Cholesterol Overview

Why is cholesterol important?

Prevention of Coronary Heart Disease (CHD)

“Evidence over the past decades have linked elevated total and LDL cholesterol and reduced HDL to the development of CHD”.¹

Cholesterol is essential for cell membrane formation, bile acid formation, and hormone production.² Triglycerides are the most common type of fat in the body and are an important source of stored energy.² Phospholipids provide structure and protection for cellular function and lipid transportation.² Together, they form lipoproteins.²

The three major lipoproteins in the blood are high-density lipoproteins (HDL), very-low-density lipoproteins (VLDL), and low-density lipoproteins (LDL).¹ Total cholesterol is composed of approximately 20-30% HDL, 10-15% VLDL, and 60-70% LDL.¹ Tagged as the
“good cholesterol”, HDL is desirable due to its function of transporting cholesterol from vascular tissue back to the liver. VLDL and LDL are considered the “bad cholesterol” because they contribute to the development of atherosclerosis. LDL encompasses the majority of total cholesterol, thus making it the primary target of therapy.

What are normal lipid panel values?1
- Total cholesterol: <200 mg/dL
- LDL cholesterol: <100 mg/dL
- HDL cholesterol: >40 mg/dL
- Triglycerides: <150 mg/dL

What are risk factors for dyslipidemia?1
- Age
  - Male: ≥45 years
  - Female: ≥55 years
- Family history of premature CHD or diabetes
- HTN (≥140/90 mmHg or on anti-HTN medication)
- Cigarette smoking
- Low HDL (below 40 mg/dL)

References:

Diet

- 2013 AHA/ACC Lifestyle Management Guideline Recommendations1:
  - Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils, and nuts
- The DASH dietary pattern1
  - High in vegetables, fruits, low-fat dairy products, whole grains, poultry, fish, and nuts
  - Low in sweets, sugar-sweetened beverages, and red meats
  - Low in saturated fat, total fat, and cholesterol
  - Rich in potassium, magnesium and calcium, as well as protein and fiber
- My Plate2
  - MyPlate is a reminder to find your healthy eating style and build it throughout your lifetime. Everything you eat and drink matters. The right mix can help you be healthier now and in the future.
- Sodium Intake1
  - Total salt intake for any patient is less than 2,400mg (~1 teaspoon)/day
  - If patient also has high BP, further sodium restriction (<1500 mg/day) is desirable

References:
Physical Activity

- Exercise reduces LDL-C and non-HDL-C
- Moderate to vigorous aerobic physical activity
- 40 minutes per session, 3-4 times a week
  - Small incremental steps to build to overall goal
  - Recommend overweight patients to lose 10% of body weight

Guide to Common Physical Activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>Calories Burned per 30 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking causally (2 mph)</td>
<td>85</td>
</tr>
<tr>
<td>Walking quickly (4 mph)</td>
<td>170</td>
</tr>
<tr>
<td>Jogging (5 mph)</td>
<td>275</td>
</tr>
<tr>
<td>Gardening</td>
<td>135</td>
</tr>
<tr>
<td>Bicycling (10 mph)</td>
<td>205</td>
</tr>
<tr>
<td>Swimming</td>
<td>240</td>
</tr>
</tbody>
</table>

*Miles per hour (mph)

Drugs Contributing to Abnormal Lipid Panels

There are a number of drugs that are able to adversely affect lipid panels. Several of these drugs/drug classes are widely used and may often be used alongside lipid-lowering medications to reduce cardiovascular risk (i.e. diuretics, beta-blockers, etc.). Included in the table below are drugs/drug classes and their adverse effects on total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG).

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>TC</th>
<th>LDL</th>
<th>HDL</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop/Thiazide-type Diuretics</td>
<td>↑5-10%</td>
<td>↑5-10%</td>
<td>-</td>
<td>↑5-15%</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>-</td>
<td>-</td>
<td>↑5-20%</td>
<td>↑10-40%</td>
</tr>
<tr>
<td>Alpha-Blockers</td>
<td>↓5%</td>
<td>↓5%</td>
<td>↑2-5%</td>
<td>↓4-14%</td>
</tr>
<tr>
<td>Estrogen Monotherapy</td>
<td>↓2-10%</td>
<td>↓7-20%</td>
<td>↑10-20%</td>
<td>↑40%</td>
</tr>
<tr>
<td>Selective Estrogen Receptor Modulators (SERMs)</td>
<td>↓5-15%</td>
<td>↓10-20%</td>
<td>-</td>
<td>↑0-30% (tamoxifen)</td>
</tr>
<tr>
<td>Retinoids (isotretinoin)</td>
<td>↑15%</td>
<td>↑15%</td>
<td>-</td>
<td>↑35-144%</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>↑10-40%</td>
<td>↑10-50%</td>
<td>↑10-90%</td>
<td>↑10-70%</td>
</tr>
<tr>
<td>Protease Inhibitors (Ritonavir)</td>
<td>↑30-40%</td>
<td>n/a</td>
<td>-</td>
<td>↑1200-300%</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↑10-50%</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>↑0-20%</td>
<td>n/a</td>
<td>↑ or ↓</td>
<td>-</td>
</tr>
</tbody>
</table>

No change (-); Not available (n/a)

References:
# Pharmacotherapy Overview

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Generic Available*</th>
<th>Effects on Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors</strong></td>
<td>Lipitor®, Lescol® XL, Mevacor®/Altoprev®, Livalo®, Pravachol®, Crestor®, Zocor®</td>
<td>atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin</td>
<td>Yes</td>
<td>High intensity LDL: ↓≥50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>Mod. Intensity LDL: ↓30-50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>Low Intensity LDL: ↓&lt;30%</td>
</tr>
<tr>
<td><strong>Fibric Acid Derivatives</strong></td>
<td>Trilipix®, Lopid®, Atromid-S®</td>
<td>fenofibrate, gemfibrozil, clofibrate</td>
<td>Yes, Yes, No</td>
<td>LDL: ↓15-27%, HDL: ↑10-30%, TG: ↓30-60%</td>
</tr>
<tr>
<td><strong>Bile Acid Sequestrants</strong></td>
<td>Prevalite®, Welchol®, Colestid®</td>
<td>cholestyramine, colesvelam, colestipol</td>
<td>Yes, No, No</td>
<td>LDL: ↓15-30%, HDL: ↑3%, TG: ↓3-10%</td>
</tr>
<tr>
<td><strong>Nicotinic Acid</strong></td>
<td>Niacor®</td>
<td>niacin, niacin ER</td>
<td>Yes, Yes</td>
<td>LDL: ↓15-30%, HDL: ↑20-35%, TG: ↓30-60%</td>
</tr>
<tr>
<td><strong>Cholesterol Absorption Inhibitor</strong></td>
<td>Zetia®</td>
<td>ezetimibe</td>
<td>No</td>
<td>LDL: ↓18-22%, HDL: ↑0-2%, TG: ↓0-5%</td>
</tr>
<tr>
<td><strong>Omega-3 Ethyl Esters</strong></td>
<td>Lovaza®, Vascepa®</td>
<td>omega-3 fatty acids</td>
<td>Yes, No</td>
<td>LDL: ↑35-45%, TG: ↓30-60%</td>
</tr>
<tr>
<td><strong>PCSK9 Inhibitors</strong></td>
<td>Praluent®, Repatha®</td>
<td>alirocumab, evolocumab</td>
<td>No, No</td>
<td>LDL: ↓50-52%</td>
</tr>
<tr>
<td><strong>Microsomal Triglyceride Transfer Protein (MTP) Inhibitor</strong></td>
<td>Juxtapid®</td>
<td>lomitapide</td>
<td>No</td>
<td>LDL: ↓40-50%, HDL: ↑0-1%</td>
</tr>
<tr>
<td><strong>Oligonucleotide Inhibitor</strong></td>
<td>Kynamro®</td>
<td>mipomersen</td>
<td>No</td>
<td>LDL: ↓~47%, HDL: ↑8%, TG: ↓27%</td>
</tr>
<tr>
<td><strong>Combination Products</strong></td>
<td>Caduet®, Vytorin®</td>
<td>atorvastatin + amlodipine, simvastatin + ezetimibe</td>
<td>No, No</td>
<td>LDL: ↓30-50%</td>
</tr>
</tbody>
</table>

References:

Update - (Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors)

**Praluent® (alirocumab)**

Praluent®, a monoclonal antibody approved in July of 2015, exhibits its pharmacological effects by inhibition of PCSK9 binding to LDL-receptors.1,2 This mechanism of action is theorized to reduce degradation of the LDL receptor; therefore, more LDL receptors will be available to extract LDL from circulation.1,2

A study conducted by Cannon P, et al., compared alirocumab versus ezetimibe as add-on therapy to patients currently receiving statin therapy.1,3 Cannon P, et al., found that there was an approximately 50.6% reduction in LDL from baseline at 24 weeks when compared to ezetimibe add-on therapy, which achieved approximately 20.7% reduction from baseline.1,3 Based on these findings, it seems that Praluent® may be a reasonable option for patients who are on maximized doses of statins or who are unable to tolerate maximally indicated doses and unable to achieve LDL-C reduction goal based on ASCVD risk. Praluent®'s effects on reduction of cardiovascular risk have yet to be determined.1,2

Current data indicates that Praluent® seems to be well tolerated in patients with most common ADRs including: allergic reaction and injection site reaction.1,2 Praluent® is administered every two weeks subcutaneously, which may be appealing to patients with suspected adherence limitations.1,2 The limiting factor for use in most patients will be related to cost. Medication cost per month is approximately $1300.4

**Repatha® (evolocumab)**

Similar to Praluent®, Repatha® is a monoclonal antibody approved in August of 2015. Repatha® also exhibits pharmacological action due to inhibition of PCSK9 binding to LDL-receptors.1,2 Current indications of Repatha® are add-on pharmacotherapy to LDL-lowering medications for patients who require additional lipid lowering.1,2

Stroes, et al., conducted a study targeting patients who were intolerant to multiple statins and only able to receive low-dose statins or none at all. Their study found that Repatha® demonstrated reductions in LDL of approximately 55% as compared to ezetimibe, which demonstrated LDL lowering effects of approximately 17%.1,5 Available studies have not determined Repatha®'s effects on cardiovascular risk reduction; therefore, Repatha® is indicated as adjunct to statin therapy or monotherapy for patients unable to tolerate statin therapy.1,2

Most common ADRs associated with Repatha® use are similar to that of Praluent®, presenting in allergic-type reactions and increased incidence of upper
respiratory tract infections. Repatha® in comparison to Praluent® is dosed subcutaneously every two weeks or once monthly. Similar to Praluent, cost will be a major factor limiting utilization of Repatha® with monthly cost of approximately $1400.4

A recent study published by Kazi DS, et al. found that the PCSK9 inhibitors are not cost-effective as compared with current therapy. Their study determined, based on 2015 wholesale price, that both PCSK9 inhibitors are approximately $14,000/year in cost and that the medication cost would have to decrease by over two-thirds to $4536 to become cost-effective. For now it seems that PCSK9 inhibitors may continue to play a secondary role in therapy; at least, for the foreseeable future.

References:


The last “dose” …

“I drive way too fast to worry about cholesterol.”
– Steven Wright [American comedian, 1955 - ]