AU InforMed

Volume 11 Number 2 (Issue 261) *Friday, February 1, 2013*

Guest Editors: William Hughes and Denise Sutter, Pharm. D. Candidates 2013

Key Inforbits

- Hyperlipidemia facts
- TLC diet information
- CHD Risk Factors
- Cholesterol Medications

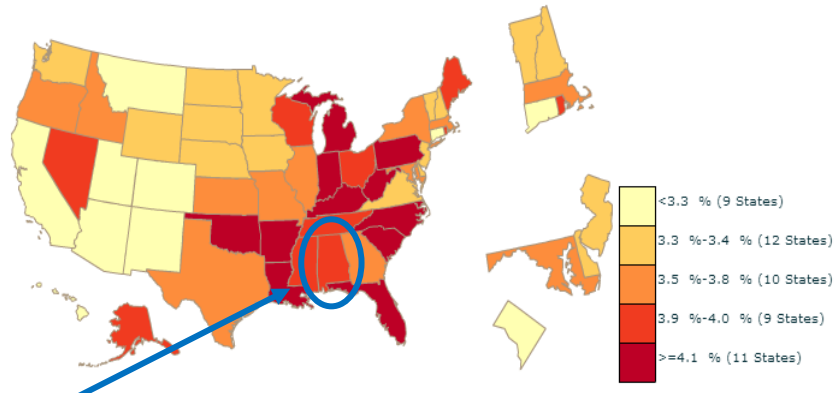
February is American **HEART** Month...

...and February 1st is wear **RED** day!!!

Did You Know[1-3]...

- In 2009-2010, ~47% of adults had at least 1 of 3 risk factors for cardiovascular disease
  - Uncontrolled hypertension
  - Current Smoker
  - **Uncontrolled high levels of LDL-cholesterol**
- 14.1% of adults ≥ 20 years old have high serum total cholesterol (≥240 mg/dL) (CDC 2007-2010)
- 2009 Prevalence of coronary heart disease among US adults (18+) in **Alabama = 4%**

2009 Prevalence of Coronary Heart Disease among US Adults (18+)



Division for Heart Disease and Stroke Prevention: Data Trends & Maps Web site. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), National Center for Chronic Disease Prevention and Health Promotion, Atlanta, GA, 2010. Available at http://www.cdc.gov/dhdsp/

Hyperlipidemia:

Heart disease is the leading cause of death in the United States. In 2010, almost 600,000 people died from heart disease.[4] High cholesterol is one of the major controllable risk factors of coronary heart disease (CHD), myocardial infarction, and stroke.[5] Hyperlipidemia can be the result of poor diet, medications, disorders of metabolism, and various disease states.[6]

Cholesterol is made up of three major classes of lipoproteins: low density lipoproteins (LDL), high density lipoproteins (HDL), and very low density lipoproteins (VLDL). Cholesterol and triglycerides are essential substrates for cell membrane formation, are utilized in hormone synthesis, and provide a source of free fatty acids.[7] Elevated LDL-cholesterol can result in atherosclerotic plaque formation through the "response-to-injury" hypothesis. According to this hypothesis, LDL-cholesterol is transported and retained in the artery wall and modified through oxidative processes. Oxidized LDL, in turn, recruits myocytes into the artery wall, and these myocytes are transformed into macrophages. Macrophages accelerate LDL oxidation and apolipoprotein B accumulation, and alter the receptor-mediated uptake of LDL into the artery wall so that is it no longer regulated by the cell content of cholesterol. Cholesterol-laden macrophages become foam cells which are the earliest recognized cell of

the arterial fatty streak. Oxidized LDL promotes coagulation by increasing plasminogen inhibitor levels, and causes vasoconstriction by inducing the expression of endothelin and inhibiting the expression of nitric oxide. Oxidized LDL also provokes an inflammatory response that contributes to both early monocyte-macrophage attachment and transmigration across the endothelium, and later lesion growth. Repeated injury and repair from oxidized LDL and foam cells eventually create plaque, a more advanced lesion of atherosclerosis that is protected by a fibrous cap. If the integrity of the fibrous cap is not maintained, the plaque may rupture resulting in thrombosis.[7,8] The outcomes of this atherogenic cascade are clinical events such as angina, myocardial infarction, arrhythmias, stroke, peripheral artery disease, abdominal aortic aneurysm, and sudden death.[7]

Treatment Steps[7,9]:

1. Determine lipoprotein levels.

- First step in selection of LDL-lowering therapy is to assess a person's risk status
- All adults aged 20 years or older should obtain a fasting lipoprotein profile once every 5 years
- If the test is non-fasting only the values for total cholesterol and HDL cholesterol will be usable
- If total cholesterol is >200 mg/dL or HDL is <40 mg/dL, a follow-up lipoprotein profile is needed for appropriate management based on LDL
- Relationship between LDL cholesterol levels and CHD risk is continuous over a broad range of LDL levels [7]

Classification of Cholesterol:

ATP III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

Taken from: ATP III guidelines at-a-glance quick desk reference[9]

2. Identify CHD Risk Equivalents and presence of other major risk factors.

- Clinical CHD
- Symptomatic carotid artery disease
- Peripheral artery disease
- Abdominal aortic aneurysm

Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

- Cigarette smoking
- Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
- Low HDL cholesterol (<40 mg/dL)*
- Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
- Age (men ≥45 years; women ≥55 years)

** HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.*

Taken from: ATP III guidelines at-a-glance quick desk reference[9]

- After a lipid abnormality is confirmed a patient evaluation should be performed and assess the following:
  - Presence or absence of cardiovascular risk factors
  - Definite cardiovascular disease in the individual
  - Family history of premature cardiovascular disease or lipid disorders
  - Presence or absence of secondary causes of lipid abnormalities, including concurrent medications
  - Presence or absence of xanthomas or abdominal pain, history of pancreatitis, renal or hepatic disease, peripheral vascular disease, abdominal aortic aneurysm, or cerebral vascular disease
  - Diabetes mellitus is also a CHD risk equivalent[7]

3. Determine risk category according to patient evaluation

Adapted from: Ito. Ann Pharmacother. 2012;46:1368-81[10]

Organization	Risk Category	LDL (Lipid Goals mg/dL)	Non-HDL (Lipid Goals mg/dL)	ApoB (Lipid Goals mg/dL)
ATP III Guidelines (2004)	High risk: CHD or CHD risk equivalent (eg. diabetes or 10y FRS > 20%)	< 100 < 70 (optional)[a]	< 130	NA
	Moderately high risk: ≥ 2 risk factors (FRS 10-20%)	< 130 < 100 (optional)	< 160	
	Moderate risk: ≥ 2 risk factors (FRS <10%)	< 130	< 160	
	Low risk: 1 or no risk factors	< 160	< 190	
ADA/ACC Consensus Report (2008)	Highest risk: CVD or diabetes + additional major CVD risk factor(s)	< 70	< 100	< 80
	High risk: No diabetes or known CVD but ≥ 2 major CVD risk factors **or** diabetes but no other major CVD risk factors	< 100	< 130	< 90
AHA/ACCF Guideline on Secondary Prevention (2011)	All patients with coronary or other atherosclerotic vascular disease	≥ 30% reduction and < 100	NA	NA
	Patients with CHD at very high risk[b]	< 70 (reasonable)		
NLA Expert Panel on FH, Clinical Guidance (2011)	Adults ≥ 20 yo with FH and LDL ≥ 190 or non-HDL ≥ 220	≥ 50% reduction	NA	NA
	Children ≥ 8 yo with FH and LDL ≥ 190 or non-HDL ≥ 200	≥ 50% reduction or < 130		

[a]Factors that favor reducing LDL to < 70 mg/dL include presence of established CVD + (1) multiple major risk factors (especially diabetes); (2) severe and uncontrolled risk factors; (3) multiple risk factors of metabolic syndrome; (4) presence of ACS

[b]Patients with CHD + (1) multiple major risk factors (especially diabetes); (2) severe and uncontrolled risk factors; (3) multiple risk factors of metabolic syndrome; (4) presence of ACS

4. Initiate Therapeutic Lifestyle Changes

- TLC should be implemented in all patients prior to considering drug therapy
- Components of TLC include:
  - Reduced intake of saturated fats and cholesterol
    - Saturated fat < 7% of total calories
    - < 200 mg of cholesterol per day
    - Trans fat < 1% of total calories
  - Dietary options to reduce LDL (eg. 2 g per day of plant sterols, 10-25 g per day of viscous (soluble) fiber)
  - Weight reduction
    - Goal BMI: 18.5-24.9 kg/m2
    - Goal waist circumference: women < 35 in; men < 40 in
  - Physical activity of moderate intensity 30 minutes per day for most days of the week[7, 11]

5. Consider pharmacological therapy

- A portion of the population will require LDL-lowering drugs in addition to TLC to reach the designated LDL goal
- Attention to TLC should always be maintained and reinforced along with prescribed medications
- Currently available drugs that affect lipoprotein metabolism and their major characteristics are listed in the table below

Adapted from: ATP III guidelines at-a-glance quick desk reference[9], Ito. Ann Pharmacother. 2012;46:1368-81[10], and Treat Guidelines. 2011 Mar;9(103):13-20.[12]

Drug Class	Trade Name	Agents (mg/day)	Lipid Effects	Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	*Lipitor* *Lescol* *Mevacor* *Livalo* *Pravachol* *Crestor* *Zocor*	Atorvastatin (10-80) Fluvastatin (20-80) Lovastatin (10-80 Pitavastatin (1-4) Pravastatin (10-80) Rosuvastatin (5-40) Simvastatin (5-80)	**LDL**:↓18-55% **HDL**:↑5-15% **TG**:↓7-30%	Myopathy Increased Liver enzymes	Absolute: Active or chronic liver disease Relative: Concomitant use of certain interactive drugs
Bile acid sequestrants	*Prevalite* *Colestid* *Welchol*	Cholestyramine (4-16g) Colestipol (5-30g) Colesevelam (4.5g)	**LDL**:↓15-30% **HDL**:↑3-5% **TG**: none	GI distress Constipation Decreased absorption of other drugs	Absolute: dysbeta-lipoproteinemia TG >400 mg/dL Relative: TG >200 mg/dL
Cholesterol absorption inhibitor	*Zetia*	Ezetimibe (10)	**LDL**: ↓18% **HDL**:↑ 1% **TG:** ↓ 8%	Diarrhea Fatigue Pain in extrmities	Absolute: Active or chronic liver disease
Nicotinic acid	*Niacin* *Niacin ER*	Immediate release nicotinic acid (3-6g) Extended release nicotinic acid (3-6g)	**LDL**:↓5-25% **HDL**:↑15-35% **TG**:↓20-50%	Flushing Hyperglycemia Hyperuricemia (gout) Upper GI distress Hepatotoxicity	Absolute: Chronic liver disease Severe gout Relative: Diabetes Hyperuricemia PUD
Fibric acids	*Lopid* *Trilipix* *Atromid-S*	Gemfibrozil (1200) Fenofibrate (48-145) Clofibrate (2000)	**LDL**:↓5-20% **HDL**:↑10-20% **TG**:↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: Severe renal disease Severe hepatic disease
Omega-3 fatty acid ester	*Lovaza*	EPA/DHA (4g)	**LDL**:↑ 45% **HDL**:↑9% **TG**:↓45%	Upper GI distress Increased liver enzymes	Absolute: Hypersensitivity

1. Fryar CD, Chen T, Li X. Prevalence of uncontrolled risk factors for cardiovascular disease: United States, 1999–2010. NCHS data brief, no 103. Hyattsville, MD: National Center for Health Statistics. 2012.
2. National Center for Health Statistics. Health, United States, 2011: With Special Feature on Socioeconomic Status and Health. Hyattsville, MD. 2012.
3. Division for Heart Disease and Stroke Prevention: Data Trends & Maps Web site. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), National Center for Chronic Disease Prevention and Health Promotion, Atlanta, GA, 2010. Available at http://www.cdc.gov/dhdsp/.
4. Leading causes of death [Internet]. Atlanta: Centers for Disease Control; updated 2013 Jan 11 [cited 2013 Jan 16]. Available from: http://www.cdc.gov/nchs/fastats/lcod.htm
5. Why cholesterol matters [Internet]. Dallas: The American Heart Association; c2013 [cited 2013 Jan 16]. Available from: http://www.heart.org/HEARTORG/Conditions/Cholesterol/WhyCholesterolMatters/Why-Cholesterol-Matters_UCM_001212_Article.jsp
6. Stone NJ. Secondary causes of hyperlipidemia. Med Clin North Am. 1994;78(1):117-41.
7. Talbert RL. Dyslipidemia. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A pathophysiologic approach. 8th ed. New York: McGraw-Hill Medical; c2011. p. 365-88.
8. Bhattacharyya G, Libby P. Atherosclerosis. In: Lilly LS, editor. Pathophysiology of heart disease: A collaborative project of medical students and faculty. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; c1997. p. 101-18.
9. NHLBI: clinical practice guidelines [Internet]. Bethesda: National Heart Lung and Blood Institute; c2001. ATP III guidelines at-a-glance quick desk reference [cited 2013 Jan 16]; [about 6 screens]. Available from: http://www.nhlbi.nih.gov/guidelines/cholesterol/atglance.pdf
10. Ito MK. Dyslipidemia: Management using optimal lipid-lowering therapy. Ann Pharmacother. 2012;46:1368-81.
11. Smith Jr SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update. J Am Coll Cardiol. 2011;58:2432-46.
12. Drugs for lipids. Treat Guidelines. 2011;9(103):13-20.

The last "dose" …

"Hear your heart. Heart your health." ~ Faith Seehill

An electronic bulletin of drug and health-related news highlights, a service of …
Auburn University, Harrison School of Pharmacy, Drug Information Center
• Phone 334-844-4400 • Fax 334-844-8366 • http://www.pharmacy.auburn.edu/dilrc/dilrc.htm
Bernie R. Olin, Pharm.D., Director
Archived issues are available at: http://pharmacy.auburn.edu/dilrc/au_informed.htm