Learning Objectives

1. Identify the primary target for cholesterol lowering therapy based upon the Adult Treatment Panel III report.
2. Categorize risk stratification for cholesterol therapy based upon LDL-C risk factors and the Framingham Risk Score.
3. Recognize the importance of hyperlipidemia therapy in the treatment of metabolic syndrome.
4. Recognize the hyperlipidemia therapy of coronary artery equivalent patients.
5. Categorize statin-related muscle complaints and identify risk factors for their development.

ATP III Basics

- Therapeutic lifestyle change is an "essential modality in clinical management," at all degrees of risk.
- Elevated LDL-C level is a major cause of CAD.
- LDL-C is the primary target for lipid-lowering therapy.
- Non-HDL-C is a secondary target for lipid-lowering therapy.

2. US Preventive Services Task Force recommendations for lipid disorder screening in adults include which one of the following?

A. Fasting lipid panel and hsCRP
B. Fasting TC, HDL and direct LDL
C. Screen all men ≥ age 35
D. Screen all adults ≥ age 35
2. US Preventive Services Task Force recommendations for lipid disorder screening in adults include which one of the following?

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Dyslipidemia Screening

- USPSTF recommends screening:
  - All men ≥ 35 (A)
  - Men 20-35 (B) and women ≥ 45 (A) at increased risk for CHD
  - CHD risk factors include:
    - Diabetes
    - CHD or non-coronary atherosclerosis
    - Family history cardiovascular disease < 50 in male relatives or < 60 in female relatives
    - Tobacco use
    - Hypertension
    - Obesity (BMI ≥ 30)

Optimal Lipid Levels

- LDL-C: <100 mg/dL
- Total cholesterol (TC): <200 mg/dL
- Triglycerides: <150 mg/dL
- HDL-C: >60 mg/dL
- Non-HDL-C (TC - HDL): <130 mg/dL

3. A 60-year-old African-American male was recently diagnosed with an abdominal aortic aneurysm. A lipid profile performed a few months ago revealed an LDL level of 125 mg/dL. You would now advise him that his goal LDL level is:

- A. < 70 mg/dL
- B. < 100 mg/dL
- C. < 130 mg/dL
- D. < 160 mg/dL
LDL Goal in CAD-Equivalent Diseases

- Goal LDL for patients with diabetes or CAD is < 100
- This LDL goal extends to CAD-equivalent diseases, including:
  - Peripheral artery disease
  - Symptomatic carotid artery disease
  - Abdominal aortic aneurysm

4. Of the following dietary factors recommended for the prevention and treatment of cardiovascular disease, which one has been shown to decrease the rate of sudden death?

- Increased intake of plant protein
- Increased intake of dietary fiber and whole grains
- Increased intake of monounsaturated oils
- Increased intake of omega-3 fats
- Moderate alcohol consumption (1-2 standard drinks per day)

Omega-3 Fats and Sudden Death

- Omega-3 fats contribute to production of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA):
  - Inhibit inflammatory immune response
  - Inhibit platelet aggregation
  - Mild vasodilators
  - Possible antiarrhythmic properties

5. A 52-year-old white male is being considered for pharmacologic treatment of hyperlipidemia because of an LDL cholesterol level of 180 mg/dL. Before beginning medication for his hyperlipidemia, he should be screened for:

- Hyperthyroidism
- Hypothyroidism
- Addison’s disease
- Cushing’s disease
- Pernicious anemia
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- **E. Pernicious anemia**

### Secondary Dyslipidemia

- Per NCEP ATP III guidelines, assess for secondary dyslipidemia before initiation of lipid-lowering therapy.
- Causes include:
  - Diabetes mellitus
  - Hypothyroidism
  - Obstructive liver disease
  - Chronic renal failure
  - Medications (thiazide diuretics, antipsychotics)

6. According to National Cholesterol Education Program guidelines, which of the following is a criteria for the diagnosis of metabolic syndrome?

- **A. HDL-cholesterol level ≤ 40 mg/dL in women**
- **B. An LDL-cholesterol level ≥ 160 mg/dL**
- **C. Serum triglycerides ≥ 200 mg/dL**
- **D. Diastolic blood pressure ≥ 90 mm Hg**
- **E. Waist circumference >40 inches in a male**

### Metabolic Syndrome

- Per NCEP ATP III guidelines, any 3 of:
  - Fasting glucose > 110 mg/dL
  - Blood pressure: systolic > 130 mm Hg or diastolic > 85 mm Hg
  - Obesity: central – waist circumference > 40” male / 35” female
  - Elevated triglycerides > 150 mg/dL
  - Low HDL < 40 mg/dL for males, < 50 for females
- LDL is NOT one of the NCEP criteria

7. According to National Cholesterol Education Program ATP III guidelines, which of the following risk factors for CHD is used to determine LDL-C goal?

- **A. Diabetes**
- **B. Obesity**
- **C. Elevated triglycerides**
- **D. Cigarette smoking**
7. According to National Cholesterol Education Program ATP III guidelines, which of the following risk factors for CHD is used to determine LDL-C goal?

- Diabetes 76%
- Obesity 4%
- Elevated triglycerides 8%
- Cigarette smoking 15%

8. A 55 year-old man with CAD and type 2 diabetes is currently taking atorvastatin 10 mg daily. His lipid panel shows: TC 222 mg/dL, HDL-C 35 mg/dL, LDL-C 110 mg/dL, triglycerides 180 mg/dL. Which one of the following statements is true regarding his lipid goals?

- An LDL-C goal of < 70 mg/dL is a therapeutic option for this patient 72%
- Extended-release niacin 500 mg qhs should be added to his atorvastatin 15%
- Ezetimibe 10 mg daily should be added 4%
- Gemfibrozil 600 mg bid should be added 8%

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Framingham Risk Score

- Includes:
  - Age
  - Gender
  - Total Cholesterol (average of at least 2 measurements)
  - HDL Cholesterol
  - Smoking (any cigarette smoking in the past month)
  - Systolic BP (regardless of whether the person is on antihypertensive therapy)

Lipid Therapy in Very High Risk Patients

- ATP III guidelines (2002) were modified in 2004, primarily based on HPS and PROVE-IT
- An LDL-C goal of <70 mg/dL is a **therapeutic option** for patients at very high risk, even if baseline LDL is < 100
- When a high-risk patient has high triglycerides or low HDL “consideration can be given to combining a fibrate or nicotinic acid with an LDL-lowering drug”
- Ezetimibe (Zetia) would lower the LDL-C but survival data is not yet available. (ENHANCE Trial)
Risk-based LDL Goals

- High-risk (10-year CAD risk ≥20%)
  - Primary CAD prevention (10-year CAD risk ≥ 20% by FRS)
  - CAD equivalent
  - Secondary CAD prevention
  - LDL-C goal <100 mg/dL
  - Intensity of therapy to achieve at least 30-40% reduction in LDL-C

- Very high-risk patients:
  - CAD plus:
    - Diabetes
    - Metabolic syndrome
    - Uncontrolled risk factors
    - Continued ischemic pain despite optimal therapy
  - LDL-C goal ≤ 70 mg/dL

9. You are evaluating an obese woman with type 2 diabetes and CAD. Her fasting lipid panel shows: TC 220 mg/dL, triglycerides 650 mg/dL, HDL-C 25 mg/dL and LDL-C 140 mg/dL. Which one of the following is most appropriate for initial therapy?

A. Therapeutic lifestyle change, with repeat lipid panel in 3 months
B. Fenofibrate 145 mg daily
C. Simvastatin 40 mg daily
D. Extended-release niacin 500 mg qhs

Fibrate Therapy

- Per ATP III guidelines, if triglycerides exceed 500 mg/dL, initial treatment should be with a fibrate to decrease the risk of pancreatitis.
- Fenofibrate reduces CHD events but does not reduce total mortality (FIELD trial).
- Fenofibrate has a lower risk of myopathy when combined with statins; gemfibrozil is most appropriate if renal dysfunction is present.
- Statins, nicotinic acid, or omega-3 fatty acids are all appropriate when the triglycerides are elevated, but < 500 mg/dL.

10. Which one of the following statements regarding statin-associated myopathy is true?

A. A normal serum creatine kinase level excludes the diagnosis.
B. Serum creatine kinase levels should be routinely monitored in patients on statins.
C. Concomitant use of macrolide antibiotics increases the risk of myopathy in patients treated with simvastatin.
D. Combination therapy with a statin and ezetimibe (Zetia) increases the risk for myopathy.
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Statin-Related Muscle Complaints

- Include:
  - Statin myopathy (any muscle complaints related to these drugs)
  - Myalgia (muscle complaints without serum CK elevations)
  - Myositis (muscle symptoms with CK elevations)
  - Rhabdomyolysis (markedly elevated CK levels, usually > 10X ULN), with elevated creatinine consistent with pigment-induced nephropathy

Statin-Related Muscle Complaints

- Lovastatin, simvastatin and atorvastatin are primarily metabolized by CYP 3A4.
- Fluvastatin and rosuvastatin are metabolized by 2C9.
- Pravastatin has minimal 3A4 metabolism and is mainly cleared by the kidneys.
- CYP 3A4 activity can vary 10-fold among patients.
- Medications that inhibit 3A4 can increase statin levels and risk of rhabdomyolysis.

Statin-Related Muscle Complaints

- Common medications that increase risk of statin-associated myopathy:
  - Fibric acid derivatives, especially gemfibrozil
  - Niacin
  - Cyclosporine
  - Azole antifungals
  - Macrolide antibiotics
  - Human immunodeficiency virus protease inhibitors
  - Nelfazodone
  - Verapamil and diltiazem
  - Amiodarone
  - Grapefruit juice, > 1 quart per day

Statin-Related Muscle Complaints

- Ezetimibe can be used in combination with statins without increasing the risk of myopathy.
- Routine measurement of CK levels in asymptomatic patients before or during statin treatment is not required, although some experts recommend baseline CK measurement.
### References: Hyperlipidemia


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### Answers

1. B  
2. C  
3. B  
4. D  
5. B  
6. E  
7. D  
8. A  
9. B  
10. C