Drugs for Lipid Disorders
Lipids and Cardiovascular Disease

• Hyperlipidemia
  – High levels of lipids in blood—major risk factor for cardiovascular disease
  – Most patients asymptomatic until cardiovascular disease produces symptoms
Lipids and Cardiovascular Disease

• Hyperlipidemia
  – Genetic and lifestyle contributors
    ▪ Diets high in saturated fat and lack of exercise contribute
    ▪ Genetics determines ability to metabolize lipids
Terms for Lipid Disorders

- Hyperlipidemia
  - High levels of lipids in the blood

- Hypercholesterolemia
  - Elevated blood cholesterol

- Dyslipidemia
  - Abnormal levels of lipoproteins, excess or deficient
Three Types of Lipids

- Triglycerides
- Phospholipids
- Steroids
Triglycerides

- Neutral fat
- Three fatty acids attached to glycerol
- Energy source
- Account for 90% of total lipids in body
Phospholipids

• Essential to building plasma membranes
• Best-known phospholipids are lecithins
• Not proven effective against high cholesterol
Steroids

- Common chemical structure is steroid nucleus or ring structure
Steroids

• Cholesterol most widely known of the steroids
  – Natural and vital component of plasma membranes
  – Necessary for production of
    ▪ Vitamin D, bile acids
    ▪ Cortisol, estrogen, progesterone, testosterone
  – Body makes about 75% of cholesterol needed
  – Remaining 25% comes from diet (animal products)
    ▪ Limit < 300 mg/day
Lipoproteins

• Carriers of lipid molecules
• Consist of cholesterol, triglycerides, and phospholipids with protein carrier
• Protein carrier is known as apoprotein
• Three types: high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL)
Low-Density Lipoprotein

- LDL transports cholesterol from liver to tissues and organs
  - Used to build plasma membranes and synthesize other steroids
- Carries highest amount of cholesterol
- “Bad” cholesterol
  - Contributes to plaque deposits and coronary artery disease
Very Low-Density Lipoprotein

- VLDL is primary carrier of triglycerides in blood
- Through bodily processes becomes LDL
High-Density Lipoproteins

• Manufactured in liver and small intestine

• Reverse cholesterol transport
  – Assist in transport of cholesterol away from body tissues and back to liver

• “Good” cholesterol
  – Transport cholesterol for destruction and removal from body
Figure 23.1 Composition of lipoproteins: (a) HDL
Figure 23.1 (continued) Composition of lipoproteins: (b) LDL
Figure 23.1 (continued) Composition of lipoproteins: (c) VLDL
# Table 23.1 Standard Laboratory Lipid Profiles

<table>
<thead>
<tr>
<th>Type of Lipid</th>
<th>Laboratory Value (mg/dL)</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>Less than 200</td>
<td>Desirable</td>
</tr>
<tr>
<td></td>
<td>200–240</td>
<td>Borderline high risk</td>
</tr>
<tr>
<td></td>
<td>Greater than 240</td>
<td>High risk</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Less than 100</td>
<td>Optimal</td>
</tr>
<tr>
<td></td>
<td>100–129</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td></td>
<td>130–159</td>
<td>Borderline high risk</td>
</tr>
<tr>
<td></td>
<td>160–189</td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td>Greater than 190</td>
<td>Very high risk</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Less than 40 (men) or</td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>50 (women)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Greater than 60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Greater than 60</td>
<td>Desirable</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>Less than 150</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>150–199</td>
<td>Borderline high risk</td>
</tr>
<tr>
<td></td>
<td>200–499</td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td>Greater than 500</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

Lifestyle Changes

• Should always be included in any treatment plan for reducing blood lipid levels

• Many patients can control dyslipidemia entirely through nonpharmacologic means
Lifestyle Changes

- Monitor blood-lipid levels
- Maintain weight
- Implement a medically supervised exercise plan
- Reduce dietary saturated fats, trans fats, and cholesterol
- Increase soluble fiber in diet
- Eliminate tobacco use
### Table 23.2 Drugs for Dyslipidemias

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route and Adult Dose (max dose where indicated)</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-COA REDUCTASE INHIBITORS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>atorvastatin (Lipitor)</td>
<td>PO: 10–80 mg daily</td>
<td>Headache, dyspepsia, abdominal cramping, myalgia, rash or pruritus</td>
</tr>
<tr>
<td>fluvastatin (Lescol)</td>
<td>PO: 20–80 mg daily</td>
<td></td>
</tr>
<tr>
<td>lovastatin (Altoprev, Mevacor)</td>
<td>PO: 10–80 mg daily (immediate release); 20-60 mg daily (extended release)</td>
<td>Rhabdomyolysis, severe myositis, elevated hepatic enzymes</td>
</tr>
<tr>
<td>pitavastatin (Livalo)</td>
<td>PO: 1–4 mg daily</td>
<td></td>
</tr>
<tr>
<td>pravastatin (Pravachol)</td>
<td>PO: 10–80 mg daily</td>
<td></td>
</tr>
<tr>
<td>rosuvastatin (Crestor)</td>
<td>PO: 5–40 mg daily</td>
<td></td>
</tr>
<tr>
<td>simvastatin (Zocor)</td>
<td>PO: 5–40 mg daily</td>
<td></td>
</tr>
<tr>
<td><strong>BILE ACID SEQUESTRANTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cholestyramine (Questran)</td>
<td>PO: 4–8 g bid–qid (max: 24 g/day)</td>
<td>Constipation, nausea, vomiting, abdominal pain, bloating, dyspepsia</td>
</tr>
<tr>
<td>colestervelam (Welchol)</td>
<td>PO: 1.875 g bid (max: 3.75 g/day)</td>
<td></td>
</tr>
<tr>
<td>colestipol (Colestid)</td>
<td>PO: 5–20 g daily in divided doses</td>
<td>Gastrointestinal (GI) tract obstruction, vitamin deficiencies due to poor absorption</td>
</tr>
<tr>
<td><strong>FIBRIC ACID DRUGS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fenofibrate (Lofibra, Tricor, others)</td>
<td>PO: 54 mg daily (max: 200 mg/day)</td>
<td>Myalgia, flulike syndrome, nausea, vomiting, increased serum transaminase and creatinine levels</td>
</tr>
<tr>
<td>fenofibric acid (Fibrinor, Trilipix)</td>
<td>PO: (Fibrinor: regular release): 35–105 mg once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PO: (Trilipix: delayed release): 45–135 mg once daily</td>
<td></td>
</tr>
<tr>
<td>gemfibrozil (Lopid)</td>
<td>PO: 600 mg bid (max: 1,500 mg/day)</td>
<td>Rhabdomyolysis, cholelithiasis, pancreatitis</td>
</tr>
</tbody>
</table>
Table 23.2 Drugs for Dyslipidemias

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route and Adult Dose (max dose where indicated)</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OTHER DRUGS FOR DYSLIPIDEMIAS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aliocumab (Praluent)</td>
<td>Subcutaneous: 75–150 mg every 2 wk</td>
<td><em>Itching, swelling, pain, or bruising at injection site,</em> <em>nasopharyngitis,</em> <em>flu</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hypersensitivity reactions</em></td>
</tr>
<tr>
<td>evolocumab (Repatha)</td>
<td>Subcutaneous: 140 mg every 2 wk</td>
<td><em>Nasopharyngitis, influenza,</em> <em>back pain</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hypersensitivity reactions</em></td>
</tr>
<tr>
<td>ezetimibe (Zetia)</td>
<td>PO: 10 mg daily</td>
<td><em>Arthralgia,</em> <em>fatigue,</em> <em>upper respiratory tract infection,</em> <em>diarrhea,</em> <em>elevation of hepatic enzymes</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Rhabdomyolysis</em></td>
</tr>
<tr>
<td>icosapent (Vascepa)</td>
<td>PO: 4 g daily with food</td>
<td><em>Arthralgia</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hypersensitivity</em></td>
</tr>
<tr>
<td>lomitapide (Juxtapid)</td>
<td>PO: 5–60 mg once daily</td>
<td><em>Abdominal pain,</em> <em>diarrhea,</em> <em>nausea,</em> <em>vomiting,</em> <em>dyspepsia,</em> <em>reduced absorption of fat soluble vitamins and fatty acids</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Fetal toxicity,</em> <em>hepatotoxicity</em></td>
</tr>
<tr>
<td>mipomersen (Kynamro)</td>
<td>Subcutaneous: 200 mg once weekly</td>
<td><em>Injection site reactions,</em> <em>flu-like symptoms,</em> <em>nausea and headache</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hepatotoxicity and elevations in serum transaminases</em></td>
</tr>
<tr>
<td>niacin (Niaspan)</td>
<td>Hyperlipidemia: PO: 1.5–3 g daily in divided doses (max: 6 g/day) Niacin deficiency: PO: 10–20 mg daily</td>
<td><em>Flushing,</em> <em>nausea,</em> <em>pruritus,</em> <em>headache,</em> <em>bloating,</em> <em>diarrhea</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Dysrhythmias</em></td>
</tr>
<tr>
<td>omega-3-acid ethyl esters (Lovaza)</td>
<td>PO: 4 g daily with food</td>
<td><em>Eructation,</em> <em>dyspepsia,</em> <em>fishy taste</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Hypersensitivity</em></td>
</tr>
</tbody>
</table>

Note: *Italics* indicate common adverse effects; *underlining* indicates serious adverse effects.
**Statins**

- Interfere with the synthesis of cholesterol
- First drugs of choice to reduce blood-lipid levels
- **Examples**: atorvastatin (Lipitor), fluvastatin (Lescol), lovastatin (Mevacor), rosuvastatin (Crestor), simvastatin (Zocor)
Figure 23.2 Cholesterol biosynthesis and excretion
HMG-CoA Reductase Inhibitors/Statins

- **Prototype drug**: atorvastatin (Lipitor)
- **Mechanism of action**: inhibits HMG-CoA reductase
- **Primary use**: reduces serum-lipid levels
- **Adverse effects**: headache, fatigue, muscle or joint pain, and heartburn, rarely rhabdomyolysis
Prototype Drug | Atorvastatin (Lipitor)

Therapeutic Class: Antihyperlipidemic  Pharmacologic Class: HMG-CoA reductase inhibitor, statin

**Actions and Uses**
The primary indication for atorvastatin is hypercholesterolemia. The statins act by inhibiting HMG-CoA reductase. As the liver makes less cholesterol, it responds by making more LDL receptors on the surface of liver cells. The greater number of LDL receptors in liver cells results in increased removal of LDL from the blood. Blood levels of both LDL and cholesterol are reduced, although at least 2 weeks of therapy is required before these effects are realized. To enhance the drug's therapeutic effects, patients receiving atorvastatin should be placed on a cholesterol-lowering diet. The primary goal in atorvastatin therapy is to reduce the risk of myocardial infarction (MI) and stroke.

**Administration Alerts**
- Administer with food to decrease GI discomfort.
- May be taken at any time of the day.
- Pregnancy category X.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 wk for lipid-lowering effect</td>
<td>1–2 h</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

**Adverse Effects**
Adverse effects of atorvastatin rarely cause discontinuation of therapy. Headache and GI complaints such as intestinal cramping, diarrhea, and constipation are common during therapy. A small percentage of patients experience liver damage; thus, hepatic function is monitored during the first few months of therapy. The most serious adverse effect is rhabdomyolysis.

**Contraindications:** Contraindications include serious liver disease, unexplained persistent elevations of serum transaminases, and prior hypersensitivity to the drug.

**Interactions**
**Drug–Drug:** Atorvastatin interacts with many other drugs. Azole antifungals, HIV protease inhibitors, and telaprevir are contraindicated due to an increased risk for myopathy and rhabdomyolysis. Atorvastatin may increase levels of digoxin and oral contraceptives containing norethindrone and ethinyl estradiol. Erythromycin may increase atorvastatin levels 40%. Risk of rhabdomyolysis increases with concurrent administration of atorvastatin with macrolide antibiotics, cyclosporine, and niacin. Ethanol should be avoided during therapy because of its effects on hepatic function.

**Lab Tests:** May increase serum transaminase and creatine kinase levels.

**Herbal/Food:** Grapefruit juice inhibits the metabolism of statins, allowing them to reach toxic levels. Red yeast rice contains small amounts of natural statins and may increase the effects of atorvastatin. Because statins also decrease the synthesis of coenzyme Q10 (CoQ10), patients may benefit from CoQ10 supplements. Manifestations of CoQ10 deficiency include high blood pressure, congestive heart failure, and low energy.

**Treatment of Overdose:** There is no specific treatment for overdose.
Bile Acid Sequestrants

• Bind with bile acids to increase excretion of cholesterol in stool
• Used in combination with statins
• **Examples**: colesevelam (Welchol), colestipol (Colestid)
Bile-Acid Resins

• **Prototype drug**: cholestyramine (Questran)

• **Mechanism of action**: bind with bile acids, increasing cholesterol excretion in stool

• **Primary use**: to lower serum-lipid levels
Bile-Acid Resins

- **Adverse effects**: GI tract, such as bloating and constipation
- Can bind other drugs, increasing potential for drug–drug interactions
Prototype Drug | Cholestyramine (Questran)

**Therapeutic Class:** Antihyperlipidemic  **Pharmacologic Class:** Bile acid sequestrant

**Actions and Uses**
Cholestyramine is a powder that is mixed with fluid before being taken once or twice daily. It is not absorbed or metabolized once it enters the intestine; thus, it does not produce any systemic effects. It may take 30 days or longer to produce its maximum effect. Questran binds with bile acids (containing cholesterol) in an insoluble complex that is excreted in the feces. Cholesterol levels decline due to fecal loss.

**Administration Alerts**
- Mix thoroughly with 60 to 180 mL of water, noncarbonated beverages, highly liquid soups, or pulpy fruits (applesauce, crushed pineapple). Have the patient drink it immediately to avoid potential irritation or obstruction in the GI tract.
- Give other drugs more than 2 hours before or 4 hours after the patient takes cholestyramine.
- Pregnancy category C.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>24–48 h</td>
<td>1–3 wk</td>
<td>2–4 wk</td>
</tr>
</tbody>
</table>

**Adverse Effects**
Although cholestyramine rarely produces serious side effects, patients may experience constipation, bloating, gas, and nausea that sometimes limit its use.

**Contraindications:** This drug is contraindicated in patients with total biliary obstruction and in those with prior hypersensitivity to the drug.

**Interactions**
**Drug–Drug:** Because cholestyramine can bind to other drugs, such as digoxin, penicillins, thyroid hormone, and thiazide diuretics, and interfere with their absorption, it should not be taken at the same time as these other medications. Cholestyramine may increase the effects of anticoagulants by decreasing the levels of vitamin K in the body.

**Lab Tests:** Aspartate aminotransferase (AST), phosphorus, chloride, and alkaline phosphatase (ALP) levels may increase. Serum calcium, sodium, and potassium levels may decrease.

**Herbal/Food:** Taking cholestyramine with food may interfere with the absorption of the following essential nutrients: beta-carotene, calcium, folic acid, iron, magnesium, vitamin B₁₂, vitamin D, vitamin E, vitamin K, and zinc. Manifestations of nutrient depletion may include weakened immune system, cardiovascular problems, and osteoporosis.

**Treatment of Overdose:** There is no specific treatment for overdose.
Niacin (Nicotinic Acid)

- B-complex vitamin
- Niacin (Niaspan)
- Decreases VLDL levels
- Has numerous adverse effects: flushing, hot flashes, nausea, excess gas, diarrhea; more serious effects like hepatotoxicity and gout possible
Fibric-Acid Agents

- **Prototype drug**: gemfibrozil (Lopid)
- **Mechanism of action**: unknown
- **Primary use**: treating severe hypertriglyceridemia
- **Adverse effects**: GI distress, watch for bleeding with patients on anticoagulants
Prototype Drug | Gemfibrozil (Lopid)

**Therapeutic Class:** Antihyperlipidemic  **Pharmacologic Class:** Fibric acid drug (fibrate)

### Actions and Uses
Gemfibrozil is indicated for the treatment of hypertriglyceridermia and hypercholesterolemia. Effects of gemfibrozil include up to a 50% reduction in VLDL with an increase in HDL. The mechanism of achieving this action is unknown. It is less effective than the statins at lowering LDL; thus, it is not a drug of first choice for reducing LDL levels. Gemfibrozil is taken orally at 600 to 1,200 mg/day.

### Administration Alerts
- Administer with meals to decrease GI distress.
- Pregnancy category B.

### Pharmacokinetics

<table>
<thead>
<tr>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 h</td>
<td>1–2 h</td>
<td>2–4 months</td>
</tr>
</tbody>
</table>

### Adverse Effects
Gemfibrozil produces few serious adverse effects, but it may increase the likelihood of gallstones and may occasionally affect liver function. The most common adverse effects are GI related: dyspepsia, diarrhea, nausea, and cramping.

### Contraindications
Gemfibrozil is contraindicated in patients with hepatic impairment, severe renal dysfunction, or pre-existing gallbladder disease, or those with prior hypersensitivity to the drug.

### Interactions
**Drug–Drug:** Concurrent use of gemfibrozil with oral anticoagulants may potentiate anticoagulant effects. Concurrent use with statins should be avoided because this increases the risk of myopathy and rhabdomyolysis. Gemfibrozil may increase the effects of certain antidiabetic agents, statins, sulfonylureas, and vitamin K antagonists.

**Lab Tests:** May increase liver enzyme values, and CPK and serum glucose levels. May decrease hemoglobin (Hgb), hematocrit (Hct), and white blood cell (WBC) counts.

**Herbal/Food:** Fatty foods may decrease the efficacy of gemfibrozil.

### Treatment of Overdose
There is no specific treatment for overdose.
Cholesterol Absorption Inhibitor

• Ezetimibe (Zetia)

• Inhibits absorption of cholesterol in small intestine, resulting in small reduction in LDL

• Serious side effects uncommon; minor side effects nasopharyngitis, myalgia, upper respiratory tract infection, anthralgia, and diarrhea
23.1 | Mechanism of Action of Lipid-Lowering Drugs

**Statin**
Interfere with HMG-CoA reductase, the critical enzyme in the biosynthesis of cholesterol

**Niacin**
Decreases both VLDL and LDL levels

**Bile acid sequestrants**
Bind bile acids, thus increasing the excretion of cholesterol in the stool

**Ezetimibe**
Blocks the absorption of cholesterol from the small intestine
Role of Nurse

• Monitor patient's condition
• Provide education on prescribed medications
• Assess patient's triglyceride, total cholesterol, LDL, and HDL levels
Statins

- Monitor liver function tests
- Do not use with pregnancy or breastfeeding
- Watch for signs of GI upset
Bile-Acid Resins

- Monitor for significant GI effects
- Obtain careful history for past GI disorders
Niacin (Nicotinic Acid)

- Monitor patient's liver function
- Monitor uric acid levels, if predisposed to gout
- Monitor blood-sugar levels, if diabetic
Fibric-Acid Agents

• Assess for complaints of GI distress before starting drug
• Use with warfarin may potentiate anticoagulant effects
  – Monitor prothrombin time/international normalized ratio (PT/INR)
Drugs for Lipid Disorders

• Assessment
  – Obtain blood samples
  – Assess laboratory tests: triglyceride, total cholesterol, LDL, HDL levels
  – Collect patient's height and weight
  – Obtain nursing history: lifestyle, current drugs, dietary habits
  – Assess patient's and family's knowledge
Drugs for Lipid Disorders

• Nursing Diagnoses
  – Deficient Knowledge (drug therapy)
  – Ineffective Health Management
  – Risk for Bleeding
Drugs for Lipid Disorders

• Planning
  – Goals for patient
    ▪ To reduce serum-lipid levels
    ▪ Ability to explain hyperlipidemia
    ▪ Ability to verbalize how to follow therapy
Drugs for Lipid Disorders

• Implementation
  – Encourage compliance with medication regimen
  – Provide education regimen
Drugs for Lipid Disorders

• Evaluation
  – Ideal outcome criteria
    ▪ Lowered serum-lipid levels
    ▪ No organ damage, no injury
    ▪ Patient verbalizes importance of prescribed medications