Learning Objectives and/or Agenda

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.

Acute Decompensated Heart Failure


Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>ADHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>4-7</td>
<td>2-4</td>
</tr>
<tr>
<td>CI</td>
<td>2.8-3.6</td>
<td>1.3-2</td>
</tr>
<tr>
<td>PCWP</td>
<td>8-12 (15-18)</td>
<td>18-30</td>
</tr>
<tr>
<td>SVR</td>
<td>800-1200</td>
<td>1500-3000</td>
</tr>
</tbody>
</table>

BP = CO x SVR

CO = SV x HR

Stroke volume depends several factors
- inotropy, afterload, preload

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

Conflict of Interest Disclosures

Sheryl L. Chow

No conflicts of interest to disclose
**Hemodynamic Classification**

Forrester’s Hemodynamic Subset

<table>
<thead>
<tr>
<th>Subset I</th>
<th>Subset II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Warm and Dry (Normal)</td>
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<tr>
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<td>Warm and Wet</td>
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<table>
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<td>PCWP 15-18 mmHg</td>
<td>Optimize oral medications</td>
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<td>CI &gt; 2.2 L/min/m²</td>
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*Compelling reason for inotrope = SBP < 90, symptomatic hypotension, or worsening renal function.

**ADHF Drug Therapy**

- **Diuretic Therapy**
  - Furosemide
  - Bumetanide
  - Torsemide

- **Inotropic Therapy**
  - Dobutamine
  - Milrinone

- **Vasodilator Therapy**
  - Nitroglycerin
  - Nitroprusside
  - Nesiritide

**ADHF Case #1 Q1**

1. DD is a 72 YOM admitted for ADHF

**Pertinent Labs**
- BNP 2300 (0-50), K⁺ 4.9
- BUN 32, Scr 2 (baseline?)
- AST 40, ALT 42, INR 1.3, PTT 42
- BP 108/62 mmHg, HR 82 BPM (O₂ 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

**Hemodynamic Classification**

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Hemodynamic Classification

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<td>CI &gt; 2.2 L/min/m²</td>
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</tr>
<tr>
<td>II - Warm and Wet (Congestion)</td>
<td>PCWP &gt; 18 mmHg</td>
<td>IV diuretics + IV vasodilators (venous)</td>
</tr>
<tr>
<td></td>
<td>CI &gt; 2.2 L/min/m²</td>
<td></td>
</tr>
<tr>
<td>III - Cold and Dry (Hypoperfusion)</td>
<td>PCWP &gt; 18 mmHg</td>
<td>If PCWP &lt;15, IVF until 15-18</td>
</tr>
<tr>
<td></td>
<td>CI &lt; 2.2 L/min/m²</td>
<td>If PCWP &gt;15, MAP &lt;50, IV dopamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If PCWP &gt;15, MAP &gt;50, IV inotrope -</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV vasodilator (arterial)*</td>
</tr>
</tbody>
</table>

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

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

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.

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

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
**Diuretic Therapy**

- Increase dose before increasing frequency of loop diuretic
  - (Note: Ceiling effect at ≈ 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

**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 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.

   - O2 sat 87% on 4-L NC
   - BP 110/75, HR 75 beats/min

   Handout Page 2-173; Answer Page 2-191

**Hemodynamic Classification**

<table>
<thead>
<tr>
<th>Subset</th>
<th>Hemodynamic Parameters</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I - Warm and Dry (Normal)</td>
<td>PCWP 15-18 mmHg CI &gt; 2.2 L/min/m²</td>
<td>Optimize oral medications</td>
</tr>
<tr>
<td>II - Warm and Wet (Congestion)</td>
<td>PCWP &gt; 18 mmHg CI &gt; 2.2 L/min/m²</td>
<td>IV diuretics + IV vasodilators (venous)</td>
</tr>
</tbody>
</table>
| III - Cold and Dry (Hypoperfusion) | PCWP 15-18 mmHg CI < 2.2 L/min/m² | If PCWP <15, IVF until 15-18
| IV - Cold and Wet (Congestion and Hypoperfusion) | PCWP > 18 mmHg CI < 2.2 L/min/m² | If MAP <50, IV dopamine

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

**Vasodilator Therapy**

<table>
<thead>
<tr>
<th></th>
<th>NTP</th>
<th>Nesiritide</th>
<th>NTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical effects</td>
<td>Vasodilator (venous and arterial)</td>
<td>Vasodilator (venous and arterial)</td>
<td>Vasodilator (venous &gt; arterial)</td>
</tr>
<tr>
<td>Indication</td>
<td>Warm &amp; wet, Cold &amp; wet alternate to inotropes, HTN Crises</td>
<td>Warm &amp; wet, Cold &amp; wet alternate to inotropes</td>
<td>Warm &amp; wet, ACS, HTN Crises</td>
</tr>
<tr>
<td>Half-life</td>
<td>&lt; 10 minutes</td>
<td>20 minutes</td>
<td>1-4 minutes</td>
</tr>
<tr>
<td>Elimination</td>
<td>Cyanide (hepatic), thiocyanate (renal)</td>
<td>NP receptor C (no renal/hepatic adjustment)</td>
<td>Inactive metabolites in urine</td>
</tr>
<tr>
<td>ADHF Case #3 Q3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. A swan-ganz hemodynamic catheter is placed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Cardiac index (CI)
  - 1.5 (2.8-3.8 L/min/m²)
- Systemic vascular resistance (SVR)
  - 2650 (800-1200 dynes/sec/cm⁵)
- Pulmonary capillary wedge pressure (PCWP)
  - 30 (8-12 mmHg, 15-18 mmHg in HF)

<table>
<thead>
<tr>
<th>Hemodynamic Classification</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Forrester’s Hemodynamic Subset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subset I</td>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Warm and Dry</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Subset III</td>
</tr>
<tr>
<td>Hypoperfusion</td>
</tr>
<tr>
<td>Cold and Dry</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CI</th>
<th>PCWP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADHF Patient Case # 3 Q3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which one of the following is the most appropriate medication now?</td>
</tr>
</tbody>
</table>

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 |

<table>
<thead>
<tr>
<th>Inotropic Therapy</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Dobutamine</th>
<th>Milrinone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of action</strong></td>
<td>β-agonist, slight peripheral vasodilation</td>
</tr>
<tr>
<td><strong>Typical dose</strong></td>
<td>5 mcg/kg/min</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td>ADHF Cold &amp; Wet – or – Cold &amp; Dry (if PCWP &gt; 15)</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>2 minutes</td>
</tr>
<tr>
<td><strong>Other comments</strong></td>
<td>Consider if hypotensive.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Arrhythmias</th>
</tr>
</thead>
</table>


### Antiarrhythmic Drug Classes

<table>
<thead>
<tr>
<th>Class I Na⁺ channel blockers</th>
<th>IA: Quinidine, procainamide, disopyramide</th>
<th>Slows depolarization</th>
</tr>
</thead>
<tbody>
<tr>
<td>IB: Lidocaine, mexiletine (phenytoin)</td>
<td>C: Propafenone, flecainide, moricizine</td>
<td></td>
</tr>
<tr>
<td>Class II β-blockers</td>
<td>Metoprolol, esmolol, atenolol</td>
<td>Slows AVN conduction (↓ HR)</td>
</tr>
<tr>
<td>Class III K⁺ channel blockers</td>
<td>Amiodarone, sotalol, dofetilide, dronedarone, ibutilide</td>
<td>Slows repolarization (↑ QT)</td>
</tr>
<tr>
<td>Class IV Ca²⁺ channel blockers</td>
<td>Diltiazem, verapamil</td>
<td>Slows AVN conduction (↓ HR)</td>
</tr>
</tbody>
</table>

### Adult Cardiac Arrest – pulseless VT, VF

CPR / DCC

- Epinephrine 1 mg IV/IO Q3-5min
- Vasopressin 40 units IV/IO x 1
  (replaces first or second epinephrine dose)

- Amiodarone 300mg IV/IO, repeat 150mg IV/IO x 1
  If amiodarone is unavailable, lidocaine may be considered.
  Lidocaine 1-1.5mg/kg IV/IO, repeat 0.5-0.75 mg/kg IV/IO q5-10min (max 3 mg/kg)

### 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

### 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

### Atrial Fibrillation

#### Rate Control

<table>
<thead>
<tr>
<th>General presentation</th>
<th>β-blockers, nondihydropyridine CCBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>Digoxin, amiodarone</td>
</tr>
<tr>
<td>Accessory pathway</td>
<td>Amiodarone</td>
</tr>
</tbody>
</table>

#### Rhythm Control

<table>
<thead>
<tr>
<th>Unstable, &lt; 48 hours</th>
<th>DCC, UFH immediately beforehand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable, unknown or &gt; 48 hrs</td>
<td>DCC, TEE+UFH immediately beforehand and AC 4 wks after DCC</td>
</tr>
<tr>
<td>Stable, unknown or &gt; 48 hrs</td>
<td>Rate control+AC 3-4 wks before and AC 4 wks after DCC</td>
</tr>
</tbody>
</table>
  - Elective DCC or CC (class I or III agents) |

#### 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
### 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%

### Class III Antiarrhythmics
- **Sotalol***
  - AF and VT maintenance alone (not conversion)
  - CI in ClCr < 40 ml/min, QT > 440 msec
- **Dofetilide***
  - AF conversion & maintenance (not VT)
  - CI in ClCr < 20 ml/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!*

- **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!*

### 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

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

### Torsades de pointes
- Primarily when QTc > 500 msec
- Withdrawal of QT-prolonging medications and correction of low Mg²⁺ and K⁺
  - 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

### 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
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 (~ ClCr 30 mL/min)

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

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

Pulmonary Arterial Hypertension


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

Lower Risk
- First line: ERA s or PDEI s (oral)
- Alternatives: epoprostenol or treprostinil (IV)

Higher Risk
- Epoprostenol or treprostinil (IV)
- Iloprost (inhaled)
- ERA s or PDEI s (oral)

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PAH Initial Algorithm

mPAP=mean pulmonary artery pressure
Drug Adverse Effects Considerations

**Calcium Channel Blockers (Class II PAH)**
- Various agents
  - Hypotension, peripheral edema, cardiac conduction delay (diltiazem)
  - Should not be used without positive response testing!
  - Selection based on HR.

**Prostacyclin Analogs (Class II-IV / III-IV PAH)**
- 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)

**Endothelin Receptor Antagonists (Class II-III* / III-IV PAH)**
- Bosentan (Tracleer)
  - Edema, hypotension, liver disease, induction/ inhibition via C2C8/9, 3A4
  - Monitor LFTs & Hgb, use two contraceptive methods
- Ambrisentan* (Letairis)
  - Higher rate edema, lower rate hypotension, liver disease
  - Monitor LFTs, use two contraceptive methods

**Phosphodiesterase Inhibitors (Class II-IV PAH)**
- Sildenafil (Revatio)
  - Headache, facial flushing
  - Augments other therapies, CI if nitrates
  - Caution with 3A4 DDIs
- Tadalafil (Adcirca)
  - Same as above

**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/pCO2 65/pO2 53/ 85%
   - PE: 3 pillow orthopnea, 3+ pitting edema
   - PMH: atrial fibrillation
   - CT angiography: enlarged pulmonary artery, mean pressure 56 mmHg

**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

**Hypertensive Crises**
**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

**Hypertensive Urgency**

- **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

### Hypertensive Emergency - IV

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroprusside*</td>
<td>Cyanide/thiocyanate toxicity</td>
</tr>
<tr>
<td></td>
<td>Cl: Renal/hepatic failure</td>
</tr>
<tr>
<td>Esmolol and</td>
<td>Bronchospasm, HF exacerbation,</td>
</tr>
<tr>
<td>Labetalol</td>
<td>bradycardia/heart block</td>
</tr>
<tr>
<td>Nicardipine*</td>
<td>Reflex tachycardia, N/V</td>
</tr>
<tr>
<td></td>
<td>Caution: Angina/Ml, acute HF, ↑ ICP</td>
</tr>
<tr>
<td>Nitroglycerin*</td>
<td>Headache, nausea, tachyphylaxis</td>
</tr>
<tr>
<td>Hydralazine*</td>
<td>Reflex tachycardia, HA, variable duration</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Renal insufficiency/failure, hyperkalemia</td>
</tr>
<tr>
<td></td>
<td>Cl: Pregnancy, renal artery stenosis</td>
</tr>
<tr>
<td>Malemidopam</td>
<td>Headache, flushing, cerebral ischemia</td>
</tr>
<tr>
<td>Clevidipine</td>
<td>Caution in elderly (renal/hepatic function), HF, β-blocker use, etc.</td>
</tr>
</tbody>
</table>

*Caution: ↑ ICP

### Hypertensive Urgency – oral drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>Renal insufficiency/failure, hyperkalemia Cl: Pregnancy, renal artery stenosis</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Sedation, dizziness Cl: Severe carotid artery stenosis</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Tachycardia, edema Cl: Angina, HF</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Flushing, headache, edema Cl: Severe aortic stenosis, coronary artery or cerebrovascular disease</td>
</tr>
<tr>
<td>Labetalol</td>
<td>Bronchospasm, HF exacerbation, bradycardia/heart block</td>
</tr>
</tbody>
</table>

**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

**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
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

Chapter and slide set developed by:

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  Medical University of South Carolina
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  Charleston, SC

Conflict of Interest Disclosures

I have no conflicts of interest to disclose

Agenda

- Acute coronary syndromes
- Peripheral Arterial Disease
- Dyslipidemia

Acute Coronary Syndromes


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

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

Goals of Therapy

- UA/NSTEMI goals
  - Prevent total occlusion
  - Antiplatelets (ASA, P2Y12, +/- 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

Invasive vs Conservative Strategy

<table>
<thead>
<tr>
<th>UA/NSTEMI</th>
<th>TIMI Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>Age &gt;65</td>
</tr>
<tr>
<td></td>
<td>More than 3 cardiac risk factors*</td>
</tr>
<tr>
<td></td>
<td>History of CAD &gt;50% stenosis</td>
</tr>
<tr>
<td>Presentation</td>
<td>Severe angina, ASA within 7 days, elevated markers, ST-segment deviation &gt;0.5 mm</td>
</tr>
</tbody>
</table>

* 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%

Invasive vs Conservative Strategy

<table>
<thead>
<tr>
<th>Invasive</th>
<th>Conservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent angina/schema at rest</td>
<td>Low risk score (TIMI, GRACE)</td>
</tr>
<tr>
<td>Elevated biomarkers</td>
<td>Patient/Physician preference in the absence of high risk features</td>
</tr>
<tr>
<td>New/presumably new ST depression</td>
<td></td>
</tr>
<tr>
<td>S/S of HF or new/worsening mitral regurgulation</td>
<td></td>
</tr>
<tr>
<td>High risk findings from noninvasive testing</td>
<td></td>
</tr>
<tr>
<td>Hemodynamic instability</td>
<td></td>
</tr>
<tr>
<td>Sustained VT</td>
<td></td>
</tr>
<tr>
<td>PCI w/6 months</td>
<td></td>
</tr>
<tr>
<td>Prior CABG</td>
<td></td>
</tr>
<tr>
<td>High risk score (e.g., TIMI, GRACE)</td>
<td></td>
</tr>
<tr>
<td>Reduced LVEF (&lt;40%)</td>
<td></td>
</tr>
</tbody>
</table>
**UA/NSTEMI & STEMI Initial Management**

- **M** = Morphine
  - Morphine 1 to 5 mg IV if symptoms not relieved by NTG or recur

- **O** = Oxygen
  - Oxygen if O2 saturation < 90% or high-risk features for hypoxemia

- **N** = Nitroglycerin NTG spray or SL tablet 0.4 mg x 3 doses (if pain unrelied after one dose, call 911)
  - NTG IV 5 mcg/min, titrate to CP relief or 200 mcg/minute

- **A** = Aspirin*
  - ASA chew and swallow non-enteric coated 162–325 mg x 1 dose

- **B** = Beta blocker*
  - PO/IV beta blocker, oral preferred

* = mortality reducing

---

**UA/NSTEMI Algorithm**

**Symptoms < 12 hours**

<table>
<thead>
<tr>
<th>Primary PCI</th>
<th>Fibrinolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLOPIDOGREL or PRASUGREL or TICAGRELOR</td>
<td>CLOPIDOGREL</td>
</tr>
<tr>
<td>UFH with (alternatively EPTIFIBATIDE or TIROFiban) or BIVALIRUDIN alone</td>
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</table>

**STEMI Algorithm**

**Symptoms < 12 hours**

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</tbody>
</table>

**Antiplatelet Agents**

**P2Y<sub>12</sub> Antagonists**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>Ticagrelor</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Indication</td>
<td>ACS managed medically or with PCI</td>
<td>ACS with PCI</td>
<td>ACS with PCI</td>
</tr>
<tr>
<td>Dosing</td>
<td>300 mg (P.I.) -600 mg (with stenting- 2011 PCI guidelines)</td>
<td>75 mg daily</td>
<td></td>
</tr>
<tr>
<td>Peak Platelet Inhibition</td>
<td>300 mg load ~ 6 hrs</td>
<td>600 mg load ~2 hrs</td>
<td></td>
</tr>
<tr>
<td>Oral/Parenteral</td>
<td>parenteral, oral</td>
<td>oral</td>
<td>parenteral (range 5-15 hours)</td>
</tr>
<tr>
<td>Non-responders</td>
<td>Increased risk of or death, MI, CHD, severe bleeding, stent thrombosis</td>
<td>Not identified</td>
<td>Not identified</td>
</tr>
<tr>
<td>Drug/Drug Interactions</td>
<td>Reduced risk of MI, death, stent thrombosis, or revascularization</td>
<td>No known issues</td>
<td>No known issues</td>
</tr>
<tr>
<td>CABG hold time</td>
<td>5 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
<tr>
<td>Study</td>
<td>CREDO, CURE, PCI-CURE, CLARITY, COMMIT, TRITON-TIMI 38, PLATO</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Clopidogrel- Plavix®**

<table>
<thead>
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<th>Prasugrel</th>
<th>Ticagrelor</th>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

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GP IIb/IIIa Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>STEMI w/o PCI</th>
<th>UA/NSTEMI w/o PCI</th>
<th>Renal Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abciximab</td>
<td>0.25 mg/kg IVB, 0.125 mcg/kg/min x 12h</td>
<td>--</td>
<td>Not necessary</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>180 mcg/kg IVB x 2 (10 min apart), 2 mcg/kg/min x 12-72h</td>
<td>IF CG &lt; 50, 4 infusion 50% If dialysis, contraindicated</td>
<td></td>
</tr>
<tr>
<td>Tirofiban</td>
<td>25 mcg/kg IVB, 0.4 mcg/kg/min x 30 min, 0.1 mcg/kg/min x 18-72h</td>
<td>IF CG &lt; 30, infusion 50%</td>
<td></td>
</tr>
</tbody>
</table>

Anticoagulants Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Classification</th>
<th>Renal Adjustment</th>
<th>Toxicity</th>
<th>Monitoring</th>
<th>Bolus</th>
<th>Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>LMWH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enoxaparin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Factor Xa inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>DTI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thrombolytics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase</td>
<td>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</td>
</tr>
<tr>
<td>Reteplase</td>
<td>10 units IV, repeat 10 units IV in 30 minutes</td>
</tr>
<tr>
<td>Tenecteplase</td>
<td>60-90 kg, 30 mg IV; 60-89 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)</td>
</tr>
</tbody>
</table>

Contraindications to Thrombolysis

<table>
<thead>
<tr>
<th>Relative Contraindications</th>
<th>Absolute Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP &gt; 180/110 mm Hg on presentation</td>
<td>ANY prior hemorrhagic stroke</td>
</tr>
<tr>
<td>History of TIA or CVA &lt; 3 months prior</td>
<td>Ischemic stroke within 3 months (except in post MI)</td>
</tr>
<tr>
<td>History of chronic poorly controlled HTN</td>
<td>Intercranial neoplasm or arteriovenous malformation</td>
</tr>
<tr>
<td>Recent trauma, major surgery, CPR, internal bleeding in 2-4 weeks</td>
<td>Active internal bleeding</td>
</tr>
<tr>
<td>Septicemia exposure &gt; 5 days earlier or prior allergic reaction</td>
<td>Bacteremic septicemia</td>
</tr>
<tr>
<td>Considerable facial trauma or closed-head trauma in past 3 months</td>
<td>Active peptic ulcer</td>
</tr>
</tbody>
</table>

UA/NSTEMI Case #1

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

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.
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 2-229)

Dual Antiplatelet Therapy after ACS

- Reduces the risk of stent thrombosis
- Aspirin plus P2Y12 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


Long-term Medications

- Beta-blockers
- ACE inhibitors
  - Within 1st 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

Q#4 Page 2-208 (Ans 2-229)

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
**Peripheral Arterial Disease (PAD)**


**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

**Diagnosis**

Ankle Brachial Index

**ABI Calculation**

Calculation of ABI

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

**ABI Interpretation**

<table>
<thead>
<tr>
<th>Level</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.4</td>
<td>Normal ABI</td>
</tr>
<tr>
<td>0.91 – 0.99</td>
<td>Borderline</td>
</tr>
<tr>
<td>&lt;0.9</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

Values >1.40 indicate noncompressible arteries

---

**STEMI Case #1**

- Home Meds: lisinopril, gemfibrozil
- Vitals: HR 68, BP 178/94, wt 100kg
- ECG:
  - 3mm ST Elevation in V2-V4, I, aVL
- Labs:
  - Serum chemistry WNL
  - Positive myoglobin
  - Positive cardiac enzymes
    - CK 175, MB 17.4, Troponin T 0.8
- Diagnosis: STEMI

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
**Risk Factors**

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

**History of PAD**

![History of PAD diagram]

**Treatment**

- **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**
  - **Statin initiation** – Goal LDL-C of less than 70 mg/dL for patients deemed very high risk
  - **Fibrin 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 HbA1C < 7%
- **Antiplatelet Agents**
  - **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

**PAD Case #6**

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

**PAD Case #1**

- 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

**Treatment-Claudication**

- **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 IIb**: Second-line agent to improve walking distance
  - **Questionable Efficacy**
  - **Additional Therapies Not Helpful**
    - Oral vasodilator prostaglandins
    - Vitamin E

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**Dyslipidemia**

### Lipid and Lipoprotein Classification

<table>
<thead>
<tr>
<th>Component</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LDL (mg/dL)</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 100</td>
<td>Optimal</td>
</tr>
<tr>
<td>100–129</td>
<td>Near optimal/above optimal</td>
</tr>
<tr>
<td>130–159</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160–189</td>
<td>High</td>
</tr>
<tr>
<td>190 or more</td>
<td>Very high</td>
</tr>
<tr>
<td><strong>HDL (mg/dL)</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 40</td>
<td>Low</td>
</tr>
<tr>
<td>60 or more</td>
<td>High</td>
</tr>
<tr>
<td><strong>TC (mg/dL)</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 200</td>
<td>Desirable</td>
</tr>
<tr>
<td>200–239</td>
<td>Borderline high</td>
</tr>
<tr>
<td>240 or more</td>
<td>High</td>
</tr>
<tr>
<td><strong>TG (mg/dL)</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 150</td>
<td>Normal</td>
</tr>
<tr>
<td>150–199</td>
<td>Borderline high</td>
</tr>
<tr>
<td>200–499</td>
<td>High</td>
</tr>
<tr>
<td>500 or more</td>
<td>Very high</td>
</tr>
</tbody>
</table>

**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

**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)
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.

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL Goal (mg/dL)</th>
<th>LDL Level to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk: CHD or CHD Risk Equivalents (10-year risk &gt;20%)</td>
<td>&lt; 100 (optional &lt; 70)*</td>
<td>≥ 100 (&lt;100: drug optional)</td>
</tr>
<tr>
<td>Moderately High Risk: 2+ Risk Factors (10-year risk 10-20%)</td>
<td>&lt; 130 (optional &lt; 100)</td>
<td>≥ 130 (≥100: drug optional)</td>
</tr>
<tr>
<td>Moderate Risk: 2+ Risk Factors (10-yr risk &lt; 10%)</td>
<td>&lt; 130</td>
<td>≥ 160</td>
</tr>
<tr>
<td>Lower Risk: 0-1 Risk Factor</td>
<td>&lt; 160</td>
<td>≥ 190 (≥160: drug optional)</td>
</tr>
</tbody>
</table>

*NCEP–ATP III Guidelines-2004

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.

Patient Case

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

Case #8

- According to NCEP guidelines, how many CHD risk factors are present?
  A. Zero
  B. One
  C. Two
  D. Three

NCEP–ATP III Guidelines-2004

Case #8 (Ans 2-230)
Approximate and Cumulative LDL Cholesterol Reduction Achievable By Dietary Modification

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

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

Non-HDL

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL Goal</th>
<th>Non-HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD and CHD risk equivalents (10-year risk &gt; 20%)</td>
<td>&lt; 100</td>
<td>&lt; 130</td>
</tr>
<tr>
<td>Multiple (2+) risk factors (10-year risk ≤ 20%)</td>
<td>&lt; 130</td>
<td>&lt; 160</td>
</tr>
<tr>
<td>0 or 1 risk factor</td>
<td>&lt; 160</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacotherapy

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.
  - (current LDL – goal LDL)/current LDL x 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.
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
  - Rhabdomyolysis
    - CK 10,000 > IU/L, or
    - CK >10 x ULN plus an elevation in serum creatinine or medical intervention with IV hydration

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

Factors That Increase the Risk of Statin-Induced Myopathy

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Statin Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>High systemic exposure</td>
<td>Female sex</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>Lipophilicity</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>High bioavailability</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Potential for drug-drug interactions metabolized by CYP pathways (particularly CYP450 3A4)</td>
</tr>
<tr>
<td>Diet (i.e. grapefruit juice)</td>
<td>Polypharmacy</td>
</tr>
</tbody>
</table>

Statin Drug Interactions

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>DNE Lova 40mg; Simva 20mg; consider limiting atorva/fluva</td>
</tr>
<tr>
<td>Azoles,Macrolides</td>
<td>Hold Lova/Simva during treatment; Limit 1 mg pitava</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>DNE Simva 20mg *Caduet=Amlodipine + Atorvastatin</td>
</tr>
<tr>
<td>Diltiazem/Verapamil</td>
<td>DNE Simva 10mg with D/V; DNE Lova 20 with D/V Consider limiting atorvastatin dose</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Avoid Atorva;Simva;Lova;DNE=Do Not Exceed</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>Rosuva 10mg; AVOID Simva and Lova; Consider limiting dose of atorva</td>
</tr>
</tbody>
</table>

Statins – Another FDA Warning

- No More Routine Periodic Monitoring of Liver Enzymes
  - LFTs 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.
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.

Statin LDL - Lowering

<table>
<thead>
<tr>
<th>Statin</th>
<th>Brand Name</th>
<th>Daily Dose (mg)</th>
<th>LDL Lowering (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluvastatin</td>
<td>Lescol</td>
<td>20 - 80</td>
<td>22 - 35</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Pravachol</td>
<td>10 - 40</td>
<td>24 - 45</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Mevacor</td>
<td>20 - 80</td>
<td>29 - 45</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Zocor</td>
<td>20 - 80</td>
<td>30 - 55</td>
</tr>
</tbody>
</table>

Pharmacokinetics

<table>
<thead>
<tr>
<th>Statin</th>
<th>Bioavail</th>
<th>T½ (hours)</th>
<th>Metabolism</th>
<th>Pro-drug</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>17%</td>
<td>1.5-2</td>
<td>na</td>
<td>No</td>
<td>Hydrophilic</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>24%</td>
<td>1</td>
<td>2C9</td>
<td>No</td>
<td>Lipophilic</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>&lt;5%</td>
<td>2-3</td>
<td>3A4</td>
<td>Yes</td>
<td>Lipophilic</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>&lt;5%</td>
<td>2</td>
<td>3A4</td>
<td>Yes</td>
<td>Lipophilic</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>13%</td>
<td>14</td>
<td>3A4</td>
<td>No</td>
<td>Lipophilic</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>30%</td>
<td>20</td>
<td>Limited 2C9</td>
<td>No</td>
<td>Hydrophilic</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>51%</td>
<td>12</td>
<td>2C9,2C8</td>
<td>Yes</td>
<td>Lipophilic</td>
</tr>
</tbody>
</table>

Dosing of Statins in Renal Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>GFR 30-59</th>
<th>GFR 15-29</th>
<th>GFR &lt; 15 or HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>10-80 mg</td>
<td>10-80 mg</td>
<td>10-80 mg</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>10-80 mg</td>
<td>10-40 mg</td>
<td>10-40 mg</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>20-80 mg</td>
<td>10-0 mg</td>
<td>10-20 mg</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20-40 mg</td>
<td>10 initial; 20-40 mg</td>
<td>20-40 mg</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>5-40 mg</td>
<td>5 mg initial; 10 mg max</td>
<td>Levels in HD are 50% higher than in normal fnc</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20-80 mg</td>
<td>5 mg initial;</td>
<td></td>
</tr>
</tbody>
</table>

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).

<table>
<thead>
<tr>
<th>Bile Acid Sequestrant</th>
<th>Dose</th>
<th>% LDL-C Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colestipol</td>
<td>5 grams</td>
<td>-12%</td>
</tr>
<tr>
<td></td>
<td>10 grams</td>
<td>-20%</td>
</tr>
<tr>
<td></td>
<td>15 grams</td>
<td>-24%</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>4-8 grams</td>
<td>-9%</td>
</tr>
<tr>
<td></td>
<td>8-12 grams</td>
<td>-13%</td>
</tr>
<tr>
<td></td>
<td>12-16 grams</td>
<td>-17%</td>
</tr>
<tr>
<td></td>
<td>16-20 grams</td>
<td>-21%</td>
</tr>
<tr>
<td></td>
<td>20-24 grams</td>
<td>-28%</td>
</tr>
<tr>
<td>Colesevelam</td>
<td>3.8 grams</td>
<td>-15%</td>
</tr>
<tr>
<td></td>
<td>4.5 grams</td>
<td>-18%</td>
</tr>
</tbody>
</table>
Niacin

Main actions
- Lowers LDL 15%–26%
- Lowers TG 20%–55%
- 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.

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

Ezetimibe

Ezetimibe (Zetia) 10 mg/day

Efficacy
- Lowers LDL 18%–20%
- May raise HDL 1%–5%
- Lowers TG 1%–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 conflicting
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 β-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

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**Patient Case**

- Which one of the following medications is best to recommend to treat M.M.’s lipids?
  - a. Ezetimibe 10 mg/day
  - b. Fenofibrate 145 mg/day
  - c. Colesevelam 625 mg 6 tablets/day
  - d. Atorvastatin 20 mg/day

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

---

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>↓22-60%</td>
<td>↑5-15%</td>
<td>↓7-40%</td>
</tr>
<tr>
<td>Niacin</td>
<td>↓15-26%</td>
<td>↑15-26%</td>
<td>↓20-50%</td>
</tr>
<tr>
<td>Ezetimibe</td>
<td>↓18-20%</td>
<td>↑1-5%</td>
<td>↓7-17%</td>
</tr>
<tr>
<td>Fibrates</td>
<td>↓5-20% (nf TG)</td>
<td>↑18-22%</td>
<td>↓30-55%</td>
</tr>
</tbody>
</table>

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**Questions?**

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

- a good mom

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2011 Updates in Therapeutics:
The Pharmacotherapy Preparatory Review & Recertification Course
Cardiology III
Robert L. Page, Pharm.D., MPH, BCPS (AQ cards), FAHA, FCCP, FASHP, FACP, CGP
University of Colorado School of Pharmacy and School of Medicine

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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

Page Pointers

- Absolutely do study this....

Page Pointers

- And this....www.americanheart.org (click Health/Research)
**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:
  - Ca 9.0
  - Mg 2.0
  - dig 0.7 ng/mL
  - Phos 2.8

**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

**Neurohormonal Blockade in HF**

<table>
<thead>
<tr>
<th>Medication</th>
<th>1st Neurohormone affected</th>
<th>Effect on mortality</th>
<th>Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitor</td>
<td>Angiotensin II</td>
<td>↓ 15%</td>
<td>↓ 30%</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>Norepinephrine</td>
<td>↓ 35%</td>
<td>↓ 35%</td>
</tr>
<tr>
<td>Aldosterone Blocker</td>
<td>Aldosterone</td>
<td>↓ 30%</td>
<td>↓ 35%</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Central sympathetic outflow</td>
<td>9%</td>
<td>↓ 6%</td>
</tr>
</tbody>
</table>

**ACEI Dosing in HF**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dosage</th>
<th>Initial Dosage</th>
<th>Maximal Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>6.25 mg BID</td>
<td>50 mg BID</td>
<td>50 mg BID</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 mg BID</td>
<td>20 mg BID</td>
<td>20 mg BID</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>2.5-5 mg/day</td>
<td>20 mg/day</td>
<td>40 mg/day</td>
</tr>
<tr>
<td>Perindopril</td>
<td>2 mg/day</td>
<td>10 mg/day</td>
<td>10 mg/day</td>
</tr>
<tr>
<td>Randipril</td>
<td>1.25-2.5 mg/day</td>
<td>5 mg BID</td>
<td>10 mg BID</td>
</tr>
<tr>
<td>Traipril</td>
<td>1 mg/day</td>
<td>4 mg/day</td>
<td>4 mg/day</td>
</tr>
</tbody>
</table>

Note: Captopril and enalapril may be used; however, they do not have the same magnitude of mortality-reducing data as the above-listed angiotensin-converting enzyme inhibitors. BID = 2 times/day; TID = 3 times/day.
### Beta Blocker Dosing in HF

<table>
<thead>
<tr>
<th>Agent</th>
<th>Starting Dosage</th>
<th>Target Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diltiazem</td>
<td>1.25 mg/day</td>
<td>10 mg/day</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 mg BID</td>
<td>25 mg BID</td>
</tr>
<tr>
<td>Metoprolol succinate XL (metoprolol CR/XL)</td>
<td>12.5–25 mg/day</td>
<td>200 mg/day</td>
</tr>
</tbody>
</table>

*50 mg 2 times/day if weight is more than 85 kg.
*Few or no data exist with metoprolol succinate.

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

### 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
    - CIs, Azole antifungals

### Other Considerations

- **Vitals**
  - BP = 112/70
  - HR = 68
- **Titration**
  - Double dose Q2 weeks maximum
  - Only 1% incidence of significant bradycardia
  - HR decreases an average of 12 bpm
  - No significant change in BP
- **Assess**
  - Edema/fluid retention, fatigue, dizziness

### Case #1 - Question??

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

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

### 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 81 mg 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
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

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<tr>
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<tr>
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<tr>
<td>furosemide 80 mg BID</td>
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<tr>
<td>cilostazol 100 mg BID</td>
</tr>
<tr>
<td>acetaminophen 650 mg QID</td>
</tr>
<tr>
<td>sertraline 100 mg QD</td>
</tr>
<tr>
<td>levothyroxine 0.1 mg QD</td>
</tr>
</tbody>
</table>

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
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<tr>
<td>acetaminophen 650 mg QID</td>
</tr>
<tr>
<td>sertraline 100 mg QD</td>
</tr>
<tr>
<td>levothyroxine 0.1 mg QD</td>
</tr>
</tbody>
</table>

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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

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 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

- Increase enalapril 10 mg 2 times/day
- Add spironolactone 25 mg/day
- Increase digoxin to 0.125 mg/day

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

- 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

- 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)

- 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

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

Harmful medications

- Promote fluid retention
  - NSAIDs
  - Corticosteroids
  - Minoxidil
  - Thiazolidinediones
  - Exacerbate HF
    - Dronedarone
  - Negative inotropic activity (cause neurohormonal activation)
    - Class I and III antiarrhythmics (except dofetilide and amiodarone)
      - Diltiazem and Verapamil
      - Itraconazole
  - Negative inotropic activity/tachycardia
    - Anagrelide
    - Amphetamines
- Increase ventricular arrhythmias
  - Class I and III antiarrhythmics (except dofetilide and amiodarone)
  - Amphetamines
  - Cilostazol
  - Acetaminophen
  - Sertraline
  - Cilostazol
  - Levothyroxine

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

**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](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

**Ventricular Rate Control**

- Beta blockade
  - Beta, 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
**Ventricular Rate Control**

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

**Anticoagulation: CHADS2**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Recent congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>H Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A Age ≥75 years</td>
<td>1</td>
</tr>
<tr>
<td>D Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>S2 History of stroke or transient ischemic attack (TIA)</td>
<td>2</td>
</tr>
</tbody>
</table>

**Anticoagulation in AF**

**Stroke Risk Reductions**

| AFASAK | SPAF | BAATAF | CAF | SPINAFA | EAF | All trails=
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin Better</td>
<td>Control Better</td>
<td>Reduction of all-cause mortality RRR 36%</td>
<td>Reduction of stroke RRR 62%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ACTIVE-W: Cumulative Risk of Stroke**

RR=1.72 (1.24-2.37), P=0.001

- Clopidogrel + aspirin
- Oral anticoagulation therapy

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Dabigatran-ACC/AHA Statement

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

Selection of patients with atrial fibrillation and stroke risk who cannot tolerate warfarin or whose control cannot be maintained may help to gain the benefits of dabigatran.

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

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)
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

Heart Failure and Atrial Fibrillation

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

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

Atrial Fibrillation in HF

- Patients usually poorly tolerant to A fib
  - 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)

Atrial Fibrillation Rhythm Control

- Dronedarone
  - Class Ia
    - Dronedarone is reasonably to decrease the need for hospitalization for cardioversion in patients with paroxysmal AF or after conversion of persistent AF. Dronedarone can be initiated during hospitalization. (Level of Evidence: B)
  - Class IIa, Norm
    - Dronedarone 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 (LVEF < 20%). (Level of Evidence: B)
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

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

<table>
<thead>
<tr>
<th>Modification</th>
<th>SBP reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Reduction</td>
<td>5-20 mm Hg/10 kg lost</td>
</tr>
<tr>
<td>DASH Diet</td>
<td>5-14 mm Hg</td>
</tr>
<tr>
<td>Sodium restriction</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>4-9 mm Hg</td>
</tr>
<tr>
<td>Limit alcohol consumption</td>
<td>2-4 mm Hg</td>
</tr>
</tbody>
</table>

Step 2: Address Lifestyle Modifications

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

Step 4: Assess for ‘Compelling Indication’

- 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? 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?
  - 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?
    - Post-MI
      - 1st 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

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? 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
- BP Goal
  - DM and renal disease (Creatinine = 1.8)
  - Goal is < 130/80 mmHg

Case #7

- Is she hypertensive? No
  - BP < 140/90 (138/88, 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?
  - DM and kidney disease
    - 1st 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

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...

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

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

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
  Exercise counsel
  Education counsel

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)
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
- Medications:
  - aspirin 325 mg/day
  - enalapril 10 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 O₂ demand
  - Increase myocardial O₂ supply

Stable Angina Management

<table>
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<tr>
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<th>Increase</th>
<th>Decrease</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Beta-blocker</td>
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<td>- goal resting HR = 55-60</td>
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<tr>
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<td></td>
<td></td>
<td>- exercise HR &lt; 75%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- pain threshold</td>
</tr>
<tr>
<td>Calcium</td>
<td>√</td>
<td>√</td>
<td>- add on to BB if needed</td>
</tr>
<tr>
<td>Antagonists</td>
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<td></td>
<td>- in place of BB 2º SE</td>
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<td></td>
<td></td>
<td></td>
<td>- avoid short-acting dihydropyridines</td>
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<tr>
<td>Nitroglycerin</td>
<td>√</td>
<td>√</td>
<td>- most useful with BB</td>
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<td></td>
<td></td>
<td>- ALWAYS PRN</td>
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<tr>
<td></td>
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<td>- can be used pre-activity</td>
</tr>
</tbody>
</table>

Case #9-Question??

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

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

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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
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 O₂ supply

**Summary**

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

All very common disease states encountered in the outpatient setting