Update on Dyslipidemia

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Objectives: At the end of the presentation, the speaker hopes that the participants will be able to:

1. Apply the ATP III guidelines to specific patient profiles.
2. Describe the recent updates to the ATP III.
3. Select the appropriate lipid-lowering agent (LLA) for the lipid abnormality.
4. Describe the indications and monitoring for combination therapy.
5. Describe the benefits of statin therapy beyond lowering of cholesterol.

Case Studies will be used throughout the presentation to facilitate application of the information.

Outline:

I. Headline News regarding lipids.
II. Summarize key points of the ATP III guidelines
III. Lipoproteins and subfractions.
IV. Medical conditions that indicate CAD equivalent.
V. Calculating 10-year risk for CAD.
VI. Lipid-lowering agents: categories, indications, dose, and effect on specific lipoproteins and triglycerides.
VII. Steps to follow in using combination therapy.
VIII. Monitoring for ADRs
IX. Beyond lipid-lowering: stroke prevention and plaque stabilization.

Bibliography:

1. Bussoletti A. Framingham Point Score: A useful tool in assessing CHD risk. *The Journal for Nurse Practitioners*. 2003; 7(9): 17-24.
2. Executive Summary of the Third Report of the National Cholesterol Educational Program (NCEP) Expect Panel on Detection, Evaluating and Treatment of High Blood Cholesterol in Adults (ATP III). *JAMA.* 2001;285(19):2486-2497.
3. Foody JM, Krumlotz HM. Are statins indicated for the primary prevention of CAD in octogenarians? Antagonist viewpoint. *The Am.Joun.Geriatric Cardiology.* 2003;12(6):357-360.
4. Jones PH, Davidson MH, Stein EA, et.al. Comparison of the efficacy and safety of Rosuvastatin versus Atorvastatin, simvastatin, and Pravastatin across doses (Stellar Trial). *The American Joun. Of Cardiology.* 2003;92:152-160.
5. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin of 20,536 high-risk individuals: a randomized placebo-controlled trial. *Lancet.* 2002;360(9326):7-22.
6. Pasternak RC, Smith SC,jr., Baiirey-Merz CN, Grundy SM, Cleeman JR, Lenfant C. ACC/AHA/NHLBI Clinical advisory on the use and safety of statins. *Circulation.* 2002;106(8):1024-1028.
7. Stone NJ. an Are statins indicated for the primary prevention of CAD in octogenarians? Protagonist viewpoint. *The Am.Joun.Geriatric Cardiology.* 2003;12(6):351-354.

Internet Resources:

1. www.Nhlbi.nih.gov/guidelines/cholesterol/atpiii.htm
2. www.heartcenteronline.com. The Cholesterol Center. Palm OS applications. 10-year Risk Calculator.
3. www.lipidhealth.org.
4. www.americanheart.org.
5. www.heartnp.com. Fran Stier's web site

Coronary Heart Disease Risk Equivalents

- Other clinical forms of atherosclerotic disease: peripheral arterial disease, abdominal aortic aneurysm, symptomatic carotid artery disease
- Diabetes
- Multiple risk factors that confer a 10-year risk for coronary heart disease> 20%

Risk Factors in the Algorithm for Primary Prevention

- Cigarette smoking
- Hypertension: ≥ 140/90 mm Hg or patient on antihypertensive medication
- Low HDL-C: <40 mg/dL*
- Family history of premature CHD: male first-degree relative < 55 years, female first-degree relative < *65* years
- Age: men ≥ 45 years, women ≥ 55 years

* High HDL-C (≥ 60 mg/dL) is a negative risk factor and decreases the total number of risk factors by one.

Clinical Identification of the Metabolic Syndrome

Risk Factor	Defining Level
Abdominal obesity* (waist circumference)#	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥ 150 mg/dl
HDL	
Men	< 40 mg/dl
Women	< 50 mg/dl
Blood Pressure	≥ 130/ ≥85 mm Hg
Fasting Glucose	≥ 110 mg/dl

* Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated body mass index (BMI). Therefore the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.

Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g. 94-102 cm (37-40 in). Such patients may have strong genetic contribution to insulin resistance and they should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

Table-B-I. Estimate of 10-Year Risk for Men
(Framingham Point Scores)

Age, y	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
5054	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

	Points				
T. Chol mg/dL	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points				
	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL, mg/dL	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year Risk, %
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥30

Table-B2. Estimate of 10-Year Risk for Women
(Framingham Point Scores)

Age, y	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
5054	6
55-59	6
60-64	10
65-69	12
70-74	14
75-79	16

	Points				
T. Chol mg/dL	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points				
	Age 20-39 y	Age 40-49 y	Age 50-59 y	Age 60-69 y	Age 70-79 y
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL, mg/dL	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year Risk, %
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥30

ATP Ill Classification of Lipids

LDL cholesterol

<100	Optimal
100-129	Near or 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

Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for 3 Risk Categories

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

* LDL indicates low-density lipoprotein; HDL, high-density lipoprotein; and CHD, coronary heart disease.

LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories*

Risk Category	LDL Goal (mg/dl)	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (mg/dl)	LDL Level at Which to Consider Drug Therapy (mg/dl)
CHD or CHD risk equivalent (10-year risk >20%)	< 100	≥ 100	≥ 130 (100-129; drug optional)
2+ Risk factors (10-year risk ≤ 20%)	< 130	≥ 130	10-year risk 10%-20%: ≥ 130 10-year risk <10%: ≥160
0-1 Risk factor	< 160	≥ 160	≥ 190

Principal Effects of Lipid-Lowering Agents on Serum Lipids

Lipid-Lowering Agent	Dose Range	Peak Effect	LDL-C	HDL-C	TG	Total Cholesterol
Statins						
Atorvastatin (Lipitor, Pfizer)	10-80 mg	4 wk	↓ 26%-60%	↑ 5%-13%	↓ 17%-53%	↓ 25%-45%
Fluvastatin (Lescol, Novartis/Reliant)	20-80 mg	4 wk	↓ 22%-36%	↑ 3%-i 1%	↓ 12%-25%	↓ 16%-27%
Fluvastatin ER (Lescol XL, Novartis/Reliant)	80 mg	4 wk	↓ 33%-35%	↑ 7%-11%	↓ 19%-25%	↓ 25%
Lovastatin (Mevacor, Merck; various)	10-80 mg	4-6 wk	↓ 21%-42%	↑ 2%-10%	↓ 6%-27%	↓ 16%-34%
Lovastatin ER (Altocor, Andrx)	20-60 mg	4-6 wk	↓ 24%-41%	↑ 9%-i3%	↓ 10%-25%	↓ 18%-29%
Pravastatin (Pravachol, Bristol-Myers Squibb)	10-80 mg	4 wk	↓ 22%-34%	↑ 2%-i 2%	↓ 15%-24%	↓ 16%-25%
Rosuvastatin (Crestor, AstraZeneca)	5-40 mg	4 wk	↓ 45%-63%	↑ 8%-i 4%	↓ 10%-35%	↓ 33%-46%
Simavastatin (Zocor, Merck)	5-80 mg	4-6 wk	↓ 26%-47%	↑ 8%-i 6%	↓ 12%-34%	↓ 19%-36%
FADs						
Fenofibrate (Tricor, Abbott; various)	54-160 mg	2 wk	↓ 20%-31%*	↑ 9%-23%	↓ 23%-54%	↓ 9%-22%
Gemfibrozil (Lopid, Pfizer; various)	1,200 mg	3-4 wk	↓ 0%-10%*	↑ 10%-3o%	↓ 20%-60%	↓ 2%-16%
Nicotinic Acid						
Niacin ER (Niaspan, Kos)	1,000-2,000 mg	3-5 wk	↓ 5%-17%	↑ 14%-26%	↓ 11%-38%	↓ 3%-25%
Niacin (various)	1,000-2,000 mg	3-5 wk	↓ 5%-25%	↑ 15%-39%	↓ 20%-60%	
Cholesterol Absorption Inhibitors						
Ezetimibe (monotherapy) (Zetia, Merck/Schering-Plough)	10 mg	2 wk	↓ 18%	↑ 1%-2%	↓ 7%-9%	↓ 3%-12%
BASs (Resins)						
Cholestyramine (Questran, Par; various)	1-6 packets	2-4 wk	↓ 15%-30%	↑ 3%-5%	May ↑ in pts with ↑ TG	↓ 10%-25%
Colesevelam (WelChol, Sankyo Pharma)	3,750-4,375 mg	2-4 wk	↓ 8%-15%	↑ 3%-5%	May ↑ in pts with ↑ TG	↓ 10%-25%
Colestipol (Colestid, Pfizer)	1-6 packets	2-4 wk	↓ 15%-30%	↑ 3%-5%	May ↑ in pts with ↑ TG	↓ 12%-13%
Combination Product						
Niacin ER and Lovastatin (Advicor, Kos)	500mg/20mg to 2,000mg/40mg		↓ 30%-42%	↑ 20%-3o%	↓ 32%-44%	Not stated