The Healthcare Medicine Institute (HealthCMI) presents

High Cholesterol Pt. 1

Western Medicine

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High Cholesterol

~ A Three Part Series ~

Outlines of all Three Courses

High Cholesterol Pt. 1: Western Medicine

Part One of this three part series on high cholesterol and high triglycerides is approved for 7 continuing education hours. Part One covers western medicine diagnosis and treatment. Part Two covers Chinese medicine theory for the treatment of hyperlipidemia. Part Three covers Chinese medicine dietetics food treatment therapy for hyperlipidemia.

Part One:
Learn the statistical prevalence, pathophysiology, signs and symptoms, and serum lipid levels relevant to an understanding of hyperlipidemia. Learn the role that chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL) play in high cholesterol and high triglycerides. Learn about drug treatment options including HMG-CoA reductase inhibitors (statins), bile acid sequestrants, nicotinic acid, and fibric acids. This course covers in detail the diagnosis and treatment of high cholesterol and triglycerides according to western medicine.

Total Cholesterol
LDL Cholesterol
HDL cholesterol
Triglycerides
VLDL Cholesterol
ATPIII Serum Lipid Level Classification (mg/dL)

1.7 Cholesterol Ratios

1.8 Determining Risk

High-risk
Intermediate Risk
Low-risk

1.9 Therapeutic Options

Drug Treatment
Effects of the major dyslipidemia drugs on serum lipid levels

1.9 Non-Mainstream Ideas about Cholesterol and Dyslipidemia

High Cholesterol Pt. 2: Chinese Medicine Theory

Part Two of this three part series on high cholesterol and high triglycerides is approved for 4 continuing education hours. Part One covers western medicine diagnosis and treatment. Part Two covers Chinese medicine theory for the treatment of hyperlipidemia. Part Three covers Chinese medicine dietetics food treatment therapy for hyperlipidemia.

Part Two:
Learn the Chinese medicine diagnostics and theoretical principles of high cholesterol and high triglycerides. Learn the syndromes associated with hyperlipidemia according to Chinese medicine. This includes a detailed look at the role of the spleen, liver, kidneys, and heart in a Chinese medicine context. Learn biomedical perspectives on Chinese medicine through an examination of modern research. This includes an examination of lipid levels in relation to Chinese medicine diagnostics. This course teaches the Chinese medicine way of diagnosing and understanding hyperlipidemia and is prerequisite to taking Part Three which covers Chinese medicine food therapy treatment for hyperlipidemia.

2. Dyslipidemia in Chinese Medicine

2.1 Introduction to Several Important Concepts in Chinese Medicine (CM)

2.2 Fundamentals of Dyslipidemia in Chinese Medicine

Symptoms of Spleen Qi Deficiency

Spleen Deficiency and Dyslipidemia in Modern Research
Liver Qi Stagnation as a Factor in Dyslipidemia
Symptoms of Liver Qi Stagnation
Liver Qi Invading the Spleen
Symptoms of Liver Qi Invading the Spleen
Liver Qi Deficiency as a Factor in Dyslipidemia
Symptoms of Liver Qi Deficiency
Liver Yin Deficiency and Deficiency Heat
Symptoms of Liver and Kidney Yin Deficiency with Deficient Heat
Symptoms of Heart Qi Deficiency

3. Prevention and Treatment of Dyslipidemia in Chinese Medicine

3.1 Lifestyle3.1.1 Sleep Hygiene

3.1.2 Elimination- Bowel Movement

3.1.3 Dietary Habits

Meals and Time Intervals
Guidelines for Breakfast, Lunch, and Dinner
General Dietary Considerations

High Cholesterol Pt. 3: Chinese medicine dietetics

Part Three of this three part series on high cholesterol and high triglycerides is approved for 12 continuing education hours. Part One covers western medicine diagnosis and treatment. Part Two covers Chinese medicine theory for the treatment of hyperlipidemia. Part Three covers Chinese medicine dietetics food treatment therapy for hyperlipidemia.

Part Three:
Learn Chinese medicine dietetics (food therapy) for treating hyperlipidemia. This includes lifestyle practices, dietary therapies, and herbal remedies. Learn Chinese medicine perspectives on the medicinal properties of individual foods and meals. Modern research is also presented with the Chinese medicine analysis for a biomedical understanding of Chinese medicine food principles. Part Two of this series is prerequisite to an understanding of this course.

3.2 Food Therapy

3.2.1 Individual Foods

1. Fruits

1. Chinese Date (Fructus Zizyphi Jujubae, Jujube)
2. Hawthorne Fruit (Fructus Crataegi)
3. Chinese wolfberry fruit

4. Sunflower Seed5. Tomato6. Kiwi Fruit
7. Fig
8. Walnuts
9. Apple

2. Vegetables

1. Cucumber
2. Celery
3. Eggplant
4. Daikon Radish
5. Carrot
6. Garlic
7. Shitake Mushroom
8. Tofu (soybean curd, doufu)

2.1 Grains

1. Buckwheat
2. Oats
3. Corn

3.2.2 Lipid-Reducing Food Formulas

1. Teas

1. Hawthorn and chrysanthemum tea
2. Lotus leaf tea (Folium Nelumbinis Nuciferae)
3. Chinese wolfberry tea
4. Reishi mushroom tea

2. Congees (rice porridge)

1. Plain-Congee
2. Corn-meal Congee
3. Carrot Congee
4. Peach Kernel Congee
5. Garlic Congee
6. Coix Congee (Job's Tears Seed Congee)
7. Mung Bean Congee
8. Peanut-skin Congee

3. Soups

1. Celery and Jujube Soup
2. Hawthorn Berry and Cassia Seed Soup
3. Chrysanthemum, Honeysuckle, Mulberry Leaf, Hawthorn Berry Soup
4. Lotus leaf, winter melon skin, and pumpkin skin drink
5. Daikon, winter melon skin and lettuce drink

Conclusion

High Cholesterol Pt. 1: Western Medicine

Introduction

Dyslipidemia affects millions of people worldwide, particularly in areas where fat-rich diets and sedentary lifestyles are prevalent, such as the United States, and is cause for concern due to the increased risk it poses for serious diseases such as coronary heart disease (CHD). While pharmaceutical drug-therapies to reduce total and LDL cholesterol may be necessary in some cases, Chinese medicine offers complementary preventative and remedial therapy options which, when appropriate, are safe, effective, and employable with a basic understanding of Chinese medical ideas. This course aims to provide nurses and other biomedical health care providers with the fundamental knowledge needed to apply Chinese medicine dietary and lifestyle practices, as well as simple herbal remedies, in the management of dyslipidemia patients.

1. Dyslipidemia in Western Medicine

1.1 Definition

Dyslipidemia is defined as disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. Dyslipidemia may include elevated plasma concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglyceride, and a decrease in high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein plasma concentrations. *Hyperlipidemia* refers to higher than normal levels of plasma lipids, including cholesterol, cholesterol esters, phospholipids, and triglycerides. All of these lipids are transported in the plasma bound to proteins, and these larger compound molecules are called *lipoproteins*. Lipoproteins have been classified on the basis of their densities into five major classes:

- chylomicrons
- very low-density lipoproteins (VLDL)
- intermediate-density lipoproteins (IDL)
- low-density lipoproteins (LDL)
- high-density lipoproteins (HDL)

When hyperlipidemia is defined in terms of elevated serum lipoproteins, the term *hyperlipoproteinemia* is used. Higher than normal serum cholesterol is termed *hypercholesterolemia*, and higher than normal serum triglyceride is termed *hypertriglyceridemia*. The main risk associated with dyslipidemia is atherosclerosis and subsequent increased risk for coronary heart disease (CHD) and other vascular diseases.

1.2 Prevalence

In recent years there are many studies showing direct correlation between incidence of coronary heart disease (CHD) and elevated total and LDL cholesterol levels. According to the third report of the Adult Treatment Panel (ATP III), issued by the National Cholesterol Education Program (NCEP) in May 2001, each year approximately 1.5 million Americans experience an acute myocardial infarction (MI), and one-third of them do not survive. Adoption of NCEP guidelines for the management of dyslipidemia means many more patients are now candidates for intensive lipid-lowering therapy. The NCEP estimated that under its 2001 guidelines, the number of Americans qualifying for dietary treatment would rise from 52 million to 65 million, and the number of candidates for drug therapy would nearly triple—from 13 million to 36 million.

1.3 Pathophysiology

The main risk of dyslipidemia is atherosclerosis (the leading cause of death and disability in the developed world) and the ensuing risk atherosclerosis poses for coronary heart disease (CHD), myocardial infarction (MI), cerebrovasular accident (CVA), peripheral arterial disease, carotid artery disease, abdominal aortic aneurysm (AAA), etc. Atherosclerosis is a subset of arteriosclerosis (hardening of the arteries), and is the formation of *atheromas* (fibrous fatty intimal plaques) in arterial walls. The exact pathogenesis of atherosclerosis is controversial and complex, but a simplified explanation is as follows:

Atherosclerosis begins when monocytes congregate on arterial walls in response to lipoprotein oxidation, creating a fatty streak (yellow streak of lipid-filled macrophage foam cells) on the arterial wall. The monocytes leave the bloodstream and enter the arterial intima where they become macrophages. The macrophages then phagocytize the oxidized LDL cholesterol and die, thus contributing to the lipid component of the fatty streak. Fatty streaks represent the initial lesion of atherosclerosis, are asymptomatic, and are present in the aorta and coronary arteries of most individuals by age 20.

As the fatty streak evolves into a more complicated atherosclerotic lesion, smooth-muscle cells accumulate within the expanding intima and the amount of extracellular matrix increases. Thus begins the formation of the fibrous cap, which separates a necrotic core of cellular debris, degenerating foam cells, and cholesterol crystals from the arterial lumen. The plaque eventually calcifies, thus stiffening and increasing the fragility of the blood vessel.

The endothelium plays a major role in the pathophysiology of atherosclerosis. Endothelial cells normally provide a permeability barrier, reduce clotting, and regulate vascular tone. In atherosclerosis, the intimal endothelium becomes dysfunctional, loses its ability to produce nitrous oxide (NO), and expresses selectins/integrins for leukocyte recruitment. NO is a vasoprotective gas released by the endothelium which has

vasodilatory, anti-thrombotic, and anti-inflammatory effects. NO activates guanylate cyclase to generate cGMP, which causes smooth muscle dilation. NO also blocks vascular inflammation by inhibiting endothelial release of inflammatory granules, and blocks platelet aggregation. Endothelial cells lose their ability to produce NO due to the presence of inflammation, toxins, atherosclerosis, or oxidized LDL.

Atherosclerosis is an inflammatory disease, which is why levels of C Reactive Protein closely correlate with and predict MI. LDL cholesterol, cigarettes and other toxins initiate vascular inflammation, damage the endothelium, and activate macrophages.

Atherosclerosis leads to vascular occlusion when the plaque ruptures or ulcerates, exposing thrombogenic material and leading to the formation of a blood clot, or thrombus. The thrombus may block the artery, causing MI or CVA, or it may become incorporated into the plaque, enlarging its size. Atherosclerotic dysfunction of the endothelium prevents NO production, inhibiting vasodilation and further aggravating the occlusion. Additionally, embolization may occur if pieces of the plaque, called atheroma, break off and become lodged in distal sites.

In the heart, increased plaque volume causes arterial remodeling, which results in an outward expansion of the coronary arteries. The arteries expand in an effort to overcome the effects of the blockage, allowing blood to flow through the stenosed arterial segment. This expansion continues until the artery reaches its maximum point of flexibility and can no longer accommodate the continued growth of the plaque. This threshold generally occurs when the arterial stenosis reaches 40%. As the plaque ages, an increasing amount of fibrous tissue accumulates, leading to the formation of a fibrous cap, which is vulnerable to rupture. Progressive arterial stenoses eventually lead to ischemic vascular disease, and the rupture of a plaque can cause a myocardial infarction.

1.4 Signs and Symptoms

The primary clinical manifestations of dyslipidemia are ischemic vascular disease, pancreatitis, and xanthomatosis. The major ischemic vascular diseases are atherosclerosis, coronary heart disease, peripheral vascular disease, and cerebrovascular disease. Pancreatitis may be associated with hypertriglyceridemia. Xanthomas are tumor-like collections of lipids (triglycerides and cholesteryl esters) that can arise in the tendons, points of continued trauma, legs, knees and elbows, as well as palms.

1.5 Description of Lipoproteins

Lipoprotein Structure
Lipoproteins are spherical particles made up of hundreds of lipid and protein molecules, yet they are smaller than red blood cells. The major lipids of the lipoproteins are cholesterol, triglycerides, and phospholipids. Triglycerides and cholesterol esters are nonpolar, hydrophobic lipids that make up the core of the lipoproteins. Phosphoplipids

and a small amount of unesterified cholesterol cover the surface of the lipoproteins, where they act as the interface between the plasma and core components. A family of proteins, known as apolipoproteins, also occupies the surface of the lipoproteins and plays an important role in the regulation of lipid transport and lipoprotein metabolism.

LDL Cholesterol (LDL-C)
LDL cholesterol typically accounts for 60-70% of total serum cholesterol. LDL is the main atherogenic lipoprotein and is the primary target of cholesterol-lowering therapy. The focus on LDL reduction has been strongly validated in recent years by clinical trials that show the efficacy of LDL-lowering therapy in reducing CHD risk. However, recent studies have also shown the significance of LDL particle size in relation to atherosclerosis and heart disease. Smaller, denser LDL carries more atherogenic potential than larger, less dense LDL particles.

HDL Cholesterol (HDL-C)
HDL cholesterol typically accounts for 20-30% of total serum cholesterol. HDL cholesterol levels are inversely correlated to CHD risk. However, recent studies[i] have shown that very high levels of HDL (≥70 mg/dL), and very large HDL particle size, are both associated with increase CHD risk. Furthermore, while some evidence suggests that HDL protects against development of atherosclerosis, a low HDL level often reflects the presence of other atherogenic factors.

VLDL Cholesterol (VLDL-C)
VLDL are triglyceride-rich lipoproteins which contain between 10-15% of total serum cholesterol. VLDL are produced by the liver and are precursors of LDL. Some forms of VLDL appear to be atherogenic, particularly VLDL remnants, which consist of partially degraded VLDL and are relatively enriched in cholesterol ester. Technically, IDL belong to these remnant lipoproteins, but IDL is included in the measurement of serum LDL.

Chylomicrons
Chylomicrons are triglyceride-rich proteins formed in the intestine from dietary fat, and which appear in the blood after a fat-containing meal. Partially degraded chylomicrons, known as chylomicron remnants, may also be atherogenic.

Characteristics of the Major Lipoprotein Classes

Lipoprotein	Density (g/dL)	Diameter (nm)	Lipid (%) *		
			Triglyceride	Cholesterol	Phospholipid
Chylomicrons	0.95	75-1200	80-95	2-7	3-9
VLDL	0.95-1.006	30-80	55-80	5-15	10-20
IDL	1.006-1.019	25-35	20-50	20-40	15-25
LDL	1.019-1.063	18-25	5-15	40-50	20-25
HDL	1.063-1.210	5-12	5-10	15-25	20-30

* The remaining percent composition is made up of the apoproteins.

Characteristics of Lipoproteins:

Lipoprotein	Normal % of Total Cholesterol	Desirable Plasma Concentration	Atherogenic Potential
Total Cholesterol	-	< 200 mg/dL	Yes
LDL	60-70%	< 100 mg/dL	High
HDL	20-30%	> 40 mg/dL < 70 mg/dL	Yes, at high levels. Moderate levels may protect against atherogenesis
VLDL	10-15%	10-31 mg/dL	Likely

1.6 Serum Lipid Levels

ATP III classified levels of serum lipids as described below. However, the actual desirable level (goal) for each individual varies depending on risk factors for CHD, and is calculated using ATP III guidelines and the Framingham Point Score tables. Therefore, the following levels are merely a rough guideline and not applicable to all individuals.

Total Cholesterol
Elevated total cholesterol is associated with increased risk of CHD. A total cholesterol level under 200 mg/dL is desirable, while a level of 200 to 239 mg/dL is borderline high, and greater than or equal to 240 mg/dL is high. However, most decisions about treatment are based upon levels of LDL or HDL cholesterol rather than total cholesterol.

LDL Cholesterol
Low-density lipoprotein (LDL) cholesterol is a more accurate predictor of CHD risk than total cholesterol, and higher LDL cholesterol concentrations are associated with increased incidence of CHD in a large number of studies.

LDL concentrations as low as 25 to 60mg/dL are physiologically sufficient. Baseline LDL levels under 100mg/dL are considered acceptable and not requiring of further LDL lowering therapies. However, individuals in this category should still follow dietary and lifestyle recommendations (TLC- Therapeutic Lifestyle Changes) that will allow for maintenance of low LDL levels.

According to ATPIII, baseline LDL cholesterol levels between 100-129 mg/dL require therapeutic intervention. Several options are available, but as in all cases of elevated cholesterol, TLC is the initial therapy. If healthy LDL levels are attained on dietary therapy alone, the use of lipid-lowering drugs may be unnecessary. If LDL remains above 100 mg/dL after 3 months of maximum dietary therapy, an LDL-lowering drug may be considered. If elevated triglyceride levels or low HDL levels are also present, another lipid-lowering drug may be considered, such as nicotinic acid or fibric acid.

For baseline LDL cholesterol levels ≥130 mg/dL, use of an LDL-lowering drug is generally considered necessary to achieve LDL cholesterol levels <100 mg/dL.

Increased LDL levels may result from the following:

1. Primary hyperlipoproteinemia
2. High fat diet
3. Acute myocardial infarction
4. Obstructive liver disease (primary biliary cirrhosis)
5. Hypothyroidism
6. Nephrotic syndrome
7. Diabetes mellitus
8. Anabolic steroid use
9. Medications
    1. Progestins
    2. Thiazide diuretics

Decreased LDL cholesterol levels may result from any of the following:

1. Abetalipoproteinemia
2. Advanced liver disease
3. Malnutrition

HDL cholesterol

It is generally accepted that elevated serum levels of HDL and larger HDL particle size lower the risk of CHD, and according to NCEP guidelines, an HDL level greater than or equal to 60 mg/dL is a negative risk factor for CHD. It is also generally accepted that low levels of HDL (<40 mg/dL) may require treatment, particularly in cases with established CHD. New research, however, shows that very high levels of HDL (≥70 mg/dL), and very large HDL particle size, are both associated with increase CHD risk. This gives rise to the hypothesis that very large HDL, which is cholesterol enriched, may at some point become a cholesterol donor instead of an acceptor. Furthermore, although it has widely been acknowledged that the anti-inflammatory capacity of HDL contributes to its antiatherogenic potency, several studies have demonstrated that HDL can also turn into a proinflammatory particle. Therefore, it is not simply a matter of higher HDL levels being better. Rather, both HDL particle size and serum levels must be considered.

Positive cardiac risk factors (atherogenic):

1. HDL < 35 mg/dL or ≥70 mg/dL
2. Total Cholesterol (TC) to HDL ratio
    1. Men > 5.0
    2. Women > 4.5

Negative cardiac risk factors according to NCEP (protective):

1. HDL > 60 mg/dL

The following may lead to increased serum HDL levels:

1. Medications
    1. Gemfibrozil
    2. Niacin

        3. Exogenous estrogens
    2. Moderate alcohol intake (1 ounce per day)
    3. Regular aerobic exercise
    4. Weight loss (for obese patients)
        1. HDL increases 2 mg/dl for each 4.5 kg of weight loss

The following may lead to decreased serum HDL levels:

1. Tobacco abuse
2. Diabetes Mellitus
3. Hypertriglyceridemia
4. Menopause
5. Obesity
6. Puberty in males
7. Uremia
8. Anabolic Steroids
9. Apolipoprotein deficiency
10. Liver disease
11. Tangier disease
12. Medications
    1. Progestins
    2. Probucol

Triglycerides

Elevated triglycerides are also associated with an increased risk of CHD. Although LDL levels are the primary focus of therapy, ATP III also recommends aggressive treatment of elevated triglyceride levels through weight management and increased physical activity. Patients whose triglyceride levels remain at 200 mg/dL or higher after they have reached their LDL goal are recommended to achieve a secondary goal based on their "non-HDL" level (total cholesterol level minus HDL level). The non-HDL goal should be 30 mg/dL higher than the LDL goal. The basis for attempting to reach this secondary goal is that all non-HDL particles are potentially atherogenic. This can be achieved through activities of daily living or the use of niacin and fibrates.

ATP III classifies triglyceride concentrations as follows:

- Normal: less than 150 mg/dL
- Borderline high: 150 to 199 mg/dL
- High: 200 to 499 mg/dL
- Very high: greater than 500 mg/dL

The following may lead to increased serum triglyceride levels:

1. Hyperlipoproteinemia (types I, IIb, III, IV, and V)
2. Pregnancy
3. Obesity
4. Alcohol abuse
5. Acute myocardial infarction
6. Pancreatitis

7. Nephrotic syndrome
8. Chronic renal insufficiency
9. Glycogen storage disease
10. Acute intermittent porphyria
11. Endocrine disease
    1. Diabetes mellitus
    2. Hypothyroidism
    3. Cushing's syndrome
    4. Hypopituitarism
12. Medications
    1. Exogenous estrogens
    2. Diuretics
    3. Glucocorticoids
    4. Ticlopidine

The following may lead to decreased serum triglyceride levels:

1. Malnutrition
2. Abetalipoproteinemia
3. Medications
    1. Gemfibrozil
    2. Nicotinic Acid
    3. Clofibrate

VLDL Cholesterol

Serum VLDL levels should ideally be below 30 mg/dL. The following may lead to increased serum VLDL levels:

1. Idiopathic increased hepatic secretion of VLDL
2. Diabetes mellitus
3. Obesity

ATPIII Serum Lipid Level Classification* (mg/dL)*:

Desirable/Optimal	Near/Above Optimal	Borderline High	High	Very High
Total Cholesterol				
< 200	-	200-239	≥ 240	-
LDL Cholesterol				
< 100	100-129	130-159	160-189	≥ 190
HDL Cholesterol				
> 40			≥ 60	
VLDL Cholesterol				
< 30	-	-	-	-
Triglycerides				
< 150	-	150-199	200-499	≥ 500

1.7 Cholesterol Ratios

Cholesterol ratios are ratios between serum levels of different types of cholesterols, the most common of which are total cholesterol to high density lipoprotein ratio (total/HDL ratio), low density lipoprotein to high density lipoprotein ratio (LDL/HDL ratio), and high density lipoprotein to low density lipoprotein ratio (HDL/LDL ratio). These are employed to help determine risk for atherosclerosis and cardiovascular disease. While the medical community is divided over the effectiveness of using these ratios for this purpose, a brief review is necessary.

Total/HDL ratio is determined by dividing the total cholesterol (TC) level by the HDL level (TC÷HDL, or TC/HDL). A ratio below 5/1 is generally considered acceptable, with 3.5/1 or below considered ideal.

LDL/HDL ratio is determined by dividing the LDL level by the HDL level (LDL÷HDL, or LDL/HDL). A ratio below 3.5/1 is generally considered acceptable, with 2.5/1 or below considered ideal.

HDL/LDL ratio is determined by dividing the HL level by the LDL level (HDL÷LDL, or HDL/LDL). A ratio above 0.3/1 is generally considered acceptable, with 0.4/1 or above considered ideal.

While these ratios may be useful in some ways, the medical community is divided on whether they are better than total cholesterol or LDL cholesterol levels in predicting CAD risk. For treatment of dyslipidemia, the absolute numbers for LDL and HDL are generally considered more relevant.

1.8 Determining Risk

While ATP III classifies levels of serum lipids from "optimal" to "very high", the optimum level for each individual varies depending on other risk factors for CHD, such as age, male gender, family history of CHD, smoking, hypertension, physical inactivity, overweight and obesity, diabetes, heavy alcohol consumption, and stress. The process used to determine CHD risk level and corresponding optimal serum lipid levels is detailed in the "ATP III Guidelines At-A-Glance Quick Desk Reference" (available n PDF download from www.nhlbi.nih.gov/guidelines/cholesterol/atglance.pdf). Below is a brief discussion of the significance of the different risk categories.

High-risk

The target LDL level for high-risk patients is <70 mg/dL. Current guidelines recommend dietary therapy for high-risk patients whose LDL levels are >100 mg/dL and drug therapy for those whose LDL levels are ≥130 mg/dL.

Intermediate Risk

The target LDL level for intermediate-risk patients is <100 mg/dL. Patients who exceed this level can begin therapeutic lifestyle changes (TLC) if their calculated 10-year risk is less than 10%. If calculated 10-year risk is between 10% and 20%, then drug treatment

should be initiated. Immediate drug therapy is recommended for intermediate-risk patients whose LDL levels are ≥160 mg/dL, even if calculated 10-year risk is less than 10%.

Low-risk
An LDL level ≤160 mg/dL is the goal for low-risk patients. Low-risk patients with LDL levels between 160 mg/dL and 189 mg/dL should begin TLC. If a 3-month trial of TLC fails to reduce LDL levels to <160 mg/dL, drug therapy can be considered. According to current guidelines, low-risk patients whose LDL levels are ≥190 mg/dL should be started on drug treatment.

1.9 Therapeutic Options:

Drug Treatment
Four major classes of medications are used to treat dyslipidemia:

- HMG-CoA reductase inhibitors (statins)
- Bile acid sequestrants
- Nicotinic acid
- Fibric acids

Statins (rosuvastatin, atorvastatin, simvastatin, pravastatin, fluvastatin, and lovastatin) can lower LDL levels 18% to 55%, and triglyceride levels 7% to 30%. They can also raise HDL levels by 5% to 15%. Major side effects include myopathy and elevation of liver enzyme levels.

Many clinical trials have shown that statins reduce incidence of major coronary events, CHD death, and stroke, and they may also reduce the need for coronary procedures, and lower total mortality. However, there is controversy.

Statins work by inhibiting the enzyme HMG-CoA reductase and are therefore also known as HMG-CoA reductase inhibitors. The process begins with acetyl-CoA. Three acetyl-CoA molecules combine to form hydroxymethyl glutaric acid (HMG). The step from HMG to mevalonate requires HMG-CoA reductase. Statin drugs work by inhibiting this enzyme, and herein lies the potential for numerous side effects because statin drugs inhibit not just the production of cholesterol, but a whole family of intermediary substances, many if not all of which have important biochemical functions.

Cholesterol is one of three end products in the mevalonate chain. The two others are ubiquinone and dilochol. Ubiquinone, also known as Co-Enzyme Q10, is a critical cellular nutrient biosynthesized in the mitochondria. It plays a role in ATP production in the cells and functions as an electron carrier to cytochrome oxidase, a major respiratory enzyme. The heart also requires high levels of Co-Q10. Ubiquinone is found in all cell membranes, where it plays a role in maintaining membrane integrity critical to nerve conduction and muscle integrity. Co-Q10 is also vital to the formation of elastin and

collagen. Side effects of Co-Q10 deficiency include muscle-wasting leading to weakness and severe back pain, heart failure (the heart is a muscle), neuropathy, and inflammation of the tendons and ligaments often leading to rupture.

Finally, there is controversy regarding the mechanism by which statins reduce CHD risk. While statins significantly reduce serum cholesterol levels, this may not be the cause of reduction of cardiac events. The fact that some studies have shown that statins can prevent heart disease, at least in the short term, is most likely explained not by the inhibition of cholesterol production but because they block the creation of mevalonate. Reduced amounts of mevalonate seem to make smooth muscle cells less active, and platelets less able to produce thromboxane. Atherosclerosis begins with the growth of smooth muscle cells in side artery walls, and thromboxane is necessary for blood clotting.

Bile acid sequestrants (cholestyramine, and colestipol) can reduce LDL levels 15% to 30% and raise HDL levels 3% to 5%. They have no effect on triglyceride levels. Major side effects include gastrointestinal distress, constipation, and a decrease in the absorption of other drugs. Clinical trials have shown that these agents reduce the incidence of major coronary events and CHD death.

Nicotinic acid (niacin/vitamin B3) can reduce LDL levels 5% to 25% and triglyceride levels 20% to 50%. Nicotinic acid also raises HDL levels 15% to 35%. Major side effects of nicotinic acid include flushing, hyperglycemia, hyperuricemia, gastrointestinal distress, and hepatotoxicity. Clinical trials have shown it can prevent major coronary events.

Fibric acids (fenofibrate, and gemfibrozil) can reduce LDL levels 5% to 20% and triglyceride levels 20% to 50%, as well as raise HDL levels 10% to 20%. Major side effects include dyspepsia, gallstones, myopathy, and unexplained noncardiac death. Clinical trials have shown that they lower the risk of major coronary events.

Effects of the major dyslipidemia drugs on serum lipid levels

Drug Type	**Effect on LDL**	**Effect on HDL**	**Effect on Triglycerides**
Statins	Reduce 18-55%	Raise 5-15%	Reduce 7-30%
Bile acid sequestrants	Reduce 15-30%	Raise 3-5%	No effect
Nicotinic acid	Reduce 5-25%	Raise 15-35%	Reduce 20-50%
Fibric acids	Reduce 5-20%	Raise 10-20%	Reduce 20-50%

Hormone replacement therapy. ATP III makes it clear that hormone replacement therapy (HRT) is not a substitute for lipid-lowering drugs in dyslipidemic women. Although HRT lowers LDL levels, studies have not shown that it reduces the risk of coronary events.

Therapeutic Lifestyle Changes (TLC)

TLC (therapeutic lifestyle changes) includes diet, weight, and exercise guidelines as set forth in ATP III. The guidelines are as follow:

- TLC Diet:
  - Saturated fat < 7% of daily calories, cholesterol < 200mg/day.
  - Consider increasing:
    - viscous fiber (10-25g/day; e.g., cereal grains, beans, peas, legumes, fruits, and vegetables).
    - plant stanols/sterols (2g/day). These are present naturally in small quantities in many fruits, vegetables, nuts, seeds, cereals, legumes, vegetable oils, and other plant sources, but the amounts are generally small. Some foods are now fortified with stanols, so these can be considered for incorporation in the diet as well.)
  - Weight management
  - Increased physical activity

1.9 Non-Mainstream Ideas about Cholesterol and Dyslipidemia

The above discussion has focused primarily on the mainstream views of cholesterol and dyslipidemia. However, there are divergent opinions that are worth examining.

While the mainstream medical establishment has interpreted the research to indicate elevated cholesterol is a major cause of cardiovascular disease and premature death, there are others who dispute these claims. One researcher, Dr. Uffe Ravnskov, who has conducted extensive reviews of the literature and conducted some meta-analyses, notes that studies show people with the highest cholesterol live the longest, and that many studies of elderly people show that high cholesterol is not a risk factor for coronary heart disease. He notes that many studies have found that total mortality was inversely associated with either total or LDL-cholesterol, or both, that high cholesterol levels are protective against infection, and that the risk of dying for patients with chronic heart failure is strongly and inversely associated with total cholesterol, LDL-cholesterol and also triglycerides; those with high lipid values live much longer than those with low values.

Ravnskov asserts that, "Most studies of young and middle-aged men have found high cholesterol to be a risk factor for coronary heart disease, seemingly a contradiction to the idea that high cholesterol is protective. Why is high cholesterol a risk factor in young and middle-aged men? A likely explanation is that men of that age are often in the midst of their professional career. High cholesterol may therefore reflect mental stress, a well-known cause of high cholesterol and also a risk factor for heart disease. Again, high cholesterol is not necessarily the direct cause but may only be a marker. High cholesterol in young and middle-aged men could, for instance, reflect the body's need for more cholesterol because cholesterol is the building material of many stress hormones. Any possible protective effect of high cholesterol may therefore be counteracted by the negative influence of a stressful life on the vascular system."[ii]

For further reading on the controversies surrounding this topic, The International Network of Cholesterol Skeptics (http://thincs.org) has a wealth of information.

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[i] van der Steeg WA, Holme I, Boekholdt M, et al. *High-density lipoprotein cholesterol, high-density lipoprotein particle size, and apolipoprotein A-I: significance for cardiovascular risk.* J Am Coll Cardiol 2008;51:634–42.

[ii] Uffe Ravnskov, MD, PhD. *The Benefits of High Cholesterol.* Wise Traditions in Food, Farming and the Healing Arts, Spring 2004.