Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

# Arrhythmias

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## Conflict of Interest Disclosures

**Dr. Tilton has no actual or potential conflict of interest in relation to this activity.**

## Learning Objectives

1. **Identify the Vaughan-Williams classification of each antiarrhythmic drug.**
2. **Describe the mechanism of action of each antiarrhythmic drug, according to the ion channel it affects and the electrophysiologic outcome.**
3. **Discuss the side effect profile of each antiarrhythmic drug.**
4. **Evaluate a patient's medication list for possible drug interactions with his or her antiarrhythmic drugs.**
5. **Develop a comprehensive treatment plan for a patient with the following arrhythmias: atrial fibrillation, atrial flutter, atrioventricular nodal reentrant tachycardia, atrioventricular reentrant tachycardia, and sustained and nonsustained ventricular tachycardia.**

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## Antiarrhythmics
### Vaughan-Williams Class Ia

- Drugs: quinidine, disopyramide
- Mechanism: $Na^+$ channel blockade
  - Intermediate association and dissociation
- Indication:
  - Supraventricular Tachycardias (SVTs)
  - Premature ventricular contractions (PVCs)
  - Ventricular tachycardia (VT)

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## Antiarrhythmics
### Vaughan-Williams Class Ia

- Clinical Pearls
  - Proarrhythmic – Torsades
    - Dose dependent
  - Disopyramide: anticholinergic side effects; however, may be useful in patients with vagally mediated paroxysmal SVT
  - Quinidine: use with AV node blocking agent

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## Antiarrhythmics
### Vaughan-Williams Class Ib

- Drugs: mexiletine
- Mechanism**:** $Na^+$ channel blockade
  - Fast association and dissociation
- Indication:
  - Ventricular tachycardias

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## Antiarrhythmics
### Vaughan-Williams Class Ib

- Clincal Pearls
  - Mexiletine
    - Side effects: CNS
      - Tremor
      - Dizziness
      - Ataxia
      - Nystagmus
  - Little affect on atrial tissue

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## Antiarrhythmics
### Vaughan-Williams Class Ic

- Drugs: propafenone, flecainide
- Mechanism: $Na^+$ channel blockade
  - Slow association and dissociation
- Indication:
  - A.Fib
  - Paroxysmal supraventricular tachycardia (PSVT)
  - Life-threatening ventricular tachycardias

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## Antiarrhythmics
### Vaughan-Williams Class Ic

- Clinical Pearls
  - Cast Trials: Avoid in patients post MI
  - Proarrhythmia – VT/VF
  - Cause wide QRS
  - Propafenone: Class II and III activity
  - Flecainide: Class III activity

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## Antiarrhythmics
### Vaughan-Williams Class II

- Drugs: β-blockers
- Mechanism: blocking catecholamine and sympathetically mediated actions
  - β-blockade, indirect $Ca^{2+}$ blockade
- Indication:
  - A.Fib
  - Atrial Flutter
  - PSVT
  - Ventricular arrhythmias

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## Antiarrhythmics
### Vaughan-Williams Class III

- Drugs: amiodarone, sotalol, dofetilide, dronedarone
- Mechanism: $K^+$ channel blockade
- Indication:
  - SVTs
  - Life-threatening ventricular arrhythmias
    - Amiodarone and sotalol only

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## Antiarrhythmics
### Vaughan-Williams Class III

- Clinical Pearls
  - Proarrhythmia – Torsades
    - Dose dependent
  - Amiodarone: Class Ib, II, IV activity
    - Monitor LFTs, TSH and CXR
  - Dofetilide:
    - REMS
  - Dronedarone: Class Ib, II, IV activity
    - Avoid in heart failure patients
    - REMS
  - Sotalol: Class II activity
    - Renally dosed

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## Antiarrhythmics
### Vaughan-Williams Class IV

- Drugs: diltiazem and verapamil
- Mechanism: $Ca^{2+}$ channel blockade
- Indication:
  - A.Fib
  - Atrial Flutter
  - PSVT

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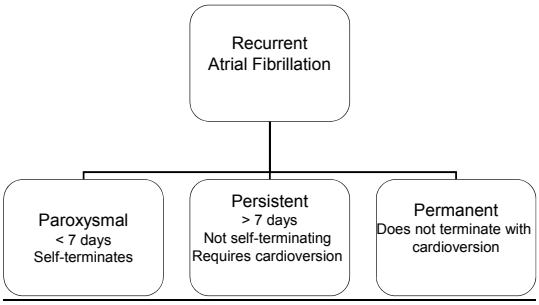
## Atrial Arrhythmias
### Atrial Fibrillation

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## Atrial Arrhythmias
### Atrial Fibrillation

- Most common arrhythmia
- Affects 0.4-1% of general population, and 8% of those > 80 years old
- 60% of those ≥ 75 years old are women
- Rate of mortality doubles compared to patients in NSR

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## Atrial Arrhythmias
### Atrial Fibrillation

- 400-600 atrial beats/minute
- Symptoms
  - Asymptomatic
  - Dizziness
  - SOB
  - Fatigue
  - Palpitation

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## Atrial Arrhythmias
### Atrial Fibrillation

- Mechanism: Enhanced automaticity in several rapidly depolarizing foci or reentry involving several circuits
- Pulmonary veins is a possible place of origin
- Can occur in both atriums
- Episodes > 24 hrs are harder to terminate

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## Atrial Arrhythmias
### Atrial Fibrillation

- Causes
  - Organic heart disease that activates the renin-angiotensin-aldosterone system through atrial stretch
  - Associated with high degree of adrenergic tone
  - Perpetuated by high cholinergic tone
  - Idiopathic

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## Atrial Arrhythmias
### Atrial Fibrillation

- Complications
  - Thromboembolic risk
  - Heart failure
  - Rapid ventricular response

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## Atrial Arrhythmias
### Atrial Fibrillation

- Treatment
  - Rate versus rhythm
  - Prevention of thromboembolism
    - Refer to Thromboembolism chapter

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## Atrial Arrhythmias
### Atrial Fibrillation

- Rate control
  - Indication
    - No symptoms or minimal symptoms
    - Treatment of choice for persistent or permanent atrial fibrillation
  - Treatment options
    - β-Blockers
    - Nondihydropyridine calcium channel blockers
    - Digoxin
    - Amiodarone
    - AV nodal ablation with pacemaker pacing

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## Atrial Arrhythmias
### Atrial Fibrillation

- Rhythm control
  - Indication
    - Symptomatic patients despite adequate rate control
    - Hemodynamically unstable
    - Heart Failure
    - A.Fib secondary to a trigger or substrate that has been corrected

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## Atrial Arrhythmias
### Atrial Fibrillation

- Rhythm control
  - Pharmacologic management
    - Class Ic
      - Flecainide
      - Propafenone
    - Class III
      - Amiodarone
      - Dofetilide
      - Dronedarone
      - Sotalol

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## Atrial Arrhythmias
### Atrial Fibrillation

- Rhythm control
  - Direct current cardioversion
  - Ablation or surgical Maze procedure

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## Patient Case
### Atrial Fibrillation

55 year-old-man complains of new onset of palpitations, fatigue, shortness of breath and dizziness while in clinic today.

PMH: HF NYHA class II (well controlled), stroke x 2, and DM

ECG: Atrial fibrillation; HR 81 beats/min

Medications: carvedilol 25 mg twice daily, lisinopril 20 mg/day, aspirin 81 mg/day, and insulin glargine 20 units at bedtime

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## Patient Case
### Atrial Fibrillation

Which one of the following is the best treatment plan?

A. Three weeks of therapeutic warfarin; then start dronedarone.
B. A transesophageal echocardiogram (TEE) today; if negative, start warfarin and dronedarone.
C. A TEE today; if negative, increase aspirin to 325 mg/day and start dronedarone.
D. Start on warfarin and change carvedilol to metoprolol succinate 200 mg/day.

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## Patient Case
### Atrial Fibrillation

If you decide to initiate dronedarone in this patient, Given the patient's current medical conditions, which one of the following potential adverse effects regarding dronedarone is most appropriate to counsel the patient?

A. Watch for signs and symptoms of ulcer.
B. Watch for signs and symptoms of hypoglycemia.
C. Watch for signs and symptoms of heart failure exacerbation.
D. Watch for blue-gray skin discoloration.

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## Patient Case
### Atrial Fibrillation

The patient returns 1 month after starting dronedarone. His ECG shows him in atrial fibrillation, and he still has symptoms that have come and gone during the past month. You find that the patient has not started the therapy because the drug was not covered by his insurance.

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## Patient Case
### Atrial Fibrillation

Which one of the following is the most appropriate alternative therapy that can be started today?

A. Amiodarone
B. Digoxin
C. Dofetilide
D. Sotalol

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## Ventricular Arrhythmias
### Ventricular Tachycardia (VT)

- Nonsustained VT (NSVT)
  - Three or more consecutive PVCs
  - Last less than 30 seconds
  - Terminates spontaneously
- Sustained VT
  - Three or more consecutive PVCs
  - Lasts more than 30 seconds
  - Or lasts less than 30 seconds, but requires termination because of hemodynamic compromise

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## Ventricular Arrhythmia
### VT

- HR greater than 100 beats/min
- Mortality risk correlates with the degree of structural heart disease
- Symptoms
  - Dyspnea
  - Syncope
  - Palpitations

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## Ventricular Arrhythmia
### VT

- Mechanism: Impulse is generated from increased automaticity of a single point in either the left or right ventricle or caused by a reentry circuit w/i the ventricle.
- Causes
  - Idiopathic
  - Sleep apnea
  - Myocardial scarring from previous MI
  - CAD
  - Hypertrophic cardiomyopathy
  - NIDCM
  - Electrolyte abnormalities
  - Right ventricular dysplasia

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## Ventricular Arrhythmia
### VT

- NSVT Chronic treatment
  - Ejection fraction greater than 40% and asymptomatic
    - Usually no treatment required
  - Symptomatic
    - B-blocker
    - Amiodarone
  - Ejection fraction less than 40%
    - Amiodarone

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## Ventricular Arrhythmia
### VT

- Sustained VT chronic treatment
  - Implantable cardioverter defibrillator (ICD)
  - If VT reoccurs after placement or if ICD not an option:
    - Ablation
    - Sotalol
    - B-blocker plus amiodarone
    - Amiodarone
    - Correct underlying cause

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## Patient Case
### VT

An 80-year-old man comes to the clinic with his holter monitor report from an outside facility showing symptomatic NSVT.

PMH: HTN, HL, obesity, DVT in right leg (newly diagnosed)

Vitals: BP 122/74 HR 75 beats/minute

Medications: Simvastatin 80 mg daily, warfarin 7.5 mg daily, lisinopril 10 mg daily, HCTZ 25 mg daily, and metoprolol succinate 150 mg daily.

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## Patient Case
### VT

The physician has determined that amiodarone is the best option for the patient. Baseline chest radiograph, LFTs, and thyroid panel have been obtained. When would be most appropriate for the patient to have these repeated?

A. 1 year

B. 1 month

C. 6 months

D. 6 weeks

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## Patient Case

VT

There is an interaction between the warfarin and amiodarone. Today's INR is 2.8. Which one of the following regimens is best regarding the warfarin dose and when should the patient return for an INR?

A. Continue current dose and return in 4 weeks.

B. Continue current dose and return in 2 weeks.

C. Reduce dose by one-third and return in 1 week.

D. Reduce dose by three-fourths and return in 5 days.

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## Patient Case

VT

Which one of the following drug interactions most appropriate to be addressed today because amiodarone was added to the patient's current medications?

A. Simvastatin

B. Lisinopril

C. Metoprolol

D. Hydrochlorothiazide

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# Dyslipidemia

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## Conflict of Interest Disclosure

**Karen McConnell**

No conflicts of interest to disclose

## Learning Objectives

- Integrate an understanding of the mechanism of action and effects of lipid medications to select appropriate pharmacologic therapy and develop a monitoring plan.
- Create an evidence-based lipid-lowering medication regimen for primary and secondary prevention.

## Learning Objectives

- Formulate an appropriate pharmacotherapeutic regimen for patients with dyslipidemia and specific case situations (e.g., chronic kidney disease, potential drug interactions, chronic creatine kinase elevations).
- Develop a treatment strategy for patients who require combination lipid-lowering therapy to achieve their lipid goals.

## Guidelines

- NCEP III
- AHA Update (2004)
- NCEP IV (due 2012)

## Fasting lipid panel

- Total cholesterol
  - Lipid in cell membranes and precursor to bile acids and steroid hormones
  - Goals
    - Less than 200 mg/dL – optimal
    - 200 – 240 mg/dL – borderline high
    - Greater than 240 mg/dL – high
  - Treatment – not a target for therapy

## Fasting lipid panel

- Triglycerides
  - Found in chylomicrons and VLDL
  - Goal less than 150 mg/dL
  - Treatment
    - Diet (limit alcohol and simple carbohydrates such as sugar, rice, pasta and bread)
    - Exercise
    - Weight loss if BMI greater than 25
    - Fibrates
    - Niacin
    - Omega-3 fatty acids (fish oil)

## Fasting lipid panel

- HDL (high density lipoprotein) – "Good"
  - Apo A-I and A-II; inversely correlated with CHD risk
  - Goals
    - Less than 40 mg/dL – low
    - 60 mg/dL – High
    - No specific goal for raising HDL identified because of lack of evidence for benefit
  - Treatment
    - Exercise
    - Niacin
    - Fibrates

## Fasting lipid panel

- LDL (low density lipoprotein) – "Bad"
  - APO-B; major atherogenic lipoprotein
  - Goals depend on risk factors and medical history
  - Treatment
    - Therapeutic lifestyle changes
      - Diet – low in saturated fat and cholesterol; high fiber
      - Exercise – 30 minutes/day most days of the week
      - Weight loss if BMI greater than 25
    - Pharmacotherapy
      - Statins
      - Niacin
      - Ezetimibe
      - Bile acid sequestrants

## Fasting lipid panel

- NonHDL – "Bad" (total cholesterol minus HDL)
  - Combination of LDL and VLDL
  - Enhances risk prediction
  - Goal 30 mg/dL above LDL goal
  - Treatment – therapies that can lower TG and LDL can improve NonHDL

## Primary Prevention Clinical Trials

## Clinical Trials – Primary Prevention

- **WOSCOPS** (1995)
  - Pravastatin 40 mg versus placebo for 5 years in 6595 male patients

| Acute coronary event | Mortality |
|---|---|
| 31% reduction | No Change |

- **AFCAPS/TexCAPS** (1998)
  - Lovastatin 20–40 mg versus placebo for 5.2 years in 6605 patients with average or below-average cholesterol concentrations

| Acute coronary event | Mortality |
|---|---|
| 37% reduction | No Change |

## Clinical Trials – Primary Prevention

- **PROSPER** (2002)
  - Pravastatin 40 mg versus placebo for 3.2 years in 5804 older patients

| Coronary events/Stroke | CHD Mortality |
|---|---|
| 15% reduction | 24% reduction |

- **ALLHAT – LLT** (2002)
  - Pravastatin 40 mg versus usual care for 4.8 years in 10,355 hypertensive patients

| Coronary events | Mortality |
|---|---|
| No difference | No difference |

## Clinical Trials – Primary Prevention

- **ASCOT – LLT** (2003)
  - Atorvastatin 10 mg versus placebo for 3.3 years in 19,342 hypertensive patients

| Coronary events | Mortality |
|---|---|
| 29% reduction | No difference |

- **JUPITER** (2008)
  - Rosuvastatin 20 mg versus placebo in healthy men and women with LDL less than 130 and C-reactive protein >1.9
  - Composite endpoint: MI, stroke, arterial revascularization, hospitalization for unstable angina, or death from CV causes

| Composite | Mortality |
|---|---|
| 44% reduction | 20% reduction |

## Secondary Prevention Clinical Trials

## Clinical Trials – Secondary Prevention

- **4S** (1994)
  - Simvastatin 10–40 mg versus placebo for 5.4 years in 4444 patients

| Coronary events | Mortality |
|---|---|
| 34% reduction | 30% reduction |

- **CARE** (1996)
  - Pravastatin 40 mg versus placebo for 5 years in 4159 patients

| Coronary events | Mortality |
|---|---|
| 24% reduction | No difference |

## Clinical Trials – Secondary Prevention

- **LIPID** (1998)
  - Pravastatin 40 mg versus placebo for 6 years in 9014 patients

| Coronary events | Mortality |
|---|---|
| 24% reduction | 23% reduction |

- **HPS** (2002)
  - Simvastatin 40 mg versus placebo for 5 years in 20,536 patients

| Major vascular events | Mortality |
|---|---|
| 24% reduction | 13% reduction |

## Clinical Trials – Secondary Prevention

- **PROVE-IT** (2004)
  - Pravastatin 40 mg versus atorvastatin 80 mg for 2 years in 4162 patients

| Composite (all-cause mortality, MI, revascularization) |
|---|
| 16% reduction |

- **TNT** (2005)
  - Atorvastatin 10 mg versus 80 mg for 4.0 years in 10,001 patients

| Major vascular events | Mortality |
|---|---|
| 22% reduction | No difference |

## Clinical Trials – Conclusion

- **Any statin that achieves significant LDL reduction remains the cornerstone of therapy for reducing CV risk.**

## Pharmacotherapy

- LDL lowering
  - Statins
  - Niacin
  - Ezetimibe
  - Bile acid sequestrants
- TG lowering
  - Fibrates
  - Omega-3 fatty acids

## LDL Lowering Agents

## Patient Case 1

- A 62-year-old man who smokes 1 pack/day presents to your clinic taking no medications. He is s/p MI with stent placement 5 years ago.
- The primary care physician would like your help in addressing his cholesterol. The patient would prefer to lower his cholesterol without medications, if possible.
- Fasting laboratory results reveal total cholesterol 187, TG 157, HDL 43, LDL 113, non-HDL 144, SCr 1.0, ALT 25, Na 140, and K 4.7. His BMI is 32.5.

Work book Page: 2-370 (Answer Page: 2-391)

## Patient Case 1 continued…

Which one of the following is the best recommendation to treat his cholesterol?

- [ ] A. Diet, exercise, and weight loss only.
- [ ] B. Diet, exercise, weight loss, and simvastatin 40 mg/day.
- [ ] C. Diet, exercise, weight loss, and ezetimibe 10 mg/day.
- [ ] D. Diet, exercise, weight loss, and fish oil supplement 1000 mg/day.

Work book Page: 2-370 (Answer Page: 2-391)

## Statins

- Mechanism of action – inhibits HMG-CoA reductase, which reduces hepatic cholesterol synthesis, lowers intracellular cholesterol and stimulates the up-regulation of the LDL receptor
- Evidence – see previous slides
- Clinical use
  - **First line** for dyslipidemia in primary and secondary prevention
    - Lowers LDL 21%–63%; for each doubling of a statin dose (e.g., simvastatin 10 mg to 20 mg), anticipate about 6% additional LDL reduction
    - Lowers TG 8%–37%; raises HDL 3%–16%

## Statin potency comparison

| Atorva (mg) | Fluva (mg) | Pitava (mg) | Lova (mg) | Prava (mg) | Rosuva (mg) | Vytorin (mg) | Simva (mg) | % ↓ LDL-C |
|---|---|---|---|---|---|---|---|---|
| — | 40 | 1 | 20 | 20 | — | — | 10 | 30 |
| 10 | 80 | 2 | 40 or 80 | 40 | — | — | 20 | 38 |
| 20 | — | 4 | 80 | 80 | 5 | 10/10 | 40 | 41 |
| 40 | — | | — | — | 10 | 10/20 | 80 | 47 |
| 80 | — | | — | — | 20 | 10/40 | — | 55 |
| | — | | — | — | 40 | 10/80 | — | 63 |

## Statins

- Clinical use (continued)
  - Pleiotropic effects
    - Improves endothelial function
    - Inhibits platelet aggregation
    - Decreases LDL oxidation
    - Reduces vascular inflammation
    - Stabilizes atherosclerotic plaques
- Contraindications
  - Pregnancy and lactation
  - Active liver disease

## FDA Drug Safety Communication: Simvastatin

- SEARCH trial
  - 7 year study comparing efficacy and safety of simvastatin 80 mg/day to 20 mg/day in patients post-MI

| | Simvastatin 80 mg/day | Simvastatin 20 mg/day |
|---|---|---|
| Myopathy | 0.9% | 0.02% |
| Rhabdomyolysis | 0.4% | 0 |

  - Risk of myopathy and rhabdomyolysis with simvastatin 80 mg/day highest in first 12 months of treatment
  - Older age and female sex increased risk
  - Supported FDA's Adverse Event Reporting System database

## FDA Drug Safety Communication: Simvastatin

| Contraindicated | NTE Simvastatin 10 mg/day | NTE Simvastatin 20 mg/day |
|---|---|---|
| Itraconazole | Amiodarone[a] | Amlodipine |
| Ketoconazole | Verapamil | Ranolazine |
| Posaconazole | Diltiazem | |
| Erythromycin | | |
| Clarithromycin | | |
| Telithromycin | | |
| HIV Protease inhibitors | | |
| Boceprevir | | |
| Telaprevir | | |
| Nefazodone | | |
| Gemfibrozil | | |
| Cyclosporin | | |
| Danazol | | |

[a]FDA approved a change to the simvastatin package labeling for maximal dose of simvastatin 20 mg/day with concomitant amiodarone.

## FDA Drug Safety Communication: Lovastatin

| Contraindicated | Avoid | NTE Lovastatin 20 mg/day | NTE Lovastatin 40 mg/day |
|---|---|---|---|
| Itraconazole | Gemfibrozil | Danazol | Amiodarone |
| Ketoconazole | Cyclosporin | Verapamil | |
| Posaconazole | | Diltiazem | |
| Erythromycin | | | |
| Clarithromycin | | | |
| Telithromycin | | | |
| HIV Protease inhibitors | | | |
| Boceprevir | | | |
| Telaprevir | | | |
| Nefazodone | | | |

## Statins

- Important adverse drug reactions
  - In general, well tolerated
  - Elevated LFTs (0.1% to 2.3%)
    - No link between statins and life-threatening liver damage
    - Elevations >3 times ULN occur in <1% of patients
    - Mild, asymptomatic transaminase elevations in 1 patient per 100,000 person-years in clinical trials
    - Elevations usually transient and resolve without intervention

## Statins

- Important adverse drug reactions (cont)
  - Myalgias (0.5% to 5%)
    - Usually without creatine phosphokinase (CPK) elevation
      - Manage by holding drug for few weeks to see whether symptoms improve; consider retrial
    - Rhabdomyolysis (0.002%)
      - CPK greater than 10,000 IU/L OR
      - CPK greater than 10 time ULN plus and elevation in Scr or medical intervention with IV hydration
      - Risk factors: advanced age (older than 65 years), small body frame, renal insufficiency, diabetes, hypothyroidism, drug interactions
      - Reversible with drug discontinuation

## Statins

- Important adverse drug reactions (cont)
  - Added to statin labels in February 2012
    - Generally non-serious and reversible cognitive side effects (memory loss, confusion, etc.)
    - Increased blood sugar and glycosylated hemoglobin (HbA1c) levels
    - FDA continues to believe that the cardiovascular benefits of statins outweigh these small increased risks.

## Statins

- Monitoring
  - Fasting lipid profile – 6 to 8 weeks after initation or titration; periodically thereafter
  - LFTS – FDA revised Feb 2012
    - Routine periodic monitoring of liver enzymes no longer recommended
    - Check before starting statin therapy and as clinically indicated thereafter
    - Serious liver injury with statins is rare and unpredictable
  - If liver enzymes elevated, important to exclude other etiologies (especially fatty liver)

## Statins

- Monitoring (cont)
  - Creatine phosphokinase (CPK)
    - Baseline levels not necessary unless patient is high risk
    - Routine monitoring not necessary in asymptomatic patients
    - Symptomatic patients: monitor CPK, thyroid function, and exacerbating factors
      - Intolerable muscle symptoms
        - Hold statin regardless of CPK level until symptoms resolved
        - If symptoms do not resolve, not likely due to statin
        - Once symptoms have resolved, the same statin at lower dose or another statin can be re-trialed
        - Recurrence of symptoms may indicate statin intolerance

## Statins

- Monitoring (cont)
  - Creatine phosphokinas (CPK)
    - Asymptomatic patients (or tolerable muscle symptoms) with mild CPK elevation, statin therapy can be continued
    - If CPK elevation is moderate or severe, or if rhabdomyolysis occurs, statin therapy should be discontinued.
    - Important to weigh risk-benefit ratio for statin use
  - Others labs to consider
    - Renal function
    - Thyroid function
    - Serum glucose

## Patient Case 2

- A 68-year-old man who suffered an MI 6 months ago and who has hypertension and peripheral artery disease presents to your clinic.
- He is adherent to simvastatin 80 mg every evening but continues to have uncontrolled cholesterol. He has been "doing his best" to improve his diet. Exercise is difficult for him and he can't afford brand-name medications. He has a history of intolerance to niacin.
- Fasting laboratory results reveal total cholesterol 174, TG 273, HDL 29, LDL 90, non-HDL 145, SCr 1.3, ALT 30, Na 143, K 4.7, uric acid 5.5, and FBG 97. His BMI is 27.0.

Work book Page: 2-376 (Answer Page: 2-391)

## Patient Case 2 continued…

Which one of the following is the best recommendation for this patient?

- A. Discontinue simvastatin and start rosuvastatin 40 mg daily.
- B. Discontinue simvastatin and start atorvastatin 80 mg every evening.
- C. Continue simvastatin and add OTC niacin, titrating up to 500 mg BID.
- D. Continue simvastatin and add a fish oil supplement, 1 capsule/day.

Work book Page: 2-376 (Answer Page: 2-391)

## Niacin (Vitamin $B_3$)

- Mechanism of action – inhibits the hepatic production of VLDL and its metabolite LDL
- Evidence
  - Coronary Drug Project
    - Niacin arm had 11% decrease in coronary mortality
  - ARBITER-6
    - Niaspan significant reduced carotid intima-media thickness (CIMT) progression compared to ezetimibe
    - Unknown if improved CIMT translates to improved clinical outcomes

## Niacin (Vitamin $B_3$)

- Evidence (continued)
  - AIM-HIGH
    - 3414 patients with established heart disease, low HDL-C levels, and raised TG
    - Trial terminated early after a 3 years because niacin showed no additional benefits over placebo
- Clinical use
  - Lowers LDL 5 to 25% and TG 20 to 50%
  - Increases HDL 15 to 35%
  - Consider 2nd line after statin therapy or as add-on to statin therapy

## Niacin (Vitamin $B_3$)

- Important adverse drug reactions
  - Flushing and itching
    - Less common with controlled-release preparations
    - Food, aspirin 30 minutes prior, night time administration and slow dose titration can improve
  - Elevated LFTs – less with immediate release
  - Increase glucose levels – importance is controversial (ADMIT study showed little impact to glucose)
  - Induce hyperuricemia – avoid with gout history
  - Myopathy – especially with concomitant statin

## Niacin (Vitamin $B_3$)

- Contraindications
  - Active hepatic disease
  - Active peptic ulcer
- Dosing and monitoring
  - OTC and prescription products available
    - Flush free niacin has no effect on lipids
  - Fasting lipid panel, ALT, fasting glucose (consider $A_{1C}$ for patients with DM), and uric acid 6 to 8 weeks after initiation or titration
  - Consider CPK if used concomitantly with statins

## Patient Case 3

- A 72-year-old woman presents with intolerance to lipid-lowering therapy (four different statins and two formulations of niacin).
- Her medical history is significant for DM and osteoporosis. She currently takes alendronate 10 mg/day. She has seen a dietitian to improve her diet and has exercised at least 200 minutes/week since her diagnosis of DM.
- Fasting laboratory results reveal total cholesterol 199, TG 115, HDL 49, LDL 127, non-HDL 150, SCr 1.6, ALT 15, and A1c 6.5%. Her BMI is 22.7.

Work book Page: 2-378 (Answer Page: 2-391)

## Patient Case 3 continued…

Which one of the following is the best recommendation to manage her dyslipidemia?

- A. Weight loss.
- B. Fenofibrate 160 mg/day.
- C. Ezetimibe 10 mg/day.
- D. Simvastatin 80 mg every evening.

Work book Page: 2-378 (Answer Page: 2-391)

## Ezetimibe

- Mechanism of action – selective inhibitor of dietary and biliary cholesterol absorption
- Evidence
  - ENHANCE trial
    - Simvastatin monotherapy: LDL reduced by 39%
    - Ezetimibe/simvastatin: LDL reduced by 56%
    - No significant difference found in primary end point
  - SEAS trial
    - Placebo: LDL reduced by 4%
    - Ezetimibe/simvastatin: LDL reduced by 54%
    - No significant difference found in primary end point
    - Cancer occurred more in ezetimibe/simvatatin group (likely incidental)

## Ezetimibe

- Evidence (continued)
  - SHARP trial
    - Simvastatin 20 mg plus ezetimibe 10 mg/day versus matching placebo
    - 9270 patients with chronic kidney disease (3023 on dialysis and 6247 not) with no known history of MI or coronary revascularization
    - Outcome was the first major atherosclerotic event (nonfatal MI or coronary death, nonhemorrhagic stroke, or any arterial revascularisation procedure).
    - 17% proportional reduction in major atherosclerotic events
    - In November 2011, FDA advisers recommend Vytorin for CVD prevention in predialysis patients with CKD.

## Ezetimibe

- Clinical use
  - LDL lowering
    - Monotherapy: 17%
    - Add on to statin therapy: additional 14 to 20%
  - Likely 3rd line agent after statins and niacin
- Contraindications – active hepatic disease
- Important adverse drug reactions – well tolerated
- Dosing and monitoring
  - Consider trial of 5 mg/day for similar efficacy of 10 mg/day
  - Fasting lipid profile and ALT at 6 to 8 weeks after initiation

## Bile Acid Sequestrants

- Mechanism of action – binds bile acid in intestine, decreasing biliary cholesterol absorption
- Evidence
  - LRC trial – cholestyramine reduced coronary events by 19%
- Clinical use
  - Lowers LDL by 15 to 30%; may raise TG
  - Almost last line for LDL lowering due to tolerability issues and drug interactions

## Bile Acid Sequestrants

- Contraindications – complete biliary obstruction
- Important adverse drug reactions
  - GI – constipation, obstruction
- Dosing and monitoring
  - Requires 3 to 20 g/day for effectiveness
  - Can bind many drugs, decreasing absorption. Recommend separating doses 2 hours prior or 4-6 hours after administration of BAS
  - Fasting lipid panel 6 to 8 weeks after initiation or titration

## Other OTC options

- Plant stanols/sterols
  - Adjunct to diet
  - 15 to 20% LDL reduction possible if taken as directed (usually large quantities required)
- Red yeast rice
  - Contains lovastatin
  - Caution warranted: lack of regulatory oversight and quality control

## TG Lowering Agents

## Patient Case 4

- A 50-year-old woman with no significant medical history presents for her annual well woman examination.
- Fasting laboratory results reveal total cholesterol 157, TG 277, HDL 39, LDL 63, non-HDL 118, SCr 0.9, ALT 20 and FBG 99. Her BMI is 30.3.

Work book Page: 2-380 (Answer Page: 2-391)

## Patient Case 4 continued…

Which one of the following is the best recommendation to manage her elevated TG?

- A. Diet, exercise, and weight loss.
- B. Fenofibrate 160 mg/day.
- C. Gemfibrozil 600 mg twice daily.
- D. Pravastatin 80 mg every evening.

Work book Page: 2-380 (Answer Page: 2-391)

## Fibrates

- Mechanism of action – induces lipoprotein-mediated lipolysis and clearance of TG
- Evidence
  - Helsinki Heart Study
    - 34% reduction in cumulative rate of cardiac end points at 5 years in gemfibrozil group
  - VA-HIT trial
    - 24% reduction in combined primary endpoint of cardiac death and nonfatal MI
  - FIELD study
    - No significant difference in coronary event rate

## Fibrates

- FDA Safety Communication: Fenofibrate (Nov 2011)
  - Based on the **A**ction to **C**ontrol **C**ardiovascular **R**isk in **D**iabetes (ACCORD) Lipid trial
  - Evaluated the efficacy and safety of fenofibrate and simvastatin combination therapy versus simvastatin alone in patients with type 2 DM
  - Fenofibric acid may not lower a patient's risk of having a heart attack or stroke
  - The benefits and risks of fenofibric acid should be considered when deciding to prescribe the drug

## Fibrates

- Clinical use
  - Lower LDL 5 to 20% (with normal TG); may raise LDL as lowers TG
  - Lower TG 20 to 50%
  - Raise HDL 10 to 20%
- Contraindications
  - Significant renal (Clcr <15 ml/min; dialysis) or hepatic dysfunction
  - Gallbladder disease
  - Biliary cirrhosis

## Fibrates

- Important adverse drug reactions
  - In general, well tolerated
  - Most common ADR is GI upset
  - More severe, but rarer: LFT elevations, myopathy, increases in SCr
- Monitoring
  - Fasting lipid panel and ALT 6 to 8 weeks after initation or titration; patients should report unusual muscle pain and CPK should be assessed
  - Dose adjust for renal insufficiency

## Patient Case 5

- A 36-year-old man with type 2 DM, gout, and hypertension presents to clinic.
- He is currently taking rosuvastatin 40 mg every evening, fenofibrate 160 mg/day, metformin 1 g 2 times/day, and lisinopril 20 mg/day.
- He "doesn't like to" exercise and won't change his eating habits at this time.
- Fasting laboratory results reveal total cholesterol 157, TG 305, HDL 41, LDL 55, non-HDL 116, SCr 1.2, ALT 45, and A1c 6.9%. His BMI is 34.4.

Work book Page: 2-381 (Answer Page: 2-391)

## Patient Case 5 continued…

Which one of the following is the best recommendation to manage his TG?

A. Change fenofibrate to gemfibrozil 600 mg twice daily.

B. Add omega-3 fatty acids that include at least 1 g of DHA/EPA a day and titrate to effect.

C. Change rosuvastatin to simvastatin 80 mg every evening.

D. No change in therapy is warranted.

Work book Page: 2-381 (Answer Page: 2-391)

## Omega-3 Fatty Acids

- Mechanism of action – inhibits hepatic secretion of TG and promotes metabolism of TG
- Evidence
  - GISSI-Prevenzione trial – significant reduction in risk of sudden death
- Clinical use
  - TG lowering (20 to 30%) – Literature reports 3 to 15 g/day. Can start DHA/EPA 1 g/day to see TG lower
  - Cardioprotection

## Omega-3 Fatty Acids

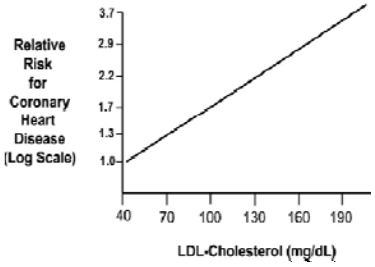
- Important adverse drug reactions
  - Fishy taste/burping; dyspepsia
  - Antiplatelet effects
- Dosing and monitoring
  - OTC (choose concentrated products) and prescription products available
  - Base dose on amount of DHA/EPA available

## Combination Therapy

- Statin plus fibrate: If TG still significantly elevated after lifestyle modification
- Statin plus niacin: After statin dose optimized, and LDL, non-HDL and/or TG remain elevated; HDL low
- Statin plus ezetimibe: Additional LDL and/or non-HDL lowering after statin dose optimized
- Others: Consider ezetimibe plus niacin if patient is intolerant of statin therapy.

## LDL Goals

## CVD Risk to LDL Level




- CVD remains the #1 cause of death in both men and women in the United States
- For every 1% reduction in LDL levels, relative risk of major CVD event is reduced by about 1%.

## Lipid Goals: Primary vs. Secondary

- Primary prevention
  - Goal <160 mg/dL
  - Goal <130 mg/dL
  - Goal <100 mg/dL
- Secondary prevention
  - Goal <100 mg/dL
  - Goal <70 mg/dL

## Primary Prevention

- Major risk factors
  - Cigarette smoking
  - Hypertension (blood pressure 140/90 mm Hg or higher or on antihypertensive agent)
  - Low HDL cholesterol (less than 40 mg/dL) – HDL cholesterol 60 mg/dL or greater counts as a "negative" risk factor; its presence removes one risk factor from the total count
  - Family history of premature CHD (CHD in male first-degree relative younger than 55 years; CHD in female first-degree relative younger than 65 years)
  - Age (men 45 years and older; women 55 years and older)

## Primary Prevention

- Less than two risk factors
  - LDL goal less than 160 mg/dL
- Two or more risk factors (Framingham risk score of 10%–20% risk of CHD within the next 10 years)
  - LDL goal less than 130 mg/dL
- CHD risk equivalents
  - LDL goal less than 100 mg/dL

## Primary Prevention

- CHD Risk Equivalents
  - Other clinical forms of atherosclerotic disease
    - Peripheral arterial disease
    - Abdominal aortic aneurysm
    - Carotid artery disease (transient ischemic attacks or stroke of carotid origin or more than 50% obstruction of a carotid artery)
  - Diabetes
  - Several risk factors that confer a Framingham risk score of greater than 20% risk of CHD within the next 10 years

## Secondary prevention (established CHD)

- LDL goal less than 100 unless
- LDL goal less than 70 (the presence of established CHD plus)
  - Several major risk factors (especially diabetes)
  - Severe and poorly controlled risk factors (especially continued cigarette smoking)
  - Many risk factors of the metabolic syndrome (especially high TG greater than 200 mg/dL plus non–HDL-C greater than 130 mg/dL with low HDL-C less than 40 mg/dL)
  - Patients with acute coronary syndromes

## LDL-C Goals and Cut Points for TLC and Drug Therapy

| Risk Category | LDL Goal | Initiate TLC | Consider Drug Therapy |
|---|---|---|---|
| High risk: CHD or CHD risk equivalents | < 100 mg/dL (optional goal: < 70 mg/dL) | ≥ 100 mg/dL | ≥ 100 mg/dL (< 100 mg/dL: consider drug options) |
| Moderately high risk: 2+ risk factors | < 130 mg/dL | ≥ 130 mg/dL | ≥ 130 mg/dL (100–129 mg/dL; consider drug options) |
| Moderate risk: 2+ risk factors | < 130 mg/dL | ≥ 130 mg/dL | ≥ 160 mg/dL |
| Lower risk: 0–1 risk factor | < 160 mg/dL | ≥ 160 mg/dL | ≥ 190 mg/dL (160–189 mg/dL: LDL-lowering drug optional) |

## Case Situations

## Patient Case 6

- A 62-year-old woman with a history of three-vessel CABG 2 years earlier and diabetes completes her fasting laboratory work.
- Medications include simvastatin 80 mg/day, glipizide 5 mg BID, metoprolol sustained release (SR) 25 mg/day, and ASA 81 mg/day.
- During the past year, she has seen a steady decline in her renal function.
- Laboratory results reveal total cholesterol 143, TG 160, HDL 42, LDL 63, non-HDL 101, SCr 2.3, CrCl (IBW) 21.9 mL/minute, ALT 45, Na 144, K 4.9, and A1c 7.5%. She weighs 180 lb and is 5'4" tall.

Work book Page: 2-384 (Answer Page: 2-391)

## Patient Case 6 continued…

Which one of the following is the best recommendation for this patient?

- A. Add omega-3 fatty acids, with at least 1 g/day of EPA/DHA.
- B. Add fenofibrate 160 mg/day.
- C. Continue therapy because her LDL is at goal.
- D. Change simvastatin to atorvastatin 40 mg/day because of her kidney function.

Work book Page: 2-384 (Answer Page: 2-391)

## Chronic Renal Insufficiency

- Dose modifications
  - Estimated CrCl less than 30 mL/minute
    - Lovastatin 10–40 mg/day
    - Simvastatin 10–40 mg/day
    - **Atorvastatin 10–80 mg/day**
    - Rosuvastatin 5–20 mg/day
    - **Pravastatin 10–80 mg/day**
    - Pitavastatin – Not recommended
    - Fluvastatin – No dosage adjustment necessary

## Chronic Renal Insufficiency (cont)

- Dose modifications (cont)
  - Estimated CrCl 30–60 mL/minute: Pitavastatin 1–2 mg/day
  - Estimated CrCl less than 50 mL/minute – Start lower dose fenofibrate (54 mg/day) and gemfibrozil (300 mg twice daily) and titrate as needed.
  - No dose adjustment needed for people on dialysis, except for pitavastatin (1–2 mg/day) and fenofibrate (avoid).

## Patient Case 7

- A 52-year-old man with a history of atrial fibrillation and hypothyroidism presents to the clinic. His cardiologist placed him on long-term amiodarone .
- Medications include simvastatin 40 mg/day, levothyroxine 137 mcg/day, warfarin as directed, and metoprolol SR 50 mg/day.
- His LDL goal has been set at less than 100 by his cardiologist.
- Laboratory results reveal total cholesterol 131, TG 100, HDL 32, LDL 79, non-HDL 99, SCr 1.8, CrCl 37 mL/minute, ALT 52, and TSH 4.32.

Work book Page: 2-388 (Answer Page: 2-396)

## Patient Case 7 continued…

Which one of the following is the best recommendation for this patient?

A. Discontinue simvastatin because it cannot be used concomitantly with amiodarone.

B. Increase simvastatin to 80 mg every evening because the patient's LDL will go up once amiodarone therapy is started.

C. Lower simvastatin to 20 mg every evening to reduce the risk of a drug-drug interaction.

D. Add niacin 500 mg twice daily to increase his HDL.

Work book Page: 2-384 (Answer Page: 2-391)

## Statin Drug Interactions

- Most statins are metabolized primarily by CYP3A4, which results in most interactions
- Alternate metabolism
  - Pravastatin – sulfation
  - Rosuvastatin – CYP2C9

## Interactions: Statins + Lipid Meds

- Gemfibrozil – Avoid using with statins because of the risk of rhabdomyolysis.
- Fenofibrate – Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.
- Niacin – Consider checking CPK after initiating or titrating combination therapy.

## Drug Interactions with Statins

- Cyclosporine
  - Preferred agents: Pravastatin or rosuvastatin (limit to 5 mg/day)
  - Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.
- HIV protease inhibitors
  - Contraindicated with: Simvastatin and lovastatin
  - Preferred agents: Pravastatin, pitavastatin or rosuvastatin (limit to 10 mg/day)
  - Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.

## Drug Interactions with Statins

- HCV protease inhibitors (boceprevir and telaprevir)
  - Contraindicated with: Simvastatin and lovastatin
  - Preferred agents: Pravastatin, pitavastatin or rosuvastatin
  - Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.
- Amiodarone
  - Limit statin doses
    - Lovastatin 40 mg/day; simvastatin 20 mg/day
  - OR convert to pravastatin or rosuvastatin.
  - Recommend waiting 3 months for complete drug metabolism before resuming high-dose statins.
  - If unusual muscle pain or weakness reported, assess CPK

## Drug Interactions with Statins

- Azole antifungals and macrolide antibiotics (except azithromycin)
  - Discontinue statin therapy for the duration of antifungal/antibiotic therapy OR
  - Convert to pravastatin or rosuvastatin
- Nefazodone
  - Preferred agents: Pravastatin or rosuvastatin
  - Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.

## NonDHP CCB + Statin Interaction

- Diltiazem
  - Limit statin doses.
    - Lovastatin 20 mg/day
    - Simvastatin 10 mg/day
- Verapamil
  - Limit statin doses.
    - Lovastatin 20 mg/day
    - Simvastatin 10 mg/day

- OR convert to pravastatin or rosuvastatin.
- Patients should report unusual muscle pain or weakness immediately, and CPK level should be assessed.

## Patient Case 8

- A 76-year-old man with a history of CAD and diabetes presents to clinic.
- For the past 2 months, he has been treated for a diabetic foot ulcer. He also recently physically exerted himself. He has been feeling achy recently.
- Lipid medications include atorvastatin 80 mg/day, niacin 500 mg twice daily, fish oil supplement 1000 mg/day
- Laboratory results reveal total cholesterol 148, TG 146, HDL 37, LDL 82 non-HDL 111, CPK 1064, SCr 1.7, CrCl 37 mL/minute, ALT 36.

Work book Page: 2-386 (Answer Page: 2-391)

## Patient Case 8 continued…

Which one of the following strategies is best to address his laboratory work?

- [ ] A. Discontinue atorvastatin because of his elevated CPK. The patient will be unable to take statin therapy in the future.
- [ ] B. Hold atorvastatin because of his elevated CPK and monitor his CPK.
- [ ] C. Continue therapy because the elevated CPK is likely caused by his diabetic foot ulcer and recent strenuous activity.
- [ ] D. Change his therapy to ezetimibe/simvastatin 10/80 mg/day because his LDL is not at goal.

Work book Page: 2-386 (Answer Page: 2-391)

## Disease States That Can Affect Lipids

- Diabetes – Elevated TG
- Hypothyroidism – Elevated TG
- Alcoholism – Elevated TG
- Recent cardiac event – Falsely lowers lipids up to 12 weeks after event

## Pharmacy Practice

- Community-based interventions
  - Medication adherence
  - Medication and lifestyle counseling
  - Treatment recommendations to providers
  - Point-of-care testing: Screening and follow-up. Most devices use fingerstick blood samples and can produce a full lipid panel in 3–5 minutes.

## Pharmacy Practice

- Primary care interventions (in clinic or telephonic)
  - Patient interview
  - Drug and lifestyle counseling
  - Treatment recommendations to providers
  - Implement therapy changes on the basis of collaborative practice agreements (see KPCO example)
  - Screening and follow-up

## Conclusion

- For every 1% reduction in LDL levels, relative risk of major CVD event is reduced by about 1%.
- Statins are first-line dyslipidemia therapy for primary and secondary prevention patients. Niacin represents an evidence based option for further optimization of lipids if needed.
- Determine LDL goal based on medical history and presence of risk factors. Lifestyle modifications key to achieving and maintaining goals.
- Recent FDA Safety Communications may change dyslipidemia therapy recommendations
- Pharmacists can play key roles in dyslipidemia management.

American College of Clinical Pharmacy

**Updates in Therapeutics® 2012:**
**Ambulatory Care Pharmacy Preparatory Review and Recertification Course**

**Primary and Secondary Prevention of Coronary Heart Disease Events**

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## Conflicts of Interest

- None

## Agenda

- Primary Prevention of Coronary Heart Disease
  - 2009 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Primary Prevention Performance Measures
  - Global Risk Assessment
    - 2008 Modified Framingham Risk Score
  - 2012 ACCP Chest Guidelines for Primary Prevention of CHD with aspirin
  - 2009 U.S. Preventive Services Task Force Guidelines on Aspirin for Prevention of Cardiovascular Disease (CVD)
  - American Diabetes Association (ADA) Recommendations for Patients with Diabetes Mellitus
    - Aspirin
    - Statins

## Agenda (Continued)

- Secondary Prevention of Coronary Heart Disease
  - Cardiac rehabilitation referral
  - Statins
    - LDL cholesterol Goal
    - Myopathy
      - Avoidance of drug-drug interactions
  - ACE inhibitors, ARBs and Aldactone
- Aspirin and P2Y12 Inhibitors
- Dosing and Duration Following Percutaneous Coronary Intervention (PCI) Stent Placement (2011 ACCF/AHA/SCAI PCI Guidelines)
  - Periprocedural Management (2011 ACCF/AHA/SCAI PCI Guidelines and 2012 ACCP Chest Guidelines)
- Patient Advocacy

## 2009 ACCF/AHA Primary Prevention Performance Measures

- **Global Risk Assessment**
  - Estimation of a patient's absolute risk of developing CHD using a multivariate risk score
- **Lifestyle and Risk Factor Screening**
  - Assessment of a patients lifestyle and physical activity risk factors for developing CHD
- **Dietary Intake Counseling**
  - Counseling to eat a health diet
- **Physical Activity Counseling**
  - Counseling to engage in regular physical activity
- **Smoking and Tobacco use Screening**
  - Risk assessment for current smoking and tobacco use behaviors
- **Smoking Cessation Counseling**
  - Cessation intervention for active smoking

Page 2-397 Table 1

## 2009 ACCF/AHA Primary Prevention Performance Measures (Continued)

- **Weight Assessment**
  - Measurement of weight and body mass index and/or waist circumference
- **Weight Management**
  - Counseling to achieve and maintain ideal body weight
- **Blood Pressure Measurement**
  - Measurement of blood pressure
- **Blood Pressure Control**
  - Effective blood pressure control or combination drug therapy
- **Lipid Profile Measurement**
  - Fasting lipid profile performed
- **Lipid Lowering Therapy and Control**
  - Low-density lipoprotein (LDL) cholesterol at target or prescribed
- **Aspirin Use**
  - Aspirin use in patients without clinical evidence of atherosclerotic disease but at high risk of events

Page 2-397 Table 1

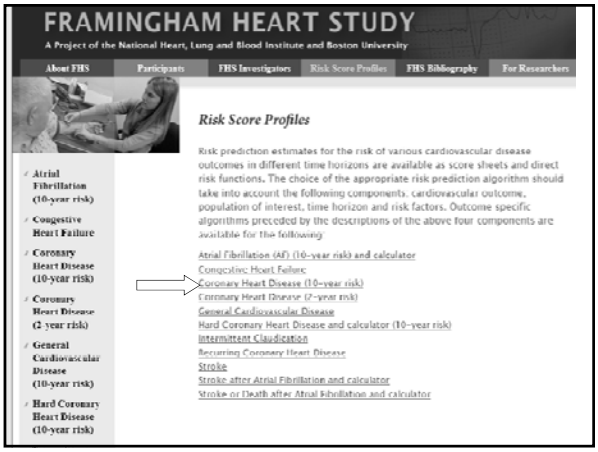
## Global Risk Assessment

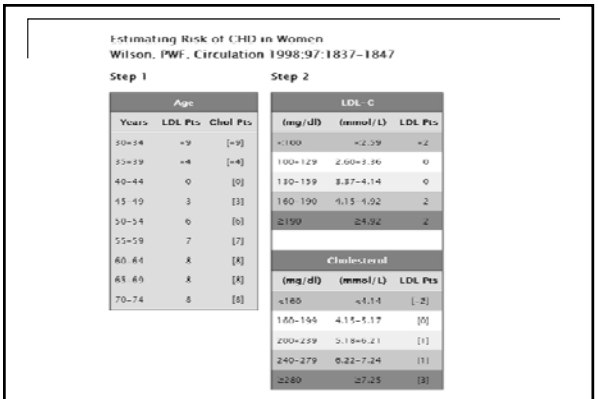
- Assess at least once every 5 years
  - All men age 35 to 80 years and all women age 45 to 80 years with at least one of the following risk factors for CHD
    - DM
    - Cigarette smoking
    - HTN
    - Elevated total or LDL cholesterol
    - Low HDL cholesterol
    - Family history of premature CHD
  - No studies that document superior patient outcomes with a formal risk assessment score versus comprehensive risk factor assessment
  - Lack of consensus about which score to use

## 2008 Update of the Framingham Risk Score

- General Cardiovascular Disease 10-year Risk
  - Age
  - DM
  - Smoking
  - Joint National Committee V BP categories
  - NCEP ATP III LDL cholesterol or total cholesterol categories
- Available from: http://www.framinghamheartstudy.org/risk/index.html

Page 2-398 to Page 2-403 Tables 2 and 3





Estimating Risk of CHD in Women
Wilson, PWF. Circulation 1998;97:1837–1847

Step 1

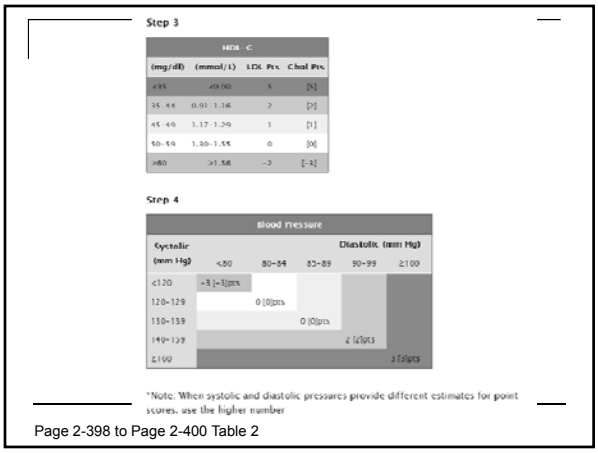
| Age | | |
|---|---|---|
| Years | LDL Pts | Chol Pts |
| 30–34 | –9 | [–9] |
| 35–39 | –4 | [–4] |
| 40–44 | 0 | [0] |
| 45–49 | 3 | [3] |
| 50–54 | 6 | [6] |
| 55–59 | 7 | [7] |
| 60–64 | 8 | [8] |
| 65–69 | 8 | [8] |
| 70–74 | 8 | [8] |

Step 2

| LDL-C | | |
|---|---|---|
| (mg/dl) | (mmol/L) | LDL Pts |
| <100 | <2.59 | –2 |
| 100–129 | 2.60–3.36 | 0 |
| 130–159 | 3.37–4.14 | 0 |
| 160–190 | 4.15–4.92 | 2 |
| ≥190 | ≥4.92 | 2 |

| Cholesterol | | |
|---|---|---|
| (mg/dl) | (mmol/L) | LDL Pts |
| <160 | <4.14 | [–2] |
| 160–199 | 4.15–5.17 | [0] |
| 200–239 | 5.18–6.21 | [1] |
| 240–279 | 6.22–7.24 | [1] |
| ≥280 | ≥7.25 | [3] |

Page 2-398 to Page 2-400 Table 2


Step 3

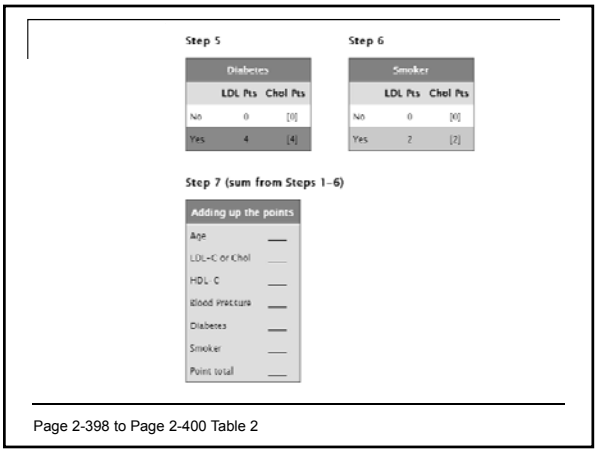
| HDL-C | | | |
|---|---|---|---|
| (mg/dl) | (mmol/L) | LDL Pts | Chol Pts |
| <35 | <0.90 | 5 | [5] |
| 35–44 | 0.91–1.16 | 2 | [2] |
| 45–49 | 1.17–1.29 | 1 | [1] |
| 50–59 | 1.30–1.55 | 0 | [0] |
| ≥60 | ≥1.56 | –3 | [–3] |

Step 4

| Blood Pressure | | | | | |
|---|---|---|---|---|---|
| Systolic (mm Hg) | Diastolic (mm Hg) | | | | |
| | <80 | 80–84 | 85–89 | 90–99 | ≥100 |
| <120 | –3 [–3]pts | | | | |
| 120–129 | | 0 [0]pts | | | |
| 130–139 | | | 0 [0]pts | | |
| 140–159 | | | | 2 [2]pts | |
| ≥160 | | | | | 3 [3]pts |

*Note: When systolic and diastolic pressures provide different estimates for point scores, use the higher number

Page 2-398 to Page 2-400 Table 2


Step 5

| Diabetes | | |
|---|---|---|
| | LDL Pts | Chol Pts |
| No | 0 | [0] |
| Yes | 4 | [4] |

Step 6

| Smoker | | |
|---|---|---|
| | LDL Pts | Chol Pts |
| No | 0 | [0] |
| Yes | 2 | [2] |

Step 7 (sum from Steps 1–6)

| Adding up the points | |
|---|---|
| Age | ___ |
| LDL-C or Chol | ___ |
| HDL-C | ___ |
| Blood Pressure | ___ |
| Diabetes | ___ |
| Smoker | ___ |
| Point total | ___ |

Page 2-398 to Page 2-400 Table 2

Step 8 (determine CHD risk from point total)

| CHD Risk | | | |
|---|---|---|---|
| LDL Pts Total | 10 Yr CHD Risk | Chol Pts Total | 10 Yr CHD Risk |
| ≤-2 | 1% | ≤21 | [1%] |
| -1 | 2% | [22-24] | [2%] |
| 0 | 2% | [25] | [2%] |
| 1 | 2% | [1] | [2%] |
| 2 | 3% | [2] | [3%] |
| 3 | 3% | [3] | [3%] |
| 4 | 4% | [4] | [4%] |
| 5 | 5% | [5] | [4%] |
| 6 | 6% | [6] | [5%] |
| 7 | 7% | [7] | [6%] |
| 8 | 8% | [8] | [7%] |
| 9 | 9% | [9] | [8%] |
| 10 | 11% | [10] | [10%] |
| 11 | 13% | [11] | [11%] |
| 12 | 15% | [12] | [13%] |
| 13 | 17% | [13] | [15%] |
| 14 | 20% | [14] | [18%] |
| 15 | 24% | [15] | [20%] |
| 16 | 27% | [16] | [24%] |
| ≥17 | ≥32% | [≥17] | [≥27%] |

Page 2-398 to Page 2-400 Table 2

Estimating Risk of CHD in Men
Wilson, PWF. Circulation 1998;97:1837–1847

Step 1

| Age | | |
|---|---|---|
| Years | LDL Pts | Chol Pts |
| 30–34 | -1 | [-1] |
| 35–39 | 0 | [0] |
| 40–44 | 1 | [1] |
| 45–49 | 2 | [2] |
| 50–54 | 3 | [3] |
| 55–59 | 4 | [4] |
| 60–64 | 5 | [5] |
| 65–69 | 6 | [6] |
| 70–74 | 7 | [7] |

Step 2

| LDL-C | | |
|---|---|---|
| (mg/dl) | (mmol/L) | LDL Pts |
| <100 | <2.59 | -3 |
| 100–129 | 2.60–3.36 | 0 |
| 130–159 | 3.37–4.14 | 0 |
| 160–190 | 4.15–4.92 | 1 |
| ≥190 | ≥4.92 | 2 |

| Cholesterol | | |
|---|---|---|
| (mg/dl) | (mmol/L) | Chol Pts |
| <160 | <4.14 | [-3] |
| 160–199 | 4.15–5.17 | [0] |
| 200–239 | 5.18–6.21 | [1] |
| 240–279 | 6.22–7.24 | [2] |
| ≥280 | ≥7.25 | [3] |

Page 2-401 to Page 2-403 Table 3

Step 3

| HDL-C | | | |
|---|---|---|---|
| (mg/dl) | (mmol/L) | LDL Pts | Chol Pts |
| <35 | <0.90 | 2 | [2] |
| 35–44 | 0.91–1.16 | 1 | [1] |
| 45–49 | 1.17–1.29 | 0 | [0] |
| 50–59 | 1.30–1.55 | 0 | [0] |
| 200 | ≥1.56 | -1 | [-2] |

Step 4

| Blood Pressure | | | | | |
|---|---|---|---|---|---|
| Systolic (mm Hg) | Diastolic (mm Hg) | | | | |
| | <80 | 80–84 | 85–89 | 90–99 | ≥100 |
| <120 | 0 [0]pts | | | | |
| 120–129 | | 0 [0]pts | | | |
| 130–139 | | | 1 [1]pts | | |
| 140–159 | | | | 2 [2]pts | |
| ≥160 | | | | | 3 [3]pts |

*Note: When systolic and diastolic pressures provide different estimates for point scores, use the higher number

Page 2-401 to Page 2-401 Table 3

Step 5

| Diabetes | | |
|---|---|---|
| | LDL Pts | Chol Pts |
| No | 0 | [0] |
| Yes | 2 | [2] |

Step 6

| Smoker | | |
|---|---|---|
| | LDL Pts | Chol Pts |
| No | 0 | [0] |
| Yes | 2 | [2] |

Step 7 (sum from Steps 1–6)

| Adding up the points | |
|---|---|
| Age | ____ |
| LDL-C or Chol | ____ |
| HDL-C | ____ |
| Blood Pressure | ____ |
| Diabetes | ____ |
| Smoker | ____ |
| Point total | ____ |

Page 2-401 to Page 2-403 Table 3

Step 8 (determine CHD risk from point total)

| CHD Risk | | | |
|---|---|---|---|
| LDL Pts Total | 10 Yr CHD Risk | Chol Pts Total | 10 Yr CHD Risk |
| ≤-3 | 1% | | |
| -2 | 2% | | |
| -1 | 2% | [≤-1] | [2%] |
| 0 | 3% | [0] | [3%] |
| 1 | 4% | [1] | [3%] |
| 2 | 4% | [2] | [4%] |
| 3 | 6% | [3] | [5%] |
| 4 | 7% | [4] | [7%] |
| 5 | 9% | [5] | [8%] |
| 6 | 11% | [6] | [10%] |
| 7 | 14% | [7] | [13%] |
| 8 | 18% | [8] | [16%] |
| 9 | 23% | [9] | [20%] |
| 10 | 27% | [10] | [25%] |
| 11 | 33% | [11] | [31%] |
| 12 | 40% | [12] | [37%] |
| 13 | 47% | [13] | [45%] |
| ≥14 | ≥50% | [≥14] | [≥53%] |

Page 2-401 to Page 2-403 Table 3

# Patient Case Question 1

- 1. A 56-year-old man with a medical history of HTN for 5 years, type 2 DM for 4 years, and dyslipidemia for 8 years presents to his primary care physician for an annual physical examination. He is a nonsmoker. His current medications include losartan 50 mg orally once daily and metformin 500 mg orally twice daily. His BP is 138/89 mm Hg and HR is 78 beats/minute. Results of today's fasting laboratory tests are as follows: SCr 0.80 mg/dL, total cholesterol 240 mg/dL, LDL cholesterol 158 mg/dL, HDL cholesterol 42 mg/dL, triglycerides 110 mg/dL, and fasting blood glucose 108 mg/dL.
- Using the Framingham risk score global risk assessment, which one of the following is the estimated risk of 10-year CHD events for this patient (using LDL points)?

A. 8%
B. 14%
C. 18%
D. 20%

Case Page 2-398. Answer Page: 2-428.

## 2012 ACCP Chest Guidelines ASA Primary Prevention

- Low-dose aspirin for persons age > 50 years

| Risk Group (10-year CHD Risk) | MIs Prevented per 1000 Patients Treated | Strokes Prevented per 1000 Patients Treated | Total Mortality Reduction per 1000 patients Treated | Major Bleeds per 1000 Patients Treated |
|---|---|---|---|---|
| Lower risk (5%) | 6 | | | 4 |
| Moderate risk (15%) | 19 | | | 16 |
| High risk (25%) | 31 | | 6 | 22 |

Page 2-405 Table 4

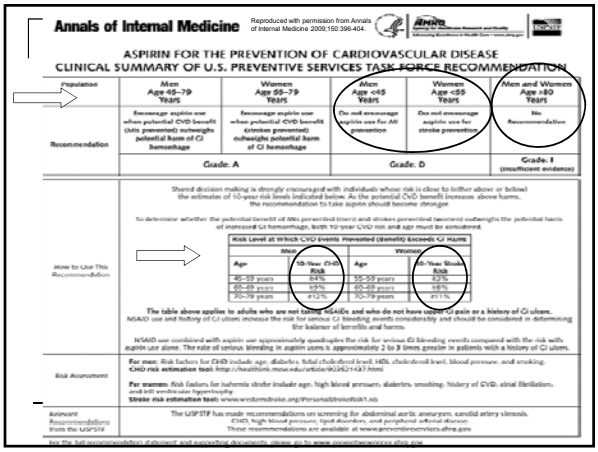
Vandvik PO, et al. Chest 2012;141:e637S–e668S.

## 2009 U.S. Preventive Services Task Force Aspirin Recommendation Statement

- **The USPSTF recommends the use of aspirin for men age 45 to 79 years when the potential benefit due to a reduction in myocardial infarctions outweighs the potential harm due to an increase in gastrointestinal hemorrhage.**
  Grade: A recommendation
- **The USPSTF recommends the use of aspirin for women age 55 to 79 years when the potential benefit of a reduction in ischemic strokes outweighs the potential harm of an increase in gastrointestinal hemorrhage.**
  Grade: A recommendation
- **The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of aspirin for cardiovascular disease prevention in men and women 80 years or older.**
  Grade: I statement
- **The USPSTF recommends against the use of aspirin for stroke prevention in women younger than 55 years and for myocardial infarction prevention in men younger than 45 years.**
  Grade: D recommendation

Page 2-406 to 2-407. Tables 5 and 6

Ann Intern Med 2009;150:396-404



Annals of Internal Medicine

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ASPIRIN FOR THE PREVENTION OF CARDIOVASCULAR DISEASE
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

| Population | Men Age 45–79 Years | Women Age 55–79 Years | Men Age <45 Years | Women Age <55 Years | Men and Women Age ≥80 Years |
|---|---|---|---|---|---|
| Recommendation | Encourage aspirin use when potential CVD benefit (MIs prevented) outweighs potential harm of GI hemorrhage | Encourage aspirin use when potential CVD benefit (strokes prevented) outweighs potential harm of GI hemorrhage | Do not encourage aspirin use for MI prevention | Do not encourage aspirin use for stroke prevention | No Recommendation |
| | Grade: A | | Grade: D | | Grade: I (insufficient evidence) |

Shared decision making is strongly encouraged with individuals whose risk is close to (either above or below) the estimates of 10-year risk levels indicated below. As the potential CVD benefit increases above harms, the recommendation to take aspirin should become stronger.

To determine whether the potential benefit of MIs prevented (men) and strokes prevented (women) outweighs the potential harm of increased GI hemorrhage, both 10-year CVD risk and age must be considered.

Risk Level at Which CVD Events Prevented (Benefit) Exceeds GI Harms

| Men | | Women | |
|---|---|---|---|
| Age | 10-Year CVD Risk | Age | 10-Year Stroke Risk |
| 45–59 years | ≥4% | 55–59 years | ≥3% |
| 60–69 years | ≥3% | 60–69 years | ≥4% |
| 70–79 years | ≥12% | 70–79 years | ≥11% |

The table above applies to adults who are not taking NSAIDs and who do not have upper GI pain or a history of GI ulcers.
NSAID use and history of GI ulcers increase the risk for serious GI bleeding events considerably and should be considered in determining the balance of benefits and harms.

NSAID use combined with aspirin use approximately quadruples the risk for serious GI bleeding events compared with the risk with aspirin use alone. The rate of serious bleeding in aspirin users is approximately 2 to 3 times greater in patients with a history of GI ulcers.

How to Use This Recommendation

Risk Assessment

For men: Risk factors for CHD include age, diabetes, total cholesterol level, HDL cholesterol level, blood pressure, and smoking.
CHD risk estimation tool: http://healthimi.mcw.edu/article/#G2421=147.html

For women: Risk factors for ischemic stroke include age, high blood pressure, diabetes, smoking, history of CVD, atrial fibrillation, and left ventricular hypertrophy.
Stroke risk estimation tool: www.westernstroke.org/PersonalStrokeRisk1.xls

Relevant Recommendations from the USPSTF

The USPSTF has made recommendations on screening for abdominal aortic aneurysm, carotid artery stenosis, CHD, high blood pressure, lipid disorders, and peripheral arterial disease.
These recommendations are available at www.preventiveservices.ahrq.gov

For the full recommendation statement and supporting documents, please go to www.preventiveservices.ahrq.gov

## Patient Case Question 2

2. A 60-year-old male smoker with no significant medical history presents to the Wellness Clinic at your hospital for BP, diabetes, and cholesterol screening. You perform the fasting screening tests, which show BP 114/75 mm Hg, LDL cholesterol 90 mg/dL, HDL cholesterol 60 mg/dL, triglycerides 80 mg/dL, and blood glucose 80 mg/dL. He asks you whether he should take a baby aspirin daily for prevention of CVD. Based on current practice guidelines, which one of the following is the best response to his question?

A. Yes, a daily aspirin will help prevent stroke.
B. Yes, a daily aspirin will help prevent heart attack.
C. No, the risk of intracranial bleeding is higher than her risk of heart attack.
D. No, the risk of gastrointestinal bleeding is higher than her risk of stroke.

Case Page 2-403. Answer Page: 2-428.

## Aspirin for Primary Prevention in Patients with Diabetes Mellitus

- 2012 ADA Standards of Medical Care
  - Estimate CVD risk
  - Aspirin 75 mg to 162 mg daily indicated if > 10% 10-year CVD risk
- 2012 ADA/ACCF/AHA Consensus Statement
  - Estimate CVD risk (various tools suggested)
  - Aspirin 75 mg to 162 mg daily indicated if > 10% 10-year CVD risk

## Aspirin for Primary Prevention in Patients with Diabetes Mellitus

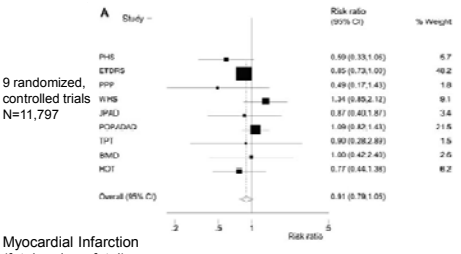
- 2012 ADA Standards of Medical Care
  - If no risk assessment
    - Men > 50 years who have at least one other risk factor for CHD
    - Women > 60 years who have at least one other risk factor for CHD
    - Risk factors for CHD
      - Family history of CVD
      - HTN
      - Smoking
      - Dyslipidemia, either
      - Low HDL cholesterol
      - Elevated LDL cholesterol
      - Elevated triglycerides
      - Albuminuria defined as ≥ 30 mg/24 hrs

## ADA/ACCF/AHA Consensus Statement on Aspirin for Primary Prevention in Patients with Diabetes Mellitus

- Aspirin resistance is higher in patients with DM but data on recommending a higher dose to overcome effects and reduce outcomes is lacking.
- Various risk assessment tools suggested

1. UKPDS Risk Engine: http://www.dtu.ox.ac.uk/riskengine/index.php
2. ARIC CHD Risk Calculator: http://www.aricnews.net/riskcalc/html/RCI.html
3. American Diabetes Association Risk Assessment Tool, Diabetes PHD: http://www.diabetes.org/phd

## Aspirin for Primary Prevention of CHD Events in Patients with DM




9 randomized, controlled trials N=11,797

Myocardial Infarction (fatal and nonfatal)

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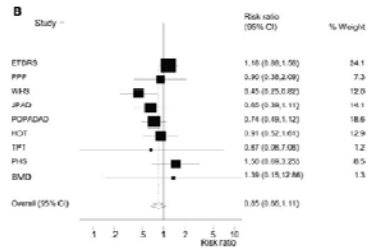
Page 2-408

## Aspirin for Primary Prevention of Stroke in Patients with DM




9 randomized, controlled trials N=11,797

Stroke

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Page 2-408

## Patient Case Questions 3 and 4

- R.R., a 56-year-old woman with a medical history of type 2 DM for 2 years, presents to her primary care physician for an annual physical examination. She is a nonsmoker and has no known drug allergies. Her current medications include metformin 500 mg orally twice daily. Her BP is 158/89 mm Hg, and her HR is 80 beats/minute, values similar to the office results obtained 6 months ago. Results of last week's fasting laboratory tests are SCr 0.90 mg/dL, LDL cholesterol 120 mg/dL, HDL cholesterol 31 mg/dL, triglycerides 100 mg/dL, hemoglobin A1c (A1c) 7.2%, and fasting blood glucose 180 mg/dL.

Case Page 2-410. Answer Page: 2-428.

## Patient Case Question 3

3. Which of the following is the best recommendation to make regarding aspirin therapy for primary prevention of CHD events in R.R. according to the ADA 2012 guidelines?

A. Aspirin 81 mg/daily orally
B. Aspirin 325 mg/daily orally
C. Aspirin 325 mg BID orally
D. No aspirin

Case Page 2-410. Answer Page: 2-428.

## Patient Case Question 4

4. Which of the following is the best recommendation for additional pharmacotherapy to initiate in R.R. at this time to prevent a CHD event?

A. Enalapril
B. Atenolol
C. Metoprolol and simvastatin
D. Lisinopril and atorvastatin

Case Page 2-410. Answer Page: 2-428.

## Secondary Prevention of Myocardial Infarction

- ACC/AHA 2008 MI Performance Measures
  - Aspirin at hospital discharge
  - β-blocker at hospital discharge
  - Statin at hospital discharge
    - For patients with LDL ≥ 100 mg/dL
  - ACE inhibitor or ARB for patients with LVEF < 40%
  - Smoking cessation counseling
  - Cardiac Rehab referral

Page 2-411 Table 7

## Secondary Prevention of Myocardial Infarction

- Statin
  - Optional LDL cholesterol goal < 70 mg/dL
  - "Regardless" of baseline LDL cholesterol
  - Select initial dose to achieve a 30% to 40% LDL-lowering
- Antiplatelets
- ACE inhibitor or ARB ± Aldactone
- Beta-blocker

## Cardiac Rehab

- 2010 AACVPR/ACCF/AHA Performance Measures for Cardiac Rehabilitation and Secondary Prevention Services
  - All patients hospitalized for myocardial infarction, PCI or cardiac surgery should be referred prior to discharge
  - All outpatients who did not participate in a program within the past 12 months following hospitalization should be referred.

## Core Components of Cardiac Rehab

- Patient assessment
- Nutritional counseling
- Lipid management
- Blood pressure management
- Smoking cessation
- Weight management
- Diabetes management
- Psychosocial management
- Physical activity counseling
- Exercise training

Page 2-410

## Aspirin Dose and Duration for Patients with ACS *NOT* Undergoing PCI

**Table 8**

| ACS | Initial Dose | Subsequent Doses Starting Day 2 and Duration of Therapy |
|---|---|---|
| **NSTE ACS Medical Management** | 162 to 325 mg nonenteric coated formulation either oral or chewed | 75 to 100 mg/day indefinitely |
| **STE MI Medical Management (including fibrinolysis)** | 162 to 325 mg nonenteric coated formulation either oral or chewed | 75 to 100 mg/day indefinitely |

**2002 UA/NSTEMI and 2004 STEMI ACCF/AHA Guideline Recommendations**

Page 2-411 Table 8

## Clopidogrel Dose and Duration for Patients with ACS *NOT* Undergoing PCI

**Table 9**

| ACS | Initial Dose | Subsequent Doses Starting Day 2 and Duration of Therapy (Class Recommendation) |
|---|---|---|
| **NSTE ACS Medical Management** | Clopidogrel 300 mg | Clopidogrel 75 mg daily for at least 1 month and ideally up to 1 year (in patients who are not at high risk of bleeding) |
| **STE MI Medical Management (including fibrinolysis)** | For patients age > 75 years: Clopidogrel 75 mg For patients age ≤ 75 years: Clopidogrel 75 mg or 300 mg | Clopidogrel 75 mg daily Days 2 to 14 |

Page 2-412 Table 9

**2007 UA/NSTE MI and STE MI ACCF/AHA Guideline Recommendations**

## Aspirin Dose and Duration for Patients with ACS Following PCI

**Table 11**

| NSTE ACS and STE MI | Initial Dose | Subsequent Doses Starting Day 2 and Duration of Therapy |
|---|---|---|
| **Bare Metal Stent** | 325 mg nonenteric coated aspirin orally prior to PCI (81 to 325 mg if already on aspirin) | 81 mg/day orally indefinitely* |
| **Drug Eluting Stent** | 325 mg nonenteric coated aspirin orally prior to PCI (81 to 325 mg if already on aspirin) | 81 mg/day orally indefinitely* |

*Class IIa recommendation

Page 2-420 Table 11 ACCF/AHA/SCAI 2011 PCI Guidelines

## P12Y12 Inhibitor Dose and Following PCI

**Table 12. STEMI Primary PCI, UA/NSTEMI PCI**

| Initial Dose | Subsequent Doses Starting Day 2 and Duration of Therapy |
|---|---|
| Clopidogrel 600 mg orally | ACS: Clopidogrel 75 mg orally daily for at least 12 months *<br>BMS Non-ACS: Clopidogrel 75 mg orally daily for at least 1 month and ideally 12 months if patient not at high risk of bleeding; if increased risk of bleeding then minimum 2 weeks<br>DES Non-ACS: Clopidogrel 75 mg orally daily for at least 12 months if patient non at high risk of bleeding |
| Prasugrel 60 mg orally | ACS: Prasugrel 10 mg daily orally for at least 12 months* |
| Ticagrelor 180 mg orally | ACS: Ticagrelor 90 mg BID orally for at least 12 months* |

* If morbidity of bleeding exceeds benefit, then earlier (< 12 months) discontinuation is reasonable (Class IIa recommendation)

Page 2-421 Table 12 ACCF/AHA/SCAI 2011 PCI Guidelines; All Class I recommendations

## Aspirin

- Low-dose aspirin
  - 2-3% GI bleeding in first year
  - Lower frequency of GI bleeding with low-dose aspirin
  - No difference in death, MI or stroke in CURRENT OASIS 7 trial

Page 2-412

## P2Y12 Inhibitors

- P2Y12 Inhibitors
  - Rash
  - Diarrhea
  - Others ticagrelor: dyspnea, bradycardia, heart block
  - Bleeding considerations (in first year)
    - REACH bleeding risk score
    - Clopidogrel adds 1% increased risk of major bleeding versus placebo
    - Prasugrel adds 0.6% increased risk of major bleeding versus clopidogrel (15 months)
    - Ticagrelor adds 0.8% increased risk of non-CABG surgery related major bleeding versus clopidogrel

Page 2-412

## Management of Periprocedural Dual Antiplatelet Therapy For Patients *WITHOUT* Stents

- Continue aspirin for patients undergoing noncardiac or CABG surgery unless low risk of events and then can discontinue
- Discontinue clopidogrel at least 5 days prior to surgery

Pages 2-413 to 2-414 2012 ACCP Chest Guidelines

## Management of Periprocedural Dual Antiplatelet Therapy For Patients *WITH* Stents

- Avoid elective surgery within 4 to 6 weeks following BMS and 12 months following DES placement.
- For urgent surgical procedures, continue aspirin and restart P2Y12 inhibitor therapy as soon as possible postoperatively.

Pages 2-422 to 2- 2011 ACCF/AHA/SCAI PCI Guidelines

## Management of Periprocedural Dual Antiplatelet Therapy For Patients *WITH* Stents

- Aspirin should be continued.
- Elective surgery should be deferred, if possible, for at least 6 weeks after bare metal stent placement and for at least 6 months after drug-eluting stent placement.
- Patients with a bare metal stent who require surgery within 6 weeks of placement should continue clopidogrel/prasugrel.
- Patients with a drug-eluting stent who require surgery within 12 months of placement should continue clopidogrel/prasugrel.
- For surgery more than 6 weeks after a bare metal stent or 6 months after a drug-eluting stent, continue aspirin and discontinue clopidogrel/prasugrel at least 5 days before to surgery.**

** Note product labeling is 5 days for clopidogrel, 5 days for ticagrelor and 7 days for prasugrel

Page 2-423 2012 ACCP Chest Guidelines

## Patient Case Questions 5-7

- J.J., a 66-year-old woman who currently smokes and has a medical history of dyslipidemia for 8 years, presents to the Cardiovascular Risk Reduction Clinic, where you are the pharmacist. She states that she was discharged from the hospital 3 weeks ago after an admission for chest pain. She reports that it was a "near miss" and that she did not have a heart attack. She states that they looked at her coronary arteries and found significant blockages and that she is scheduled for CABG surgery in 2 weeks. Her current medications are aspirin 81 mg orally once daily, ticagrelor 90 mg orally twice daily, atorvastatin 80 mg orally once daily, metoprolol succinate 100 mg 24-hour tablets orally once daily, and lisinopril 40 mg orally once daily.
- She reports that she is concerned about her risk for bleeding with her antiplatelet medications and feels she is taking "too much".

Case Page 2-414. Answer Page: 2-428.

## Patient Case Question 6

6. Which one of the following is the best recommendation to make to J.J. and her cardiologist now regarding her aspirin?

A. Discontinue now in preparation for surgery.
B. Continue current regimen of 81 mg/day.
C. Increase dose to 325 mg/day.
D. Reduce dose to 81 mg every other day.

Case Page 2-414. Answer Page: 2-428.

## Patient Case Question 7

7. Which one of the following is the best recommendation to make to J.J. and her cardiologist now regarding her ticagrelor?

A. Discontinue in 1 week because surgery will increase her bleeding risk.
B. Discontinue 3 days before surgery.
C. Continue current regimen of 90 mg twice daily.
D. Decrease dose to 90 mg once daily.

Case Page 2-414. Answer Page: 2-428.

## Statin Myopathy

- National Lipid Association Definition
  - Myalgia, weakness, cramping
  - Rhabdomyolysis
    - Any elevation in CK with renal dysfunction
- Statin clinical trials often used different definitions of myopathy or rhabdomyolysis
- Occurs in approximately 3% of clinical trial study patients receiving moderate- to high-dose statins
- Community practice reports 10% to 20%
- Common cause of statin discontinuation
- Proposed mechanism
  - Induction of apoptosis in smooth muscle cells via by depleting the isoprenoid farnesyl pyrophosphate which increases cystosolic calcium levels activating capsase-3 and capsase-9

Page 2-442 to 2-443

## Risk Factors for Myopathy with Statins

- Increased statin and statin active metabolite concentrations
  - Statin dose
  - Low BMI
  - Drug-drug interactions
  - Genetic variants affecting statin pharmacokinetics
    - *SLCO1B1* reduced function alleles
- Concomitant fibrate or niacin
- Advanced age
- Uncontrolled hypothyroidism
- Renal impairment
- Alcohol abuse
- Crack cocaine use

Page 2-416

## Key Statin Drug Interaction Examples: Warnings, Precautions, "Do not Exceed"

- Simvastatin – Amiodarone
  - Limit simvastatin doses to 20 mg or less
  - Limit lovastatin doses to 40 mg or less
  - Select pravastatin, rosuvastatin or atorvastatin
- Simvastatin – Amlodipine
  - Limit simvastatin dose to 20 mg
- Cyclosporine
  - Limit rosuvastatin dose to 5 mg
  - Limit atorvastatin dose to 10 mg
  - Limit pravastatin dose to 20 mg or less
  - Contraindicated with pitavastatin, simvastatin and lovastatin

Page 2-416 See statin product labeling for a complete list of drug interactions.

## Key Statin Drug Interaction Examples: Warnings, Precautions, "Do not Exceed"

- Gemfibrozil
  - Contraindicated with simvastatin and lovastatin
  - Limit doses of rosuvastatin to 10 mg
  - Limit atorvastatin dose to 10 mg
  - Select fenofibrate or fenofibrinic acid

Page 2-443 See statin product labeling for a complete list of drug interactions.

## New Statin ADEs

- Cognitive impairment
  - Studies inconclusive
  - Labeling change based on case reports/case series/AERs
  - Reversible memory loss, confusion
  - Withdraw statin for 1 to 3 months
  - Switch to rosuvastatin or pravastatin
  - Not associated with Alzheimer's dementia

http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm. Rojas-Fernandez CH, et al. Ann Pharmacother 2012;46:549-57.

## New Statin ADEs

- Increased blood glucose and $A_{1c}$
- Sattar N, et al. Meta-analysis of 13 statin placebo- and standard care-controlled trials of more than 1 year in duration (N > 90,000)
  - Statin therapy was associated with a 9% increased risk of developing diabetes
    - 1 additional patient developing diabetes for every 3 patients protected from major CV disease
    - Risk was not related to LDL-reduction, baseline cholesterol levels or individual statin
  - Proposed mechanism unclear

http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm. Sattar N, et al. Lancet. 2010 Feb 27;375(9716):735-42.

## Patient Case Question 8

8. A 76-year-old man with a medical history of HTN for 15 years, MI 2 years ago, and chronic stable angina for the past year has the following fasting lipid panel: LDL cholesterol 110 mg/dL, HDL cholesterol 28 mg/dL, and triglycerides 80 mg/dL. Current medications include aspirin 81 mg/day orally, clopidogrel 75 mg/day orally, amlodipine 10 mg/day orally, metoprolol XL 200 mg/day orally, isosorbide dinitrate extended release 60 mg/day orally, lisinopril 40 mg/day orally, and simvastatin 20 mg/day orally for 3 months.

Which one of the following changes in dyslipidemia medications will best help this patient achieve his goal lipid values for secondary prevention of CHD?

A. Increase simvastatin dose to 40 mg daily orally.
B. Increase simvastatin dose to 80 mg daily orally.
C. Change simvastatin to rosuvastatin 40 mg daily orally.
D. Add gemfibrozil 600 mg twice daily orally.

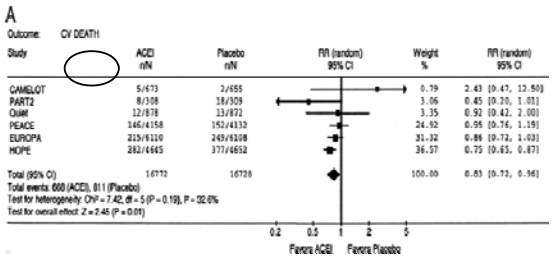
Case Page 2-417. Answer Page: 2-428 to 2-429.

## ACE Inhibitor or ARB ± Aldactone

- ACE Inhibitor
  - Class I indication for patients with LVEF < 40%
    - Performance measure
  - Class IIa indication for all post-MI patients
    - Not a performance measure
- ARB
  - Alternative to ACE inhibitor if not tolerated
    - E.g. cough with ACE inhibitor
    - Performance measure
- Aldactone
  - Eplerenone or spironolactone for patients who present with LVEF < 40% already taking ACE inhibitor (or ARB) plus β-blocker
  - Not a performance measure
  - Monitor for hyperkalemia

Pages 2-417 to 2-418

## ACE Inhibitors For Secondary Prevention of MI in Patients with Preserved Systolic Function




Systematic Review N=33,500

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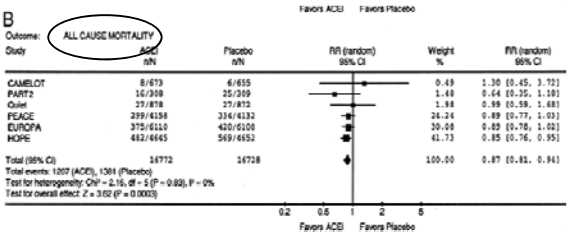
## ACE Inhibitors For Secondary Prevention of MI in Patients with Preserved Systolic Function

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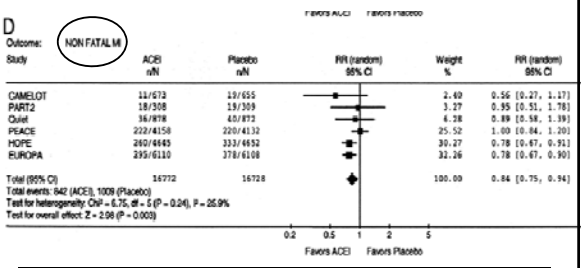
## ACE Inhibitors For Secondary Prevention of MI in Patients with Preserved Systolic Function




Systematic Review N=33,500



Reproduced with permission from Al-Mallah NH, et al. J Am Coll Cardiol 2006;47:1576-83.

## Patient Advocacy: Medication Reconciliation Pearls

- At each visit, assess compliance with performance measures.
- Document any medication allergies and intolerances for indicated but not prescribed medications.
- Avoid duplicate prescriptions
  - Patient taking ACE inhibitor or ARB or two ACE inhibitors
  - Patient taking two statins
- Reassess whether preferred alternatives can be tried. Examples:
  - High-dose statin monotherapy (other than simvastatin) rather than low-dose statin plus ezetimibe if no history of statin intolerance
  - Ticagrelor if clopidogrel allergy and low bleeding risk
  - ARB if cough with an ACE inhibitor
  - Clopidogrel if patient refuses to take aspirin due to gastrointestinal upset.
  - Rechallenge with the same or a different statin if patient discontinued due to myalgia.
  - Recommend aspirin desensitization in patients with MI who in the past had experienced allergy (respiratory or skin) to aspirin.
  - Re-initiate low-dose ACE inhibitor for patients with left ventricular dysfunction and unclear reasons for discontinuation



## Premature Discontinuation of Dual Antiplatelet Therapy in Patients with Stents

- Primary nonadherence 7%
- Premature discontinuation 20% to 30%
  - Associated with increased risk of
    - Stent thrombosis
    - MI
    - Death

Ko DT, et al. Am Heart J 2009;158:592-598e.1.

## Patient Assistance Programs

- Low cost pharmacy generic drug programs
  - Some low-dose statins
- RxAssist.org
- NeedyMeds.org
- Patientassistance.com

## Improving Adherence

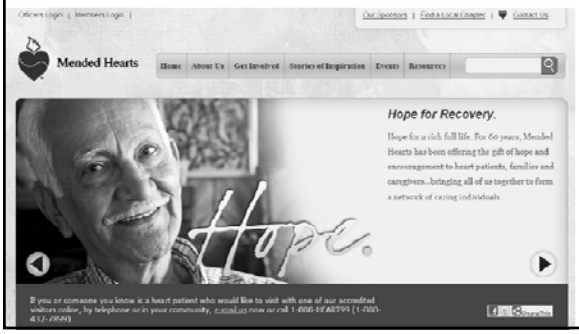
- Mypillbox.org
  - Schedule
  - Medication list



## AHA's Life's Simple 7


## AHA's Life's Simple 7: Example Manage Blood Pressure


## Patient Support Group: MendedHearts.org



**Correction to Primary and Secondary Prevention of Coronary Heart Disease Events Chapter**

Page 2-414

Question 7, Answer C – the “75 mg” should be deleted.

Updates in Therapeutics® 2012:
Ambulatory Care Pharmacy Preparatory Review and Recertification Course

**Emergency Medicine**

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## Conflict of Interest Disclosures

None

## Learning Objectives

1. Assess effective cardiopulmonary techniques in the management of sudden cardiac arrest and factors that contribute to improved survival.
2. Recommend appropriate interventions to care for the arrest victim when advanced care is being provided.
3. Distinguish between the types of allergic reactions and management strategies.
4. Recognize the signs and symptoms of anaphylaxis and plan treatment strategies based on presentation.

## Learning Objectives

5. Create a plan for treating angioedema caused by medications or genetic deficiencies (i.e., hereditary angioedema).
6. Develop a treatment plan for a victim of a toxic exposure including initial treatments and antidote administration.
7. Describe the functions of an emergency department–based pharmacist.

## What is your certification status?

A. CPR only

B. CPR and ACLS

C. Neither

## Patient Case 1

- Samantha leaves her house at 6:00 in the morning to go to work. She sees her 76-year-old neighbor Walter holding his chest and slumped over on the sidewalk. As she walks up to him, he collapses in front of her. Which one of the following is the best action for Samantha to take?

Workbook Page 2-442

## Patient Case 1 Answer Choices

A. Open the airway and give 2 breaths; then start 30 chest compressions; repeat

B. Perform chest compressions only at a rate of 100 per minute

C. Cycle 30 chest compressions with 2 breaths for 2 minutes; then check pulse

D. Check for a pulse; then begin CPR with cycles of 30 compressions and 2 breaths

Answer: Page 2-468

## Cardiopulmonary Resuscitation (CPR)

- Bystander CPR is essential
  - Survival decreases without blood to vital organs
    - Chest compressions = SBP 60 mm Hg
  - Return to a perfusing rhythm
    - VF is the Initial arrest rhythm in 40% victims
  - EMS response times >7 min
  - Early CPR and defibrillation increases survival

Workbook Page 2-437

## CPR Sequence

- Verify unresponsiveness
- Activate EMS*
- Compressions
- Airway
- Breathing

C-A-B

- Compression-only CPR
- Compression to ventilation ratio
  - Adults-30:2 Peds-30:2

* If a pediatric or respiratory arrest victim, complete 2 minutes of CPR before activating EMS


Workbook Page 2-437 to 2-439

## Appropriate Technique

**Chest Compressions**

- Infants (<1 year)
  - Two finger or two-thumb encircling
  - Depth: 1.5 inches
- Children (1-8 years)
  - Heel or hand over heel
  - Depth: 2 inches
- Adults (>8 years)
  - Hand over heel
  - Depth: >2 inches

**Airway**

- Head tilt-chin
- Jaw thrust

**Ventilations**

- Barrier device or mouth to mouth
- Visible chest rise
  - 6-7 mL/kg

Workbook Page 2-438 to 2-439

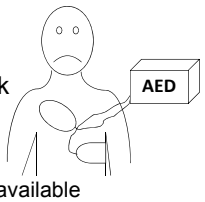
## Compression Only CPR

- May improve willingness to perform CPR
- Superior to no CPR
- Similar survival rates to standard CPR
- Indicated for lay rescuers
  - Not trained or unwilling to provide rescue breaths
- Not recommended for asphyxial causes and pediatric victims
- Compression rate 100 per minute

Workbook Page 2-439

## AED

- Public access
- Minimize time to shock
- Compressions after shock
- Adults
- Pediatric
  - Use pediatric attenuator if available
- Infants
  - Manual defibrillator preferred




Workbook Page 2-441

## Advanced Cardiovascular Life Support (ACLS)

- CPR Cornerstone
  - Remember C-A-B
- Rhythm analysis
  - Ventricular fibrillation (VF)
  - Ventricular tachycardia (VT)
  - Pulseless electrical activity
  - Asystole
- Defibrillation
  - VF or VT

Workbook Page 2-442 to 2-443

## Medications During ACLS

- Vasopressors (VF/VT/PEA/Asystole)
  - Epinephrine 1mg IV/IO Q3-5 min
  - Vasopressin 40 units IV/IO x 1
    - Replaces 1 dose of epinephrine
  - Atropine not recommended
- Antiarrhythmics (VF/VT)
  - Amiodarone 300mg IV bolus
  - Lidocaine 1-1.5mg/kg IV bolus

Workbook Page 2-445

## Medication Administration Principles

- Medications require circulation
  - Coordinate time with chest compressions
- Fluid bolus with 0.9% sodium chloride
- Elevate extremity
- IV/IO preferred
- Use endotracheal route if no IV/IO access
  - Higher doses required

Workbook Page 2-446

## Advanced Airway

- Asynchronous rates
  - Compressions-100 per min
  - Ventilations- 8 to 10 breaths/min
- Blind
  - Esophageal-tracheal combitube
  - Laryngeal mask airway
- Direct vocal chord visualization
  - Endotracheal tube

Workbook Page 2-443 to 2-444

## Reversible Causes

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hyper/hypo- kalemia
- Hypothermia
- Toxins
- Tamponade
- Thrombosis (coronary)
- Thrombosis (pulmonary)
- Tension pneumothorax


Workbook Page 2-444 to 2-445

## Pharmacists Role (AEIOU)

- Anticipate
- Ensure dosing and administration are appropriate
- Investigate reversible causes
- Observe and recommend drugs when indicated
- Use CPR skills when necessary

Workbook Page 2-447

## Patient Case 3

- A 51-year-old man presents to the ED with decreased mental status. His initial vital signs in the ED include a blood pressure of 78/49 mm Hg, heart rate 90 beats/minute, respiratory rate 28 breaths/minute, oxygen saturation 93%, and temperature 97.6°F. His bedside glucose is greater than 700 mg/dL. An arterial blood gas reveals severe metabolic acidosis (pH 6.8). He rapidly deteriorates with worsening mental status and a widening QRS complex on his ECG. No pulse is detected, and CPR is initiated. After 2 minutes of CPR, a rhythm is detected with a rate of 35 beats/minute, but there is no pulse, so CPR is reinitiated. Which one of the following is the best intervention at this time?

Workbook Page 2-447

## Patient Case 3 Answer Choices

A. Administer epinephrine 1 mg intravenously and deliver a shock.

B. Administer epinephrine 1 mg intravenously and atropine 1 mg intravenously and deliver a shock.

C. Administer vasopressin 40 units intravenously and epinephrine 1 mg intravenously.

D. Administer vasopressin 40 units intravenously

Answer: Page 2-468

## Allergy

- Immune mediated
- Some reactions mimic allergy
- Immunogenicity
  - Molecular size
  - Haptens
- Adverse drug reactions

Workbook Page 2-448

## Allergy Classification

- Type I
  - Immediate hypersensitivity
    - Bronchospasm, anaphylaxis, angioedema, urticaria
- Type II
  - Cytotoxic
    - Hemolytic anemia, thrombocytopenia, granulocytopenia
- Type III
  - Serum sickness
    - Delayed, fever, rash, urticaria, arthralgia, lymphadenopathy

Workbook Page 2-448 to 2-449

## Allergy Classification

- Type IV
  - Delayed hypersensitivity
    - Contact dermatitis
    - Maculopapular rash
    - Bullous exanthema: Stevens Johnson Syndrome and Toxic Epidermal Necrolysis
    - Fixed drug eruption
    - Drug rash with eosinophilia and systemic symptoms

Workbook Page 2-449

## Drug Reaction Evaluation

- History
  - Name
  - Timing
  - Symptoms
  - Previous exposure
  - Management
- Exam
  - Systemic signs
  - Edema
  - Skin
- Laboratory
  - CBC
  - CMP
  - UA
  - Coombs
  - RAST

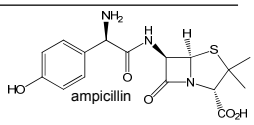
Workbook Page 2-450

## Management

- Stop drug
- Symptomatic treatment
  - Antihistamines, glucocorticoids, NSAIDs
- Severe skin hypersensitivity
  - Supportive care

Workbook Page 2-451

## β-Lactams




- β-lactam ring
- Most common documented allergy
- Rare cross-reactivity
  - Penicillins vs cephalosporins
  - Avoid if Type I or positive skin test
- Aztreonam no cross-reactivity
- Urticaria history requires skin testing

Workbook Page 2-453

## Sulfonamide Antibiotics

- Second most common
- Rare Type I allergies
- Immunogenic structure
- No cross reactivity
  - Sulfonamide diuretics (loops, thiazides, carbonic anhydrase inhibitors)
  - Sulfonylureas

Workbook Page 2-453

## Non-allergic Reactions

- Mimics true allergy
- Direct release of mast cell mediators
- No previous exposure
- Examples
  - Radiocontrast media
  - Intravenous acetylcysteine
  - Iron dextran

Workbook Page 2-453

## Skin Testing

- Useful for environmental allergens
- Limited use with drugs
  - β-lactam testing
- Type I and type IV reactions
- Not useful for type II and type III
- Desensitization for type I

Workbook Page 2-451

## Principles for the Pharmacist

- Accurate allergy documentation
- Patient counseling
- Role of medications in treatment
  - Glucocorticoids
  - H1-antagonists
  - H2-antagonists
  - Epinephrine
- No re-challenge situations
  - SJS and TEN
  - Type I reactions
- Cross reactivity
  - β-lactams
  - Sulfonamide antibiotics
  - Local anesthetics

Workbook Page 2-452

## Patient Case 6

- A 31-year-old man has a medical history significant for native valve endocarditis (tricuspid valve) 2 years ago caused by *Streptococcus bovis.* At that time, he was desensitized with penicillin because of an anaphylactic allergic reaction to penicillin and received a 6-week course of intravenous penicillin G without problems. He presents to the ED because his primary care physician was notified of positive blood cultures (gram-positive cocci) drawn 1 day earlier. In the ED, he has a temperature of 102°F, blood pressure 115/72 mm Hg, and heart rate 92 beats/minute. The infectious diseases physician on call recommends that the ED physician initiate penicillin G intravenously immediately after two additional blood cultures are obtained. Given this patient's allergy to penicillin in the past and assuming penicillin G is the drug of choice, which one of the following is the best recommendation?

Workbook Page 2-454

## Patient Case 6 Answer Choices

A. Initiate desensitization procedures with penicillin.
B. Administer penicillin G as ordered.
C. Recommend changing to oral administration to decrease risk of an allergic reaction.
D. Perform a skin test with the major penicillin determinant, and administer penicillin if negative.

Answer: Page 2-468 to 2-469

## Anaphylaxis

- Immune mediated
  - IgE
- Mediator release from basophil and mast cells
  - Cytokines
  - Leukotrienes
  - Histamine
  - Tryptase
- Causes
  - Medications
  - Food
  - Blood products
  - Latex
  - Seminal fluid
  - Venoms

Workbook Page 2-454

## Clinical Features

- Rapid onset
  - Minutes to hours
- Life threatening
- Systemic
  - Skin: urticaria, rash, swelling, pruritis
  - Swelling: lips, tongue, uvula, ears, genitalia, eyes
  - Respiratory: nasal, upper and lower
  - Gastrointestinal: nausea and vomiting
  - Cardiovascular: hypotension, tachy- or brady- cardia

Workbook Page 2-455

## Anaphylaxis Diagnostic Criteria

| **One of the following criteria need to be met** | | | |
|---|---|---|---|
| 1 | Acute onset of cutaneous and or mucosal symptoms | AND | Respiratory compromise |
| | | | OR |
| | | | Hypotension or symptoms of end-organ damage |
| 2 | At least two of the following after exposure to a likely antigen<br>• Respiratory compromise<br>• Hypotension or symptoms of end-organ damage<br>• Acute onset of cutaneous and/or mucosal symptoms<br>• Persistent gastrointestinal symptoms | | |
| 3 | Acute onset of hypotension after exposure to a known antigen | | |

Workbook Page 2-455

## Treatment

- Close monitoring
  - Hemodynamic
  - Respiratory
- Oxygen
- Medications
  - Reverse acute symptoms
  - Prevent late or secondary reactions

Workbook Page 2-456

## Medication Management

- Epinephrine
  - Cornerstone
  - Adults: 0.2-0.5mg IM and Pediatrics: 0.01mg/kg
- Histamine-1 antagonists
  - Treats urticaria and pruritis
- Histamine-2 antagonists
  - Additive effect to histamine-1 antagonists for cutaneous symptoms
- Glucocorticoids
  - Slow onset limits utility in acute reactions
  - Prevents late secondary reactions

Workbook Page 2-456 to 2-457

## Long Term Management

- Allergy database
- Patient knowledge
- Medical alert identification
- Self-injectable epinephrine
  - <30kg: 0.15mg product
  - ≥30kg: 0.3mg product
- Action plan
- Allergist

Workbook Page 2-457

## Patient Case 8

- A 6-year-old boy (52 lb) is being discharged from the ED after being stung by a bee at a water park while on vacation. He was given a diagnosis of anaphylaxis. As the ED pharmacist, you are asked by the ED physician for your recommendations regarding self-injectable epinephrine in this patient. Which one of the following is the best response about self-injectable epinephrine?

Workbook Page 2-458

## Patient Case 8 Answer Choices

A. It is indicated, and the patient should receive a prescription for the 0.3-mg product.

B. It is indicated, and the patient should receive a prescription for the 0.15-mg product.

C. It is not indicated, and the patient should be referred to an allergist to receive appropriate immunotherapy.

D. It is not indicated because the patient is unlikely to understand the instructions, and he would be at risk of inadvertent injection into the thumb.

Answer: Page 2-469

## Angioedema

- Clinical features
  - Non-pitting edema
  - Skin
  - Mucous membranes
  - Sudden
  - Variable severity
- Causes
  - Allergic
    - Usually associated with anaphylaxis
  - Nonallergic
  - Medications
  - Genetics

Workbook Page 2-458

## ACE Inhibitor Induced Angioedema

- Low incidence
- Class effect
- Onset: days to years
- Bradykinin
- Some cross-reactivity with ARBs
- Treatment
  - Supportive
- “Anaphylaxis” medications not effective

Workbook Page 2-459

## Hereditary Angioedema (HAE)

- C1-inhibitor (C1-INH) dysfunction
  - Type I: low C1-INH levels
  - Type II: normal C1-INH levels, but decreased activity
- Clinical features
  - Recurrent
  - Duration
  - Triggers

Workbook Page 2-459

## Acute HAE Treatment

- Replacement therapy using C1-INH 20 units/kg IV
- Kallikrein inhibitor
  - Ecallantide 30mg SQ divided into 3 injections
- Fresh frozen plasma
  - Historical use
  - Risk of worsening angioedema

Workbook Page 2-459

## Self Assessment Question 9

- A 43-year-old African American man has a medical history of hypertension and diabetes mellitus; both disease states have been well controlled with enalapril and metformin, respectively, without medication changes during the past year. He presents to the ED with significant lower lip swelling without difficulty breathing or hypoxia. No recent changes have been made in his diet. He does remember being stung by a wasp on the hand at the beach yesterday. Which one of the following is the most likely diagnosis and cause in this patient?

Workbook Page 2-436

## Self Assessment Question 9 Answer Choices

A. Angioedema from taking enalapril.

B. Anaphylaxis from wasp sting.

C. Angioedema caused by genetics.

D. Anaphylactoid reaction caused by enalapril.

Answer: Page 2-471

## Toxicology

- Poison Control Centers
  - Regional
  - 1-800-222-1222
  - 2.5 million human exposure calls annually
- National Poison Data System
  - Real-time database
  - Annual report

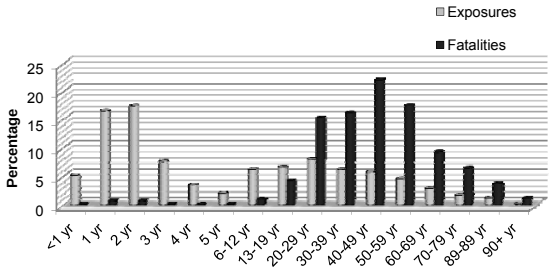
Workbook Page 2-460

## Human Exposures

- Residential exposures
  - 94% occur at a home
- Acute
- Most unintentional
- Management
  - 75% outpatient
- Fatalities
  - 1158 in 2009
  - Sedatives/hypnotics/ antipsychotics accounted for 14% deaths
  - 50% medication related

Workbook Page 2-461

## Age Distribution of Poisoning Exposures and Fatalities




Workbook Page 2-461

## Patient Evaluation

- History
  - Time, route, type, amount, intent
- Physical exam
  - Vital signs
  - Eyes
  - Skin
  - Odor
- ECG
  - QT
  - QRS
- Labs
  - Glucose, electrolytes, ABG, drug levels

Workbook Page 2-462

## Characteristic Vital Sign Changes

| | |
|---|---|
| Bradycardia | β-Blockers, calcium channel blockers, clonidine, digoxin, opioids |
| Tachycardia | Cocaine, anticholinergics, antihistamines, amphetamines, theophylline |
| Hyperthermia | Neuroleptics, antihistamines, salicylates, sympathomimetics |
| Hypothermia | Carbon monoxide, opioids, insulin, ethanol, sedative hypnotics |
| Hypertension | Cocaine, thyroid, sympathomimetics, caffeine, anticholinergics, nicotine |
| Hyperventilation | Phencyclidine, salicylates |
| Hypoventilation | Ethanol, sedative hypnotics |

Workbook Page 2-462

## Treatment

- Supportive care
- Gastric decontamination
  - Activated charcoal < 1 hr
    - Not effective for acids, alkalis, lithium, iron, hydrocarbons, pesticides
  - Orogastric lavage <1 hr
  - Whole bowel irrigation
    - Body packers

Workbook Page 2-463

## Treatment

- Most toxins do not have an antidote
- Antidote use depends on the clinical situation
- Selected antidotes
  - Acetylcycteine
  - Antivenins
  - Atropine/pralidoxime
  - Calcium
  - Digoxin immune Fab
  - Flumazenil
  - Fomepizole
  - Hydroxycobalamin
  - Methylene blue
  - Naloxone
  - Pyridoxine
  - Sodium bicarbonate

Workbook Page 2-464

## Final Thoughts

- Recognition and appropriate treatment of the arrest victim improves chances of survival
- Allergy is an important cause of adverse drug reactions
- Anaphylaxis treatment may be initiated in the outpatient setting because of epinephrine auto-injectors
- Most patients with poisoning can be managed outpatient and only require supportive care