. Eckman, Margaret C. Fang, Elaine M. Hylek, Sam Schulman, Alan S. Go, Michael Hughes, Frederick A. Spencer, Warren J. Manning, Jonathan L. Halperin and Gregory Y. H. Lip

Chest 2012;141:e531S-e575S  
DOI 10.1378/chest.11.2304

[http://chestjournal.chestpubs.org/content/141/2\\_suppl/e531S.full.pdf+html](http://chestjournal.chestpubs.org/content/141/2_suppl/e531S.full.pdf+html)

## Atrial Fibrillation

### ■ Goals of therapy

- Ventricular rate control
  - 60-80 at rest, 90-115 during exercise
  - RACE-2: HR<110 beats per min (lenient) not inferior to strict rate control of < 80 beats/min
  - Select agent(s) based on
    - concomitant disease states
    - individual response
- Anticoagulation
  - Aspirin or warfarin based on risk factors

Page Number 249

## Ventricular Rate Control

### ■ Beta blockade

- Beta<sub>1</sub> selective agents preferred
- Labetalol or carvedilol may be used if additional BP effects required (concomitant alpha blockade)
- Sotalol or propafenone useful if maintenance of NSR is to be pursued for symptom control (Class III antiarrhythmic properties)
- Beta blockers particularly useful to control HR increases with exercise

Page Number 249

## Ventricular Rate Control

- Calcium Channel Blockers
  - Verapamil or diltiazem
- Preferred over beta blocker if:
  - severe asthma/COPD
  - undesirable side effects
    - sexual dysfunction
    - fatigue

Page Number 249

## Ventricular Rate Control

- Digoxin
  - Often ineffective as a single agent, especially during exercise
- Should be included in rate control regimen in patients with systolic HF

Page Number 249

## Anticoagulation: CHADS2

Risk Factors	Score
C Recent congestive heart failure	1
H Hypertension	1
A Age ≥75 years	1
D Diabetes mellitus	1
S <sub>2</sub> History of stroke or transient ischemic attack (TIA)	2

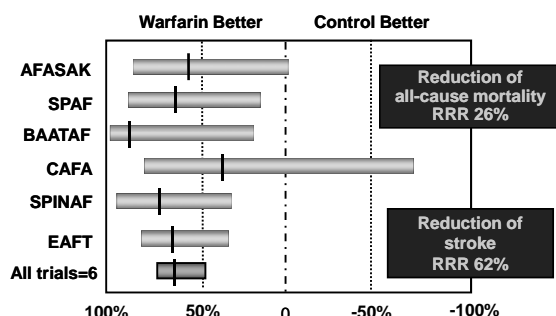
Page Number 251 Table 10

## Anticoagulation: CHADS2 Old vs New

CHADS <sub>2</sub> SCORE	Old Recommendations	New 2012 Recommendations
0 (Low risk)	Aspirin 81-325 mg/day	No therapy rather than antithrombotic therapy (Grade 2B) If antithrombotic therapy is required, then ASA 75-325 mg/day (Grade 2B)
1 (Intermediate Risk)	Aspirin 81-325 mg/day or warfarin (INR of 2-3 in nonvalvular AF)	Oral Anticoagulation with warfarin (INR 2-3) or dabigatran 150 mg BID (Grade 1D) Dabigatran is suggested rather than warfarin (Grade 2B) If unsuitable for oral anticoagulation, then aspirin + clopidogrel rather than aspirin alone (Grade 1D)
≥ 2 (High risk)	Warfarin (INR of 2-3 in nonvalvular AF) or dabigatran (in nonvalvular AF only)	Oral Anticoagulation with warfarin (INR 2-3) or dabigatran 150 mg BID (Grade 1A) Dabigatran is suggested rather than warfarin (Grade 2B) If unsuitable for oral anticoagulation, then aspirin + clopidogrel rather than aspirin alone (Grade 1D)

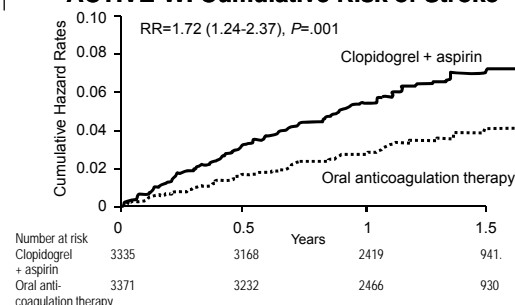
Page Number 251 Table 10

## Anticoagulation in AF Stroke Risk Reductions



Page Number 250

## ACTIVE-W: Cumulative Risk of Stroke



\*ACTIVE=Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events.  
Primary outcome: stroke, systemic embolus, MI, vascular death.  
Clopidogrel + aspirin=5.6% risk/year vs warfarin=3.93% risk/year.  
Connolly S, et al. *Lancet*. 2006;367:1903-1912.

Page Number 252

## Dabigatran-ACC/AHA Statement

<sup>1</sup> Class I Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance  $\leq 15$  mL/min), or advanced liver disease (impaired baseline clotting function). (Level of Evidence: B)

The update does not recommend routinely switching patients to dabigatran who are already successfully taking warfarin:

<sup>2</sup> Because of the twice-daily dosing and greater risk of nonhemorrhagic side effects with dabigatran, patients already taking warfarin with excellent INR control may have little to gain by switching to dabigatran.





Here is the discussion about choosing between dabigatran and warfarin:

<sup>3</sup> Selection of patients with AF and at least 1 additional risk factor for stroke who could benefit from treatment with dabigatran as opposed to warfarin should consider individual clinical features, including the ability to comply with twice-daily dosing, availability of an anticoagulation management program to sustain routine monitoring of INR, patient preferences, cost, and other factors.

Page Number 251-252

## Case #4-Question??

What is the most appropriate approach to manage his atrial fibrillation?

-  Begin digoxin 0.25 mg/day (HR controlled)
-  Begin diltiazem 240 mg/day (HR controlled)
-  Begin warfarin (titrate to INR of 2.5)
-  Begin dabigatran 150 mg 2 times/day

## Case #5

- 67 year-old male
- HTN
- Moderate mitral valve insufficiency
- Atrial fibrillation x 4 years
- Medications:
  - Ramipril 5mg 2 times/day
  - Sotalol 120 mg 2 times/day
  - Digoxin 0.125 mg daily
  - Warfarin 5 mg daily

Page Number 254-Case #5

## Case #5

CC: ↑ shortness of breath, palpitations, and some bilateral lower extremity edema

Vitals: BP 115/70 mmHg, HR = 88 beats/minute





Labs: All WNL, except INR = 2.8

ECG: Atrial fibrillation

Echocardiogram: EF of 35-40 %, moderate mitral valve insufficiency

## Case #4-Question??

What is the most appropriate approach to manage his atrial fibrillation?

-  Begin digoxin 0.25 mg/day (HR controlled)
-  Begin diltiazem 240 mg/day (HR controlled)
-  Begin warfarin (titrate to INR of 2.5)
-  Begin dabigatran 150 mg 2 times/day

## Heart Failure and Atrial Fibrillation

- Biggest issue: Rate vs Rhythm Control in a patient with symptoms?
  - Symptoms may be attributed to both:
    - HF (SOB, edema)
    - Atrial fibrillation (SOB, palpitations)

Page Number 254-256

## Heart Failure and Atrial Fibrillation

- **Biggest issue: Rate vs Rhythm Control in a patient with symptoms?**
  - Symptoms may be attributed to both:
    - HF (SOB, edema)
    - Atrial fibrillation (SOB, palpitations)
- **Fact: Rate Control preferred**
  - Increased hospitalizations and GI side effects when Rhythm Control is pursued with antiarrhythmic therapy

Page Number 254-256

## Heart Failure and Atrial Fibrillation

- **General rules**
  - Optimize HF and Rate Control therapies
  - Consider antiarrhythmic therapy if unacceptable symptoms persist

Page Number 254-256

## Anticoagulants and Antiarrhythmics

- **Prior to attempting cardioversion, the risk of stroke must be minimized**
  - Stroke rate with thrombus present + cardioversion = 91%
- **Without anticoagulation, AFib for**
  - < 48 hours = < 1 % rate of thrombus
  - > 48 hours = 15% rate of thrombus
  - > 72 hours = 30% rate of thrombus

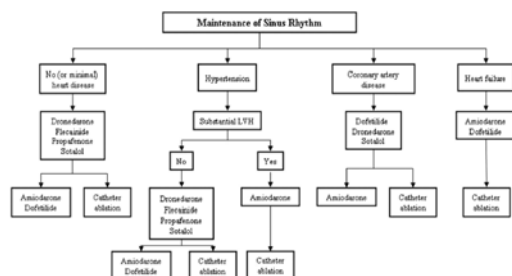
Page Number 254-256

## Atrial Fibrillation in HF

- **Patients usually poorly tolerant to Afib**
  - loss of atrial kick (15 - 20% of CO)
- **Only dofetilide and amiodarone have been proven SAFE in this population**
  - some other agents (not all) have been shown to increase mortality in patients with HF
- **Rate control options**
  - beta-blocker (metoprolol or carvedilol) preferred
  - digoxin useful adjunct
  - avoid CCBs (negative inotropes, contraindicated in HF)

Page Number 254-256

## Atrial Fibrillation Rhythm Control



Page Number 257-Figure 4

## Dronedaron

2011 Focused Update Recommendations	Comments
Class IIIa	
1. Dronedaron is reasonable to decrease the need for hospitalization for cardiovascular events in patients with paroxysmal AF or after conversion of persistent AF. Dronedaron can be initiated during outpatient therapy. <sup>29</sup> (Level of Evidence: B)	New recommendation
Class III-Harm	
1. Dronedaron should not be administered to patients with class IV heart failure or patients who have had an episode of decompensated heart failure in the past 4 weeks, especially if they have depressed left ventricular function (left ventricular ejection fraction $\leq 35\%$ ). <sup>30</sup> (Level of Evidence: B)	New recommendation

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## Case #5

### Medications:





Ramipril 5 mg BID  
Sotalol 120 mg BID  
Digoxin 0.125 mg daily  
Warfarin 5 mg daily (INR = 2.8)

### ■ Important Points:

- Pt with hx Afib, new diagnosis of HF and symptoms of SOB, edema, and palpitations.
- HF regimen needs improvement
- INR = 2.8 (therapeutic)

## Case #5-Question??

What is the most appropriate approach to manage his atrial fibrillation?

-  Discontinue sotalol and begin metoprolol succinate 12.5 mg/day
-  Discontinue sotalol and begin dronedarone 400mg 2 times/day
-  Discontinue sotalol and begin amiodarone 400mg 2 times/day, tapering to goal of 200mg/day x 6 weeks
-  Continue sotalol and begin metoprolol tartrate 25 mg 2 times/day





## Case #6

- 50-year old African-American male
- Hospital discharge s/p AMI
- PMH = HTN (was on HCTZ 25 mg daily)
- EF = > 60%
- Vitals: BP = 150/94 mmHg, HR = 80 beats/minute

Page Number 259-Case #6

## Case #6-Question??

What is the most appropriate approach to manage his hypertension?

-  Discontinue hydrochlorothiazide and add diltiazem
-  Continue hydrochlorothiazide and add metoprolol
-  Discontinue hydrochlorothiazide and add losartan
-  Continue hydrochlorothiazide and add losartan

## Step 1: Define HTN

- BP ≥ 140/90 mmHg
- Taking antihypertensive drug therapy

BP Classification	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Lifestyle Modification
Normal	< 120	AND < 80	Encourage
Prehypertension	120-139	OR 80-89	Yes
Stage 1 hypertension	140-159	OR 90-99	Yes
Stage 2 hypertension	≥ 160	OR ≥ 100	Yes

BP = blood pressure

Page Number 259 Table 14

## Step 2: Address Lifestyle Modifications

- Encouraged in ALL individuals
- Recommended in:
  - Prehypertensive
  - Stage 1 HTN
  - Stage 2 HTN

Modification	SBP reduction
Weight Reduction	5-20 mm Hg/10 kg lost
DASH Diet	8-14 mm Hg
Sodium restriction	2-8 mm Hg
Physical Activity	4-9 mm Hg
Limit alcohol consumption	2-4 mm Hg

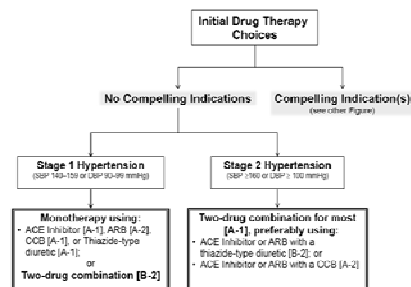
Page Number 258

### Step 3: Define Treatment Goal

- JNC-7 goals are < 140/90 mmHg for all patients EXCEPT those with DM and/or CKD OR albuminuria then goal is <130/80 mmHg
- Other guidelines are the AHA 2007, ISHB 2010, ACC/AHA Consensus in the Elderly 2011 however these are controversial!

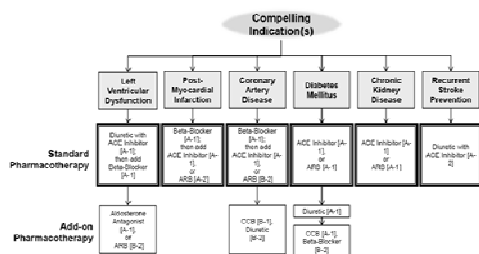
Page Number 260-261

### Step 4: Assess for 'Compelling Indication'



Page Number 261. Figure 5.

### Step 4: Assess for 'Compelling Indication'



Page Number 261 Figure 6.

### Case #6

- 50-year old African-American male
- Hospital discharge s/p AMI
- PMH = HTN (was on HCTZ 25 mg QD)
- EF = > 60%
- Vitals: BP = 150/94 mmHg, HR = 80 beats/minute

### Case #6

- Is he hypertensive?

### Case #6

- Is he hypertensive? Yes
  - BP > 140/90 mmHg (150/94 mmHg, Stage 1)
  - Takes antihypertensive medication

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90 mmHg (150/94 mmHg, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
- 

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90 mmHg, (150/94 mmHg, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
    - Has HTN
- 

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90, (150/94, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
    - Has HTN
  - BP Goal
- 

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90 mmHg, (150/94 mmHg, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
    - Has HTN
  - BP Goal
    - No DM and/or CKD OR albuminuria
    - Goal is < 140/90 mmHg
- 

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90 (150/94, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
    - Has HTN
  - BP Goal
    - No DM and/or CKD OR albuminuria
    - Goal is < 140/90 mmHg
  - Any compelling indications?
- 

### Case #6

- Is he hypertensive? Yes
    - BP > 140/90 mmHg, (150/94 mmHg, Stage 1)
    - Takes antihypertensive medication
  - Recommend Lifestyle Modifications? Yes
    - Has HTN
  - BP Goal
    - No DM and/or CKD OR albuminuria
    - Goal is < 140/90 mmHg
  - Any compelling indications? Yes
    - Post-MI
      - 1<sup>st</sup> line = Beta Blocker
      - Then add ACEI or ARB also recommended
-

### Case #6-Question??

What is the most appropriate approach to manage his hypertension?

- ☐ Discontinue hydrochlorothiazide and add diltiazem
- ☐ Continue hydrochlorothiazide and add metoprolol
- ☐ Discontinue hydrochlorothiazide and add losartan
- ☐ Continue hydrochlorothiazide and add losartan

### Case #7

- 45-year old Caucasian female
- PMH: Type II diabetes (on glyburide 5mg daily)
- + for macroalbuminuria
- BP today = 138/88 mm Hg, HR = 70 bpm
- BP at last visit was 136/85 mmHg
- Labs: 

140	102	14
4.0	28	1.8

 NR

Page Number 259-Case #7

### Case #7-Question??

What is the most appropriate approach to manage her hypertension?

- ☐ Begin lifestyle modifications
- ☐ Begin lifestyle modifications and add amlodipine 5 mg/day
- ☐ Begin lifestyle modifications and add lisinopril 2.5 mg/day
- ☐ Begin lifestyle modifications and add atenolol 25 mg/day

### Case #7

- Is she hypertensive?

### Case #7

- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)

### Case #7

- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)
- Recommend Lifestyle Modifications?

### Case #7

- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)
- Recommend Lifestyle Modifications? Yes
  - Has prehypertension

### Case #7

- Is she hypertensive? No
  - BP < 140/90 (138/88, prehypertension)
- Recommend Lifestyle Modifications? Yes
  - Has prehypertension
- BP Goal

### Case #7

- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)
- Recommend Lifestyle Modifications? Yes
  - Has prehypertension
- BP Goal
  - DM and renal disease (Creatinine = 1.8)
  - Goal is < 130/80 mmHg

### Case #7





- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)
- Recommend Lifestyle Modifications? Yes
  - Has prehypertension
- BP Goal
  - DM and renal disease (Creatinine = 1.8)
  - Goal is < 130/80 mmHg
- Any compelling indications?

### Case #7

- Is she hypertensive? No
  - BP < 140/90 mmHg (138/88 mmHg, prehypertension)
- Recommend Lifestyle Modifications? Yes
  - Has prehypertension
- BP Goal
  - DM and renal disease (Creatinine = 1.8)
  - Goal is < 130/80 mmHg
- Any compelling indications? Yes
  - DM and kidney disease
    - 1<sup>st</sup> line = ACEI or ARB
    - Diuretic then CCB or Beta-blocker

### Case #7-Question??

What is the most appropriate approach to manage her hypertension?

-  Begin lifestyle modifications
-  Begin lifestyle modifications and add amlodipine 5 mg/day
-  Begin lifestyle modifications and add lisinopril 2.5 mg/day
-  Begin lifestyle modifications and add atenolol 25 mg/day





## Case #8

- 58-year old white male
- PMH = HTN (was on HCTZ 12.5 mg/day)
- Hospital discharge for AMI
- EF > 60%
- Vitals: BP = 130/65 mmHg, HR = 64 beats/min
- Current medications (for discharge)
  - ASA 81 mg daily      - Atorvastatin 80 mg daily
  - Atenolol 50 mg QD    - SL NTG prn chest pain
  - HCTZ 25 mg daily

Page Number 265 -Case #8

## Case #8-Question??

Which of the following represents the best action to take in response to his discharge regimen?

-  Discontinue HCTZ; add diltiazem extended release 240 mg/day
-  Continue HCTZ; add amlodipine 5 mg/day
-  Discontinue HCTZ; add ramipril 5 mg/day
-  Continue HCTZ; add vitamin E 400 IU/day

## NEW Guidelines Expected...

### CHRONIC ANGINA FOCUSED UPDATE

#### 2007 Chronic Angina Focused Update of the ACC/AHA 2002 Guidelines for the Management of Patients With Chronic Stable Angina

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to Develop the Focused Update of the 2002 Guidelines for the Management of Patients With Chronic Stable Angina

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*Writing on behalf of the 2002 Chronic Stable Angina Writing Committee*

## Assess in all Patients with CAD

A = Aspirin and Antianginal therapy, ACEI

B = Beta-blocker and Blood pressure

C = Cigarette smoking and Cholesterol

D = Diet and Diabetes

E = Education and Exercise

### Unhelpful/potentially harmful therapies in CAD

Vitamin E

Hormone replacement therapy

Antibiotic Therapy

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## Case #8 - Patient Assessment

A	Aspirin (alt. Clopidogrel)	✓
	Antianginal therapy	NA
	ACEI	-
B	Beta-blocker	✓ (HR = 64)
	Blood pressure (goal 140/90)	✓ (BP = 130/65)
C	Cigarette Smoking	NA
	Cholesterol	✓ (follow-up)
D	Diet	counsel
	Diabetes	NA
E	Exercise	counsel
	Education	counsel

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## Case #9

- 64-year old white female
- PMH: MI x 2, stent x3, EF > 60%
- CC: SOB and chest heaviness with activity x 3 months
- Vitals: BP 132/80 mmHg, HR 72 beats/minute
- Medications:
  - aspirin 325 mg/day      - simvastatin 40 mg QPM
  - enalapril 10 mg BID    - metoprolol 50 mg BID
  - prn sl NTG (uses ~ 3/day)





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### Case #9

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- CC: SOB and chest heaviness with activity x 3 months
- Medications:
  - aspirin 325 mg/day
  - simvastatin 40 mg QPM
  - enalapril 10 mg BID
  - metoprolol 50 mg BID
  - prn sl NTG ~ 3/day
- Dx: stable angina

### Case #9-Question??

Which of the following regimens is best to improve her stable angina symptoms and increase her level of activity?

-  Discontinue metoprolol tartrate and begin diltiazem extend release 240 mg/day
-  Add ranolazine 500 mg 2 times/day
-  Add isosorbide mononitrate 30 mg every morning
-  Increase metoprolol tartrate to 100 mg 2 times/day and add isosorbide mononitrate 30 mg every morning

### Stable Angina Management

- Revascularization
  - Stent placement, balloon angioplasty, CABG, brachytherapy
- Goals of medication management
  - Decrease myocardial O<sub>2</sub> demand
  - Increase myocardial O<sub>2</sub> supply

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



### Stable Angina Management

Medication	Increase supply	Decrease demand	Comments
Beta-blocker		✓	- goal rest HR = 55-60 - exercise HR < 75% pain threshold
Calcium Antagonists	✓	✓	- add on to BB if needed - in place of BB 2° SE - avoid short-acting dihydropyridines
Nitroglycerin	✓	✓	- most useful with BB - ALWAYS PRN - can be used pre-activity

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### Case #9

What do you recommend in order to improve her stable angina symptoms and increase her level of activity?

- a. Discontinue metoprolol, begin diltiazem 240 mg daily
  - Goal resting HR is < 60 (HR = 72)
  - BB is first-line therapy
- b. Add ranolazine 500mg 2 times/daily
- c. Add isosorbide mononitrate 30 mg every morning
- d. Increase metoprolol to 100 mg BID, and add isosorbide mononitrate 30 mg every morning

### Case # 9

What do you recommend in order to improve her stable angina symptoms and increase her level of activity?

- a. Discontinue metoprolol, begin diltiazem 240 mg daily
- b. Add ranolazine 500 mg 2 times/day
  - can be done, but after other therapies maximized
- c. Add isosorbide mononitrate 30 mg every morning
- d. Increase metoprolol to 100 mg BID, and add isosorbide mononitrate 30 mg every morning

### Case # 9

What do you recommend in order to improve her stable angina symptoms and increase her level of activity?

- a. Discontinue metoprolol, begin diltiazem 240 mg daily
- b. Add ranolazine 500 mg 2 times/day
- c. Add isosorbide mononitrate 30 mg every morning
  - will both increase supply and decrease demand
  - good add-on after HR at goal
- d. Increase metoprolol to 100 mg BID, and add isosorbide mononitrate 30 mg every morning

### Case # 9

What do you recommend in order to improve her stable angina symptoms and increase her level of activity?

- a. Discontinue metoprolol, begin diltiazem 240 mg daily
- b. Add ranolazine 500 mg 2 times/day
- c. Add isosorbide mononitrate 30 mg every morning
- d. Increase metoprolol to 100 mg BID, and add isosorbide mononitrate 30 mg every morning
  - will work towards goal of rest HR < 60 beats/minute
  - will also increase O<sub>2</sub> supply

### Summary

- Heart failure
- Atrial Fibrillation
- Hypertension
- Chronic Stable Angina
- Chronic Coronary Artery Disease

**All very common disease states  
encountered in the outpatient setting**