



A PHARMACY CONTINUING EDUCATION PROGRAM

W-F Professional Associates, Inc. 400 Lake Cook Rd., Suite 207 Deerfield, IL 60015 847-945-8050

February 2009 "Pharmacy Guide & Review---Cholesterol Management" #707-000-09-002-H01-P

31st Year



THIS MONTH  
"Cholesterol  
Management"

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**Cholesterol Management** is one of those topics that you continue to tell us is significantly important. One reason is because it is covered so much in the consumer media. Therefore, we as pharmacists must be prepared to share understandable & current information with patients. These are the reasons that we review this topic quite often. Additionally, the statins have become one of the largest prescribed drug classes. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-09-002-H01-P. Pharmacists completing this lesson by February 29, 2012 may receive full credit.**

**To obtain continuing education credit for this lesson**, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page (for continuous participants only).**

**The objectives of this lesson are such that upon completion the participant will be able to:**

1. Name & describe the plasma lipids.
2. List the types of lipoproteins.
3. Discuss cholesterol transport, metabolism & regulation within the plasma.
4. Comment upon the guidelines for lipid blood levels.
5. Describe drug & nondrug treatments for hyperlipidemia.

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There is a misconception among a portion of the general public that cholesterol and other plasma lipids are harmful substances that trigger many disorders. While elevated levels are a concern for cardiovascular disease (coronary heart disease, CHD), normal levels are important in maintaining routine body functions such as providing energy to many tissues of the body, maintaining regular body temperature, and serving as a chemical precursor to substances required by the body such as hormones, adrenal corticoids, and vitamin D. Despite improvement in lifestyle and the use of cholesterol-lowering medications, CHD and strokes remain principle causes of death in the U.S.

### CONSTITUENTS OF PLASMA LIPIDS

Plasma lipids consist of the following main components: **sterols, triglycerides, fatty acids, and phospholipids.**

#### **Sterols, (Cholesterol and Ester Cholesterol)**

**Sterols** are found in plants (Phytosterols) and animals (Zoosterols), but are absent among bacteria. They differ from triglycerides in structure. Instead of hydrocarbon chains, sterols possess hydrogen rings. Cholesterol, the animal sterol, is a waxy alcohol with a fatty appearance and is present in body tissues including the brain, nerves, muscles, skin, liver, kidneys, intestines and most other internal organs. The word sterol is derived from steroid and alcohol. The term cholesterol comes from chola (bile), stereos (solid), and "ol" (alcohol). About 20% of cholesterol in the blood stream is produced by food, and 80% is synthesized by the body. The body uses only a small amount of cholesterol present in the blood to synthesize hormones, vitamin D and bile acids. If the unused cholesterol in the blood is excessive, it may be deposited in the arterial walls, especially the coronary arteries, leading to clogging and narrowing of the arteries that supply oxygen and nutrients to the heart. Clogging occurs as a result of deposition of atherosclerotic plaques, resulting in an increased risk of CHD and myocardial infarctions. On the other hand, studies have shown that plant sterols (campesterol, sitosterol, and stigmasterol) can cause a reduction in cholesterol in the plasma.

#### **Triglycerides**

Triglycerides consist of a molecule of glycerol together with fatty acids on each side of the –OH groups. It is the main component of vegetables and animal oils as well as fatty acids. It is present in blood plasma in association with cholesterol. The main sources of triglycerides are fats eaten in food or the carbohydrates that are not used immediately by the body and eventually are transformed to triglycerides that are stored as fat cells. Triglycerides may be released by the body as a source of energy. Such lipids exist in nature as solids (fats) or liquids (oils). This depends on room temperature, length of fatty acid chain, and the extent of the hydrogen bond saturation. Triglycerides with a short fatty acid chain and or unsaturated fatty acids exist as liquids at room temperature (i.e., plant oils like olive oil, corn oil, etc.). Those with long fatty chains and or saturated fatty acids, exist in solid form at room temperature (i.e., fat like butter, fat from meat, etc.)

#### **Fatty Acids**

Fatty acids are aliphatic monocarboxylic acids usually with a long straight aliphatic chain. They are either saturated or unsaturated. When not attached to other molecules, they are known as free fatty acids. Carboxylic acid can be short—containing 4 carbon atoms (butyric acid), or long—derived from natural oil fats that usually contain from 8 to 28 carbon atoms (i.e. caprylic, oleic, stearic, linoleic and linolenic acids). They are formed from the hydrolysis of the ester linkage of triglycerides found in animal or vegetable fat, oil or wax. The human body produces all of the required fatty acids except for linoleic and linolenic, which are formed in plant oils. These acids are essential for the human body which cannot synthesize them, hence the name essential fatty acids. Omega-3 oil and the fatty acids eicosapentaenoic and docosahexaenoic acids are contained in fish oils. Essential fatty acids are necessary for proper functioning of the immune system, formation of prostaglandins that assist in blood pressure regulation, and control of mechanical and electrical processes of the heart. Trans fatty acids contain a trans double bond between carbon atoms. Such bonds occur when plant oils are hydrogenated. It has been shown that trans fats raise the LDL cholesterol (harmful), lower HDL (useful) cholesterol, and increase triglycerides and lipoprotein.

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### Phospholipids

A phospholipid consists of a triglyceride, a phosphate group, and an organic molecule such as choline, (e.g. lecithin). These compounds are the main constituents of biological membranes. Within the cell, they form a lipid bilayer (a head that is hydrophilic and a hydrophobic tail).

The major components of an atherosclerotic plaque, also known as atheroma, are cholesterol, cholesterol esters and other lipids. The initial plaque is deposited in the smooth cells of the inner coat of large and medium-sized arteries. Lipoprotein, especially LDL, adheres to the smooth muscle cells, causing them to proliferate. The smooth muscle cells also produce collagen, elastin, and other proteins that become components of the plaque. The presence of collagen results in the accumulation of fibrotic tissue. The plaque will not only reduce the flow of oxygenated blood and nutrient to the heart muscle, but if unstable it may break away to produce a nonocclusive or occlusive blood clot, that may lead to myocardial infarction or death. The higher the cholesterol blood level, the higher the risk of CHD, responsible for over 500,000 deaths annually in the U.S.

### LIPID TRANSPORT

All lipids in the blood stream do not exist in the free form. Cholesterol and other lipids do not mix with water. Consequently, they are unable to travel in the blood stream. To facilitate their transport, lipids and cholesterol bind to plasma protein (i.e., albumin, globulin) to form a complex known as lipoproteins. This lipoprotein carries cholesterol through the circulation. The lipoprotein complexes are composed of spheres that are smaller than red blood cells. Each sphere is composed of an inner core of hydrophilic lipid (cholesterol, cholesteryl esters and triglycerides) surrounded by an outer core of protein that acts as the interface between the plasma and the lipid core. Because the protein portion of the outer core is hydrophilic in nature, the entire sphere becomes dispersible or soluble in the aqueous blood plasma, and is transportable.

### TYPES OF LIPOPROTEINS

There are three distinct types of lipoproteins: **1) very low-density lipoproteins (VLDL)** have an inner core that consists mainly of triglycerides; **2) low-density lipoproteins (LDL)** consist of a predominantly cholesterol inner core; and, **3) high-density lipoproteins (HDL)** that have a total lipid content slightly less than the weight of protein in the outer membrane and, consequently, its density is high. The inner core of HDL is made of cholesterol.

### Chylomicrons

These are the largest lipoproteins and possess the lowest density. They consist of 85%-95% triglycerides and 3%-7% cholesterol. Their main function is to transport digested triglycerides in food from the intestines via the thoracic duct to the bloodstream. The majority of chylomicrons are cleared from the blood by the enzyme lipoprotein lipase after 12 to 14 hours. The glycerol produced as a result of the breakdown of chylomicrons penetrates the cells for providing energy or storage for later use.

### Very Low-Density Lipoproteins (VLDL)

This lipoprotein is produced endogenously in the liver and consists of 50%-65% glycerols, and 20%-30% cholesterol. Its main function is to transport triglycerides synthesized in the liver to adipose and muscular tissues. After the transport process has been completed, the residues of the VLDLs are converted to LDL. Elevated levels of VLDL may contribute to the development of atherosclerosis.

### Low-Density Lipoproteins (LDL)

Production of LDLs occurs as a result of the breakdown or metabolism of VLDL. They consist of 51%-58% cholesterol and 4%-8% triglyceride. This lipoprotein carries most of the cholesterol in the blood and accounts for 60%-75% of all plasma cholesterol. LDLs are considered the most harmful of the lipoproteins. The main function of LDL is to deliver cholesterol to the liver and peripheral tissues. Absorption of LDL by tissue cells is accomplished by means of endocytosis (engulfment), and requires the presence of LDL receptors on the cell surface. As the cell demands for cholesterol increase, the cell begins to synthesize more LDL receptors, thereby absorbing more LDL. However, if the cell fails to increase the formation of LDL receptors, then LDL absorption will be impaired. LDL has been associated with the development of atherosclerosis (unstable blockage made of a fatty plaque) and the development of CHD. Moreover, unstable plaques can break loose and form a clot that could lead to heart attacks and strokes. Reduction of LDL can result in a decrease in the development of CHD and regression of coronary atherosclerosis. The risk of CHD in men over 45 years of age increases when total plasma cholesterol is over 200mg/dl. Conversely, a 25% reduction in plasma LDL level may reduce the level of CHD by 50%.

### **High-Density Lipoprotein (HDL)**

HDL is the smallest and densest of lipoproteins. It consists of 18%-25% cholesterol and 2%-7% triglycerides. Normally, HDL contributes approximately 20%-30% of the total cholesterol in plasma. While LDL is responsible for delivery of cholesterol to tissues including liver, the function of HDL is to remove cholesterol (about 25% of blood cholesterol) from other tissues of the body. This removal process is useful in preventing the accumulation of cholesterol and lipids in the arterial wall. Physical exercise has been shown to increase the HDL level. In contrast to LDL and VLDL, a high level of HDL is beneficial and has been shown to reduce the incidence of CHD, thus provides protection from such diseases.

### **CHOLESTEROL METABOLISM & REGULATION**

About 20% of cholesterol in the blood stream is provided by food and 80% is synthesized by the body. Synthesized cholesterol contributes about 900-1000 mg of the total cholesterol pool, while the amount of cholesterol contributed by diet is 300-500 mg daily.

The enzyme lipoprotein lipase (LPL) is synthesized in fatty and muscular tissues. Its main function is to mediate the triglycerides of both chylomicrons and VLDL to release fatty acids that are deposited into the adjacent tissues where they are utilized for energy or stored as fat. Insulin plays a role in the synthesis and secretion of LDL. Thus, impaired synthesis of LDL caused by low levels of insulin, as in diabetes, can cause impaired triglyceride clearance.

The endogenous transport system is responsible for transferring the lipids from the liver to the peripheral tissues and from peripheral tissues back to the liver. Only 10% of the total cholesterol produced in the body originates from the liver. The remainder is synthesized by the peripheral tissues. Endogenous cholesterol production occurs as a result of enzymatically-mediated reactions such as the conversion of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) to mevalonic acid, which is catalyzed by HMG-CoA reductase enzyme. Once cholesterol is produced by the liver and peripheral tissues, it is released into the bloodstream in the form of VLDL, which rapidly becomes an intermediate density lipoprotein (IDL). Within 2 to 6 hours, IDL is either taken by liver receptors or remains in the circulation where it breaks down and loses more glycerides and becomes LDL. Therefore, the main source of LDL is VLDL.

Diet is the source of exogenous cholesterol. In industrialized societies, a normal individual consumes approximately 70-150 gm of fat and 0.5 gm of cholesterol during 3 meals. Usually, the body disposes of the circulating fat within 8 hours of the last meal. However, some individuals with dyslipidemia may have fat in their bloodstream for up to 24 hours after this last meal. Triglycerides are absorbed from the intestinal lumen where they are engulfed by chylomicron particles. The chylomicron carries the triglycerides from the intestines to the venous system. Once it reaches adipose and muscular tissues, the vast majority of chylomicron glyceride is hydrolyzed. The fatty acids and glyceride derived from the hydrolysis enter the cells as energy sources or are stored. Remnants of chylomicrons, which are mostly cholesterol-rich particles, are removed from the bloodstream by receptors located in the liver. This exogenously obtained cholesterol joins the endogenously synthesized cholesterol in the liver to be utilized in forming bile acids or incorporated into VLDL and then released into circulation where it is converted to LDL. About 60% of plasma LDL is removed by the liver and the remainder by active receptor sites located on fibroblasts and other cells that bind to the protein of LDL. A small quantity of LDL is believed to be removed by ingestion of scavenger macrophages that may reach arterial walls and form part of the atherosclerotic plaque.

### **GUIDELINES FOR THE EVALUATION AND TREATMENT OF HYPERLIPIDEMIA**

The National Institutes of Health (NIH) established a National Cholesterol Education Program (NCEP) whose guidelines were instituted in 1987, and the Adult Treatment Panel (ATP) of the NCEP periodically issues updated reports as warranted by newer advances to guide health care professionals for the testing, evaluation, monitoring and treatment of hyperlipidemia. The NCEP guidelines suggest that every person aged 20 years or older should have their blood lipids measured at least every 5 years. The most recent update was issued by ATP III in 2001. An important component of ATP guidelines is the development of treatment goals for hyperlipidemia based on patient's risk for CHD. ATP I established criteria for prevention of CHD in individuals with high levels of LDL ( $\geq 160$  mg/dl) or with borderline high LDL (130-159 mg/dl) and multiple (2+) risk factors. ATP II added criteria concerning the management of LDL in individuals with established CHD. For such persons, ATP II affirmed a new lower LDL goal of  $\leq 100$  mg/dl. The main part of ATP III is based on ATP I and ATP II, but placed emphasis on primary prevention in persons with multiple risk factors, as well as on more intensive LDL-lowering treatment. Patients with high risk for CHD will gain benefits from more aggressive LDL-lowering therapy than recommended in ATP II. The primary goal of ATP III is to lower LDL, since it has been shown that this results in reduction in the risk of CHD.

***ATP III classification of blood LDL levels, as well as total and HDL levels is as follows:*****LDL Cholesterol (mg/dl)**

≤ 100	Optimal
100- 129	Near or above optimal
130-159	Borderline high
160-189	High
≥ 190	Very High

**Total Cholesterol (mg/dl)**

< 200	Desirable
Borderline high,	risk for heart diseases
240	High risk for heart disease

**HDL Cholesterol (mg/dl)**

< 40	Low, high risk for heart disease
≥ 60	High, less risk for heart disease

**Triglycerides (mg/dl)**

< 150	Normal, low risk of heart disease
150-199	Borderline high, normal risk for heart disease
200-499	high, high risk for heart disease
> 500	Very high, very high risk for heart disease.

The ATP III included new aspects such as consideration of diabetes without CHD as equivalent to the risk factors of CHD; use of Framingham projection of 10-year absolute CHD risk; consideration of persons with multiple metabolic factors as candidates for intensified therapeutic lifestyle changes; recommendation for initial tests that include total, LDL and HDL cholesterol and triglycerides rather than that for total cholesterol; recommendation for the use of plant sterols and soluble fiber in diet to enhance lowering of LDL cholesterol; adherence to therapeutic lifestyles changes; and, treatment beyond LDL lowering in the presence of triglycerides of ≥ 200 mg/dl. ATP III includes the following major risk factors for atherosclerotic vascular disease: 1) cigarette smoking; 2) blood pressure ≥ 140/90 mm Hg; 3) low HDL (< 40 mg /dl); 4) family history of premature CHD; and, 5) age (men ≥ 45 years, women ≥ 55 years).

ATP III instituted recommendations regarding LDL levels at which to initiate therapeutic lifestyles changes, as well as LDL levels at which to consider drug therapies:

1. Persons with CHD or CHD risk equivalents (10-year risk > 20%) should attain an LDL level of < 100 mg/ dl. The LDL level at which to initiate therapeutic lifestyle changes (TLC) is ≥ 100 mg and the LDL levels at which to consider drug therapy is ≥ 130 mg/dl;
2. For persons with 2+ risk factors (10-year risk ≤ 20%), the LDL goal is < 130 mg/dl; the LDL level at which to initiate TLC is ≥ 130 mg/dl, and the LDL at which to consider drug therapy for 1-year risk 10 %- 20 % is ≥ 130 and for 10-year risk is ≥ 160mg/dl;
3. For persons with 0 – 1 risk factor, the LDL goal is < 160 mg/dl, and the LDL level at which to initiate TLC is ≥ 160 mg/dl and the LDL level of 160- 189 mg/dl, drug therapy is optional. It is important to realize that when LDL lowering drugs are utilized, one should maintain TLC.

**TREATMENT OF HYPERLIPIDEMIA**

ATP III recommends two methods of treatment: **1) therapeutic lifestyle changes (TLC);** and, **2) drug therapy.**

**1. Therapeutic Lifestyle Changes (TLC)**

The main causes of hyperlipidemia are: heredity, unhealthy diet, obesity, sedentary lifestyle, age, excessive alcohol consumption and mental stress.

**Heredity**

Familial hypercholesterolemia, which may lead to early heart disease, is influenced by acquired genes. These genes play an important role in determining how fast LDL is manufactured and removed. Drug therapy may be the only way for management of such hyperlipidemia.

**Unhealthy diet**

A healthy diet is an important element in the management of hyperlipidemia, especially that which is not due to heredity. Diet modification may lead to an acceptable blood level of cholesterol. The NCEP dietary guidelines are: total fat less than 30% of daily calories; polyunsaturated fat less than 7% of calories; polysaturated fat less than or equal to 10 % of calories; nonsaturated fat approximately 10-15 % of calories; cholesterol less than 200mg per day; and carbohydrate 50-60 % of calorie intake.

**Overweight**

Weight loss may help in lowering LDL levels and raising HDL levels.

### Regular Physical Exercise

This may lower triglycerides levels and increase those of HDL.

### Age

Cholesterol blood levels gradually increase until about the age of 60-65.

### Excessive Alcohol Consumption

Moderate alcohol consumption may increase HDL levels, but has no effect on lowering LDL. Excessive alcohol consumption may cause liver and heart muscle damage.

### Mental Stress

Extended mental stress may increase blood cholesterol levels. Cessation of smoking is highly recommended.

## 2. Drug Therapy

Diet, exercise and weight reduction may be inadequate to achieve the goals set by ATP III. High LDL, presence of risk factors, and documentation of CHD should justify instituting drug therapy along with TLC. Monotherapy has been shown to be effective in treating dyslipidemia, but combination therapy may be required for a comprehensive approach. There are a number of lipid-lowering drugs that are currently used most often: **1) Statins 2) Ezetimibe, 3) Bile acid sequestrants or bile binding resins, 4) Niacin, 5) Fibric acid derivatives, and 6) Plant sterols.**

### STATINS

The statins are considered the foundation for treatment, as they are well tolerated and possess a predominant effect on lowering LDL. These medications are useful for high-risk patients such as those with CHD and diabetes.

The mechanism of action by which the statins reduce LDL concentration is to competitively inhibit HMG- CoA reductase, the enzyme that catalyzes the rate-limiting step in hepatic cholesterol biosynthesis. Statins tend to cause an alteration in the formation of LDL.

In spite of their effectiveness and use in clinical practice, statins have a number of limitations that need to be taken into consideration. At the standard doses used, statins are capable of reducing LDL levels by 30%-40%. Studies have shown that when such doses are administered, the LDL levels of over 40% of high-risk patients failed to reach the ATP III LDL goal of < 100 mg/dl. Increasing the dose of statins has its disadvantages: 1) Doubling, tripling, and quadrupling the dose will result in only 6%, 12% and 18% respectively in LDL lowering; 2) the higher the dose of statin, the greater the potential for toxicity, the most serious of which is myopathy; and, 3) some patients have low-tolerance to higher doses due to the occurrence of adverse effects such as elevation of transaminase, weakness, fatigue and muscular pain.

Currently the following are the statins in use: lovastatin, pravastatin, simvastatin, fluvastatin, atorvastatin and rosuvastatin. Comparison of efficacy of these revealed that atorvastatin resulted in the highest reductions of LDL (42%), lovastatin and simvastatin, each (36%). Results of triglycerides reduction were atorvastatin (19%) simvastatin (13%) and lovastatin (12%). Serum HDL level increased by 5 %-6% with all five statins.

**Lovastatin (Mevacor®)** is partially absorbed from the GI tract and undergoes first-pass metabolism. Food appears to enhance the rate of absorption after oral administration. It is excreted in urine and feces. The main side effects involve the GI tract. They are usually transient, mild and include abdominal pain, inflammation, cramps, diarrhea, nausea, and dyspepsia. An increase in serum concentration of hepatic transaminase, as well as elevated creatine phosphokinase, may occur in some patients. Headache, rash and pruritus have been experienced.

Dosage should be determined in accordance with the requirements and response of the patient. The usual initial dose in adults is 20 mg daily given in the evening with dinner. The dose may be increased at an interval of 4 weeks or more until the desired lipoprotein concentration is achieved, or a maximum daily dose is reached. The usual maintenance dose is 10-80 mg daily given in a single or divided dose. Care must be exercised when giving lovastatin to patients with renal impairment due to its slow excretion in the urine.

**Pravastatin (Pravachol®)**: Side effects include nausea and/or vomiting, diarrhea, abdominal cramps, heartburn, flatulence, constipation, increased serum aminotransferase, muscular pain, headache, skin rash and increased serum creatine kinase. The usual initial dosage in healthy adults is 20 mg at bedtime, while that of individuals with renal or hepatic impairment and geriatric patients is 10 mg daily. The usual maintenance dose is 10-40 mg daily.

**Simvastatin (Zocor®)**: The most frequently encountered side effects include: abdominal discomfort, constipation, flatulence, nausea, dyspepsia, anorexia, heartburn, increased serum creatine kinase, rash and headache. The usual initial dose in adults is 20 mg daily at bedtime. A dosage of 10 mg daily is initiated until a maximum dosage of 80 mg daily is reached.

**Fluvastatin (Lescol®)**: The most encountered adverse effects include GI disturbances, back pain, headache, upper respiratory infections, a potentially serious increase in hepatic aminotransferase, myopathy, elevated creatine kinase concentration, rash and headache.

**Atorvastatin (Lipitor®):** Like fluvastatin, this drug is synthetically prepared and differs structurally from lovastatin, pravastatin, and simvastatin. Atorvastatin calcium is used to reduce elevated serum total, LDL and triglyceride concentrations. The drug is used orally without restriction to meal-type or time of day. It is contraindicated in patients with liver diseases.

Adult dosage should be personalized and adjusted within 2-4 weeks after the initial dose of 10 mg daily. The maintenance daily adult dose is 10-80 mg.

**Rosuvastatin (Crestor®):** Rosuvastatin is the newest marketed statin in the U.S. and is the most potent. It is effective in reducing high cholesterol level and useful when patients do not respond to other drugs.

#### **EZETIMIBE (Zetia®)**

Ezetimibe is the first drug of a new class to be used in the management of dyslipidemia. This drug, which was approved by the FDA in October 2002, appears to be effective as monotherapy for patients with a low risk of CHD, but cannot tolerate the statins. For patients with moderate to high risk for CHD, ezetimibe has been shown to be capable of reducing LDL comparable to that achieved following the administration of high doses of statins, with short-term safety levels identical to placebo.

The mechanism of action differs from the currently available lipid-lowering medications. The drug is a selective cholesterol absorption inhibitor. Following a meal, approximately 50% of the total cholesterol contributed by food is absorbed by the intestines, and the remainder is excreted in the feces. In the intestines, the cholesterol is stored as triglyceride-rich chylomicrons. Ezetimibe acts by blocking the absorption of dietary and biliary cholesterol. The precise mechanism of action by which ezetimibe blocks the uptake of cholesterol into the intestines is not known, but it is believed that it interacts with a cholesterol transport protein.

#### **BILE ACID SEQUESTRANTS**

The bile acid-binding resins, cholestyramine, colestipol and colesevelam, combine with bile acids present in the intestine to form an insoluble complex. The bile acid sequestrants can be used alone or in combination with statins. When used concurrently with TLC, they can produce a 15%-30% reduction in LDL levels. When used along with statins, they can reduce LDL levels by approximately 18% beyond what is achieved by statins alone. Because the bile acid-binding resins are not absorbed from the GI tract, they do not have systemic adverse effects. However, these drugs are associated with side effects that are limited to the GI tract such as constipation, nausea, flatulence and indigestion. These adverse effects may become unpalatable enough to limit patient compliance.

#### **Cholestyramine**

The usual initial adult dose is 3 gm, 3 times daily before meals. The usual maintenance adult dose is 4 gm, 3 to 4 times daily before meals and at bedtime. Similar results may be achieved by administering the drug twice daily. The patient should be instructed to mix the powder with liquids such as water, fruit juices, soups, or with pulpy fruits such as applesauce or crushed pineapple.

#### **Colestipol Hydrochloride**

This is a high molecular weight basic anion-exchange resin. The mechanism of action, adverse effects and mode of administration are similar to those of cholestyramine.

#### **NIACIN**

Niacin is capable of reducing LDL (15%-25%), VLDL (25%-35%) and triglyceride concentration, and at the same time results in elevation of HDL (15%-25%). The mechanism of action is not fully understood, but it has been postulated that niacin can partially inhibit free fatty acid release from adipose tissue and reduce the rate of synthesis of VLDL. The most frequent adverse reactions include uncomfortable and potentially dose-limiting flushing of the skin, itching, skin rash, GI disturbances, hepatotoxicity, and an increase in blood sugar and uric acid. Niacin is available in tablets, extended-release capsules, and elixirs. The usual adult maintenance dose is 1 to 2 gm, three times daily after meals.

#### **FIBRIC ACID DERIVATIVES**

**Gemfibrozil (Lopid®)** and **fenofibrate (Tricor®)** have a minimal effect on lowering LDL serum concentration, but are effective in reducing plasma triglyceride content by increasing fatty acid oxidation in the liver, thereby reducing secretion of VLDL. Additionally, they can increase HDL levels. The drugs may be used in combination with niacin or bile acid sequestrants in order to assist in lowering of HDL levels. Fibric acid derivatives should be given at least two hours after the ingestion of the sequestrants. The most frequently encountered adverse effects are rashes and GI disturbances. Statin-fibrate combination therapy resulted in a 35%-42% decrease in LDL, a 48 %-57% decrease in triglycerides and an increase of 14%-17% in HDL.

#### **PLANT STEROLS**

Plant sterols are capable of lowering LDL by approximately 10%. They act by blocking cholesterol absorption from the intestines. Plant sterols are available as nonprescription drugs and should not be recommended as primary therapy, especially in high-risk patients.

**SUMMARY**

High cholesterol level in the blood is a serious threat to a healthy heart, and atherosclerotic plaques within the walls of the arteries may occur. The accumulation of such material can result in blockade of heart arteries, thereby increasing the risk of CHD and strokes. Lipid profiles should be regularly checked and monitored. Hypercholesterolemia may be managed by following a healthy lifestyle, and implementing drug therapy.

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**EMAIL Address (we need this)** \_\_\_\_\_

**LESSON EVALUATION**

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Name & describe the plasma lipids Yes No

List the types of lipoproteins Yes No

Discuss cholesterol transport, metabolism & regulation within the plasma Yes No

Comment upon the guidelines for lipid blood levels Yes No

Describe drug & nondrug treatments for hyperlipidemia Yes No

2. Was the program independent & non-commercial Yes No

	Poor		Average		Excellent
	1 2	3	4 5	6	7

3. Relevance of topic \_\_\_\_\_

4. What did you like most about this lesson? \_\_\_\_\_

5. What did you like least about this lesson? \_\_\_\_\_

**Please Select the Most Correct Answer**

1. Which statement is true about sterols?
  - A. Found in plants, animals & bacteria
  - B. About 20% of cholesterol in the blood is produced by food
  - C. Only body-produced cholesterol is used to synthesize hormones & Vitamin D
  - D. Campesterol is an animal sterol
2. Triglycerides:
  - A. May be released in the body as a source of energy
  - B. At room temperature exist in nature as liquids
  - C. Found in body tissue but not in blood
  - D. Have a structure similar to cholesterol
3. Lecithin is:
  - A. A free fatty acid
  - B. A pure form of triglyceride
  - C. The only component of an atheroma
  - D. A phospholipid
4. Chylomicrons are the smallest lipoprotein & have the highest density.
 

A. True      B. False
5. Which statement is true about evaluation of serum cholesterol?
  - A. 160-189 mg/dl of LDL in the blood is considered normal
  - B. 150-199 mg/dl of triglyceride is considered very high
  - C. Every person 20 years of age & older should have blood lipids measured every 5 years
  - D. Main goal of ATP III is to lower HDL

6. All of these are causes of hyperlipidemia, except:
  - A. Heredity
  - B. Obesity
  - C. Age
  - D. Bone density
7. The following is true about the statins:
  - A. Doubling statin dose results in 40% lowering of LDL
  - B. Competitively inhibit HMG-CoA
  - C. Atorvastatin has the lowest reduction of LDL
  - D. The higher the statin dose, the lower the potential of toxicity
8. What is true about atorvastatin?
  - A. Effective only to reduce triglyceride blood level
  - B. Contraindicated in patients 65 years of age & older
  - C. Used orally without restriction to meal type
  - D. The maintenance adult dose daily is 80 to 120 mg
9. The most potent statin is:
  - A. Simvastatin
  - B. Fluvastatin
  - C. Pravastatin
  - D. Rosuvastatin
10. This drug causes flushing of the skin.
  - A. Cholestyramine
  - B. Ezetimibe
  - C. Niacin
  - D. Gemfibrozil

**Contributing Author**

Farid Sadik, Dean Emeritus  
University of South Carolina  
College of Pharmacy  
Columbia, SC

**Executive Editor**

William J. Feinberg,  
BS Pharm, MBA



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