

Treatment of dyslipidemias in HIV-infected individuals (reviewed 1/11/06)

Introduction:

The NCEP (National Cholesterol Education Program) released guidelines in 2001 titled ATP III (Adult Treatment Panel III). "Optimal" LDL was defined as less than 100 mg/dL. It had been noted that there is an exponential relationship between cardiovascular risk and rising LDL (for each 30 mg/dL increase in LDL the relative risk of CHD is increased in proportion by 30%). This relationship is consistent even at very low levels of LDL. However, until recently it was not known whether lowering LDL with medications to very low levels (ie to levels substantially below 100 mg/dL) would decrease morbidity and mortality. However, the Heart Protection Study randomized 20,536 patients with diabetes, coronary artery disease or other occlusive arterial disease to simvastatin 40mg or placebo. The study found that even with patients with a baseline LDL<100 mortality was significantly reduced. In addition, PROVE IT compared simvastatin 40mg and atorvastatin 80mg in patients following acute coronary syndromes. The average LDL attained in the simvastatin group was 95 mg/dl and in the atorvastatin group was 62 mg/dL. With atorvastatin there was a 16% reduction in the composite cardiovascular endpoint following 2 years of therapy.

These two studies led the NCEP to revise their 2001 guidelines. The guidelines focus heavily on management of LDL with lesser emphasis on HDL and triglycerides. The steps to manage lipids are as follows:

I. Baseline Labs

Obtain fasting (9-12 hours) lipid profile prior to starting ARVs, within 3-6 months of starting new regimen, and yearly unless abnormalities are detected or therapeutic interventions are initiated. On average, non-fasting labs falsely elevate TG by 20-30 and falsely lower LDL by 4- 6. Lipid levels may need to be repeated fasting for more accurate measurements.

II. Determine # of Risk Factors for CHD (diabetes is a CHD risk equivalent); Refer to Nutrition/Smoking Cessation

| |
|--|
| Cigarette smoking |
| BP ≥ 140/90 mmHg or on antihypertensive medication |
| HDL < 40 mg/dL (HDL ≥ 60 mg/dL is a “negative” risk factor; removes one risk factor from the total count) |
| Family history of premature CHD (< 55 years in 1 st degree male relatives; < 65 years in female 1 st degree relatives) |
| Age: men ≥ 45; women ≥ 55 |

III. For pts with ≥ 2 RF estimate 10-year risk of MI or cardiac death - see table on next page or online calculator at <http://hin.nhlbi.nih.gov/atp/iii/calculator.asp>

IV. Lipid goals and treatment decisions (Any pt at high or moderately high risk who has lifestyle-related risk factors is a candidate for Therapeutic Lifestyle Changes (TLC) regardless of LDL level)

| Risk category | LDL mg/dL | | |
|---|------------------------------|--------------|--|
| | Goal | Initiate TLC | Consider drug therapy |
| High risk CHD or CHD risk equivalents*§ | <100 optional goal < 70** | ≥ 100 | ≥ 100 (<100 consider drug options) |
| Moderately high risk 2+ risk factors(10-yr risk 10% to 20%) | < 130 optional goal <100 | ≥130 | ≥ 130 100-129 consider drug options |
| Moderate risk 2+ risk factors (10 yr risk < 10%) | <130 | ≥ 130 | ≥ 160 |
| Lower risk 0-1 risk factor | <160 | ≥160 | ≥190 160-189; LDL -lowering drug optional |

*CHD risk equivalents: peripheral vascular disease, AAA, symptomatic carotid stenosis, DM, and 2+ risk factors with 10-year risk for CHD >20%

** Very high risk pts: existing CVD + multiple RF (esp diabetes), severe & poorly controlled single RF (ie. cont. smoking) or metabolic syndrome; pts with recent ACS are also considered high risk

§ If a high-risk person has high TG or low HDL-cholesterol, may consider adding a fibrate or nicotinic acid with an LDL-lowering drug. When TG >200, non-HDL-cholesterol (TC-HDL) is a secondary target of therapy, with a goal of 30 higher than the identified LDL goal.

Therapeutic Lifestyle Changes (TLC) Features:

- 1) TLC Diet: Saturated fat <7% of calories, cholesterol <200 mg/day, consider increased viscous (soluble) fiber (10-25 g/day) and plant stanols/sterols
- 2) Weight Management
- 3) Increased physical activity

V. Drug therapy

| | |
|-------------------------------------|---|
| Elevated LDL only | STATIN (pravastatin 40mg QD or atorvastatin 10mg QD b/c of lack of / low potential for drug interactions); if inadequate response to full dose of statin, (in HIV PI containing regimens: Pravachol max dose 80 mg, atorvastatin max dose 40 mg) may consider adding Niaspan (0.5g QHS for 1 month, then increase by 0.5g monthly up to 1.5-2g QHS) or add a fibrate (gemfibrozil 600mg BID or fenofibrate 160mg QD) |
| Elevated LDL with TGs 200-500 mg/dL | STATIN (pravastatin or atorvastatin); alternatives: 1 st fibrate, 2 nd Niaspan; may consider combining statin with a fibrate or Niaspan if inadequate response to full dose of statin |
| TGs > 500 mg/dL | FIBRATE (gemfibrozil or fenofibrate); alternatives: Niaspan or fish oil (1-2g TID with meals); may consider combining fibrate with niacin or fish oil if inadequate response |

Effects of drugs on lipids

| | LDL | HDL | TG |
|--------------|----------|------------|----------|
| Atorvastatin | ↓ 38-54% | ↑ 0.1-5.5% | ↓ 13-25% |
| Pravastatin | ↓ 19-43% | ↑ 3-6% | ↓ 3-10% |
| Gemfibrozil | ↓↑ 10% | ↑ 10-20% | ↓ 60% |
| Fenofibrate | ↓↑ 10% | ↑ 10-20% | ↓ 30-60% |
| Niacin | ↓ 5-25% | ↑ 15-35% | ↓ 20-50% |
| Fish oil | | | ↓ 30-60% |

Monitoring Labs

> When using a statin, obtain LFTs at baseline and at 12 weeks following both the initiation of therapy and dose elevation. Check every 6 months thereafter.
> Repeat lipid panel every 6 weeks after the initiation of therapy until LDL goal achieved, then every 4-6 months.

Antiretroviral therapy associated with dyslipidemias

In one study, protease inhibitor based regimens were associated with fasting TG inc of 50%, TC and LCL inc 10% and no change in HDL-cholesterol compared to non-PI based regimens. Atazanavir has a more favorable effect on all lipid parameters. Stavudine has been variably associated with increases in fasting TG, TC and LDL. Nevirapine has superior lipid profile to efavirenz.

Men

Estimate of 10-Year Risk for Men

(Framingham Point Scores)

| Age | Points |
|-------|--------|
| 20-34 | -9 |
| 35-39 | -4 |
| 40-44 | 0 |
| 45-49 | 3 |
| 50-54 | 6 |
| 55-59 | 8 |
| 60-64 | 10 |
| 65-69 | 11 |
| 70-74 | 12 |
| 75-79 | 13 |

| Total Cholesterol | Points | | | | |
|-------------------|-----------|-----------|-----------|-----------|-----------|
| | Age 20-39 | Age 40-49 | Age 50-59 | Age 60-69 | Age 70-79 |
| <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 | Age 40-49 | Age 50-59 | Age 60-69 | Age 70-79 |
| 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 (mmHg) | 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 |

10-Year risk _____%

Women

Estimate of 10-Year Risk for Women

(Framingham Point Scores)

| Age | Points |
|-------|--------|
| 20-34 | -7 |
| 35-39 | -3 |
| 40-44 | 0 |
| 45-49 | 3 |
| 50-54 | 6 |
| 55-59 | 8 |
| 60-64 | 10 |
| 65-69 | 12 |
| 70-74 | 14 |
| 75-79 | 16 |

| Total Cholesterol | Points | | | | |
|-------------------|-----------|-----------|-----------|-----------|-----------|
| | Age 20-39 | Age 40-49 | Age 50-59 | Age 60-69 | Age 70-79 |
| <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 | Age 40-49 | Age 50-59 | Age 60-69 | Age 70-79 |
| 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 (mmHg) | 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 |

10-Year risk _____%

References:

Cannon CP, Intensive versus moderate lipid lowering after acute coronary syndromes, NEJM 2004; 350:1495-504

Heart Protection Study Collaborative Group, MRC/BHF Heart Protective Study of cholesterol lowering with simvastatin, Lancet 2002; 360:7-22.

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