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# Dyslipidemia

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## Continuing Education Activity

Dyslipidemia refers to abnormal levels of lipids in the bloodstream, which poses a significant risk factor for cardiovascular (CV) diseases. Dysregulation in these lipid levels, whether due to genetic predispositions or lifestyle factors, can lead to atherosclerosis and other CV complications. Diagnosis often relies on lipid profile tests, with recommended target levels for optimal CV health. Treatment strategies work to mitigate risks by targeting specific lipid abnormalities, emphasizing lifestyle modifications, and considering comorbidities to individualize care. Given the multifaceted nature of dyslipidemia management, a multidisciplinary approach is essential for comprehensive patient care.

This course is designed to provide healthcare professionals with a comprehensive understanding of dyslipidemia, its diagnosis, treatment strategies, and the importance of a multidisciplinary approach in patient care. Throughout this activity, learners explore various aspects of dyslipidemia management. Essential lipids such as cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides, evaluating their roles in physiological processes and the implications of dysregulation are discussed. One of the key themes of this course is the vital role of interprofessional collaboration in dyslipidemia management. Learners gain insights into how collaborative efforts among healthcare professionals, including cardiologists, endocrinologists, nurses, pharmacists, dietitians, and educators, contribute to developing tailored treatment plans for managing dyslipidemia.

**Objectives:**

- Evaluate the etiology and mechanisms underlying dyslipidemia, including impaired lipoprotein synthesis, secretion, and clearance.
- Identify the risk factors and clinical presentations indicative of dyslipidemia.
- Differentiate the management options for dyslipidemia, including lifestyle modifications, pharmacological interventions, and potential benefits or risks of each class of lipid-lowering medications.
- Implement patient-centered care and shared decision-making in dyslipidemia management to include collaborative efforts between healthcare professionals.

Access free multiple choice questions on this topic.

**Introduction**

Lipids, such as cholesterol or triglycerides, are absorbed from the intestines and carried throughout the body via lipoproteins for energy, steroid production, or bile acid formation. Major contributors to these pathways are cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and high-density lipoprotein (HDL). An imbalance of any of these factors, either from organic or nonorganic causes, can lead to dyslipidemia.[1] Dyslipidemia results in abnormal levels of lipids (fats) in the blood, which can increase the risk of cardiovascular diseases.

Lipids include LDL cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. Dyslipidemia is classified into 2 types: primary and secondary. Primary dyslipidemia is inherited and caused by genetic mutations that affect lipid metabolism.[2] Secondary dyslipidemia is acquired and caused by lifestyle factors or other medical conditions that alter lipid levels. The most common forms of dyslipidemia are:

- LDL cholesterol is considered “bad” cholesterol because it can form plaques in the arteries and reduce blood flow.
- HDL cholesterol is considered “good” cholesterol because it can help remove LDL from the blood and protect against atherosclerosis.
- Triglycerides are stored in fat cells and released as energy when needed. High triglycerides can also contribute to plaque formation and inflammation in the arteries.
- Total cholesterol is the sum of LDL, HDL, and half of the triglyceride level. High total cholesterol can indicate an increased risk of heart disease and stroke.[3]

Dyslipidemia usually does not cause any symptoms, but it can be detected by a blood test measuring different lipids levels. The optimal lipid level varies depending on the individual's age, sex, and other risk factors, but generally, the following ranges are recommended:

- LDL cholesterol: less than 100 mg/dL
- HDL cholesterol: more than 40 mg/dL for men and more than 50 mg/dL for women
- Triglycerides: less than 150 mg/dL
- Total cholesterol: less than 200 mg/dL

The treatment of dyslipidemia depends on the type and severity of the condition and the presence of other risk factors, such as diabetes, hypertension, obesity, or smoking. The main goals of treatment are to lower LDL cholesterol, raise HDL cholesterol, and reduce triglycerides.

Preventing dyslipidemia is essential to reduce the risk of cardiovascular complications and improve the quality of life. The prevention strategies include:

- Screening for dyslipidemia regularly, especially for people with a family history or other risk factors. The frequency and type of screening depend on the individual's age, sex, and health status, but generally, a lipid profile test is recommended every 4 to 6 years for adults and every 2 years for children and adolescents.
- Adopting a healthy lifestyle by eating a balanced diet with plenty of fruits, vegetables, whole grains, lean proteins, and healthy fats, such as omega-3 fatty acids from fish, nuts, and seeds. Avoid foods high in cholesterol, saturated fats, trans fats, added sugars, and salt. If possible, engage in physical activity for at least 150 minutes weekly. Maintaining a healthy weight and body mass index, quitting smoking, and limiting alcohol intake are all recommended.
- Comorbidities such as diabetes, hypertension, hypothyroidism, chronic kidney disease, or liver disease can affect lipid levels or increase the risk of cardiovascular disease; therefore, it is important to remain compliant with any medications.[4]

**Etiology**

Dyslipidemia, characterized by aberrations in lipid metabolism, has multifaceted etiologies influenced by genetic, environmental, and lifestyle factors. Understanding these etiologies is crucial for developing targeted interventions and preventive strategies. Dyslipidemia can be classified into 2 types based on the etiology:

**Primary Dyslipidemia**

This type of dyslipidemia is caused by genetic mutations that affect the metabolism of lipids. Primary dyslipidemia can be inherited as an autosomal dominant, autosomal recessive, or X-linked. Some examples of primary dyslipidemia are familial hypercholesterolemia, familial hypertriglyceridemia, familial combined hyperlipidemia, and familial dysbetalipoproteinemia. The estimated prevalence of familial hypercholesterolemia ranges from 1 in 500 to 1 in 250 in most populations. Still, it can be as high as 1 in 67 in some ethnic groups, such as Afrikaners, French Canadians, and Lebanese.[5] The prevalence of familial hypertriglyceridemia is estimated at 1 in 500 in the general population. However, it is higher in certain populations, such as Hispanics and Native Americans.[6] The prevalence of familial combined hyperlipidemia is estimated at 1 in 100 in the general population. However, it can be higher in patients with premature coronary artery disease. The prevalence of familial dysbetalipoproteinemia is estimated at 1 in 10,000 in the general population, but it can be higher in patients with diabetes or obesity.

The mechanisms of primary dyslipidemia involve defects in the synthesis, transport, or degradation of lipoproteins, which are the main carriers of lipids in the blood. These defects result in the accumulation or deficiency of lipoproteins and lipids in the blood, increasing the risk of atherosclerosis and cardiovascular disease. For example, familial hypercholesterolemia is caused by mutations in the LDL receptor gene, impairing LDL cholesterol uptake from the blood and leading to high LDL cholesterol levels and premature atherosclerosis.

Familial hypertriglyceridemia is caused by mutations in the LPL gene or the apo C-II gene, which impair the hydrolysis of triglycerides in chylomicrons and very low-density lipoproteins (VLDL), leading to high triglyceride levels and pancreatitis. Familial combined hyperlipidemia is caused by the overproduction of apo B-containing lipoproteins, such as VLDL and LDL, by the liver, leading to high cholesterol and triglyceride levels and insulin resistance. Familial dysbetalipoproteinemia is caused by mutations in the apo E gene, which impair the clearance of chylomicron and VLDL from the blood, leading to high cholesterol and triglyceride levels and xanthomas.[7][8]

**Secondary Dyslipidemia**

This type of dyslipidemia is caused by lifestyle factors or other medical conditions that alter the levels of lipids in the blood. Secondary dyslipidemia is reversible or modifiable by addressing the underlying cause. Some examples of secondary dyslipidemia risk factors include physical inactivity, unhealthy nutrition, obesity, diabetes, hypothyroidism, chronic

kidney disease, liver disease, alcohol abuse, smoking, and the use of certain drugs.[9] Results from a study in the United States (US) found that 28% of new patients referred to a lipid clinic had 1 or more potential causes of secondary dyslipidemia, with excessive alcohol intake (10%) and uncontrolled diabetes mellitus (8%) as the most prevalent.

- For example, obesity is associated with increased production of very low-density lipoprotein and decreased liver clearance of chylomicrons, leading to high triglyceride and low high-density lipoprotein cholesterol levels.
- Diabetes mellitus is associated with insulin resistance and hyperglycemia, impairing triglyceride lipolysis and the uptake of LDL cholesterol; this leads to high triglyceride and LDL cholesterol levels and low HDL cholesterol levels.
- Hypothyroidism is associated with decreased expression of LDL receptors and lipoprotein lipase, which impair the clearance of LDL cholesterol and triglycerides from the blood, leading to high LDL cholesterol and triglyceride levels.
- Chronic kidney disease is associated with impaired catabolism of apo B-containing lipoproteins and reduced activity of lipoprotein lipase and hepatic lipase, which impair the clearance of triglycerides and cholesterol from the blood, leading to high triglyceride and LDL cholesterol levels and low HDL cholesterol levels.
- Liver disease is associated with impaired synthesis and secretion of lipoproteins and bile acids, which impair the transport and excretion of cholesterol and triglycerides from the liver, leading to high or low cholesterol and triglyceride levels depending on the type and severity of the liver disease.
- Alcohol abuse is associated with increased synthesis of VLDL and decreased oxidation of fatty acids by the liver, leading to high triglyceride levels.
- Smoking is associated with increased oxidative stress and inflammation, which impair the function and synthesis of HDL cholesterol, leading to low HDL cholesterol levels.
- Use of certain drugs, such as corticosteroids, beta-blockers, oral contraceptives, and antiretroviral agents, can affect the metabolism of lipids and lipoproteins by various mechanisms, leading to high or low cholesterol and triglyceride levels depending on the type and dose of the drug.

**Epidemiology**

Dyslipidemia is a global public health problem that affects millions of people and increases the risk of cardiovascular disease, the leading cause of death worldwide. The epidemiology of dyslipidemia varies by region, age, sex, and ethnicity and is influenced by genetic and environmental factors.[10] According to a systematic review protocol, the global prevalence of dyslipidemia in adults is estimated to range from 20% to 80%, depending on the definition and criteria used.[11] However, comprehensive and updated data on the epidemiology of dyslipidemia is currently lacking in different populations and settings. The awareness, treatment, and control of dyslipidemia are also suboptimal in many countries, especially in low- and middle-income countries.[11] From 2005 to 2008, 33.5% of U.S. adults older than 20 had high LDL levels. Of these individuals with elevated LDL levels, only 48.1% received treatment, and 33.2% had LDL control. The prevalence of LDL control was lowest amongst uninsured individuals, Mexican Americans, or those who had income below the poverty level.[12]

The incidence and mortality of dyslipidemia are challenging to measure directly, as dyslipidemia is usually asymptomatic and often coexists with other risk factors, such as hypertension, diabetes, obesity, and smoking. Therefore, most studies use surrogate endpoints, such as cardiovascular events, to assess the impact of dyslipidemia on morbidity and mortality. A large-scale trial showed that lowering LDL cholesterol by 1 mmol/L reduced the risk of major vascular events by about 20%, regardless of the initial LDL level. A meta-analysis of 26 randomized trials found that statin therapy reduced the risk of all-cause mortality by 10%, coronary mortality by 18%, and stroke mortality by 9%. The economic burden of dyslipidemia is also substantial, as it increases the direct and indirect costs of healthcare and productivity losses. Results from a US study showed that the estimated annual cost of dyslipidemia was $34.4 billion in 2006, of which $19.7 billion was attributed to direct medical costs and $14.7 billion to indirect costs.[13]

The epidemiology of dyslipidemia also reveals gender differences, as women tend to have higher HDL cholesterol and lower LDL cholesterol than men, but this advantage diminishes after menopause. Women are also less likely to receive adequate screening, diagnosis, and treatment for dyslipidemia than men and have worse outcomes after cardiovascular events. The prevalence of dyslipidemia in children and adolescents is increasing, especially in developed countries, due to the rising rates of obesity, sedentary lifestyles, and unhealthy diets.[14] Results from another US study reported that 7% of children and adolescents aged 6 to 19 had high total cholesterol, and 22% had at least one abnormal lipid level. Dyslipidemia in childhood can persist into adulthood and increase the risk of premature cardiovascular disease. Dyslipidemia is a modifiable risk factor for cardiovascular disease, and prevention and management are essential to reduce the global burden of morbidity and mortality. The epidemiology of dyslipidemia provides

valuable information for developing and implementing effective strategies to improve dyslipidemia awareness, treatment, and control in different populations and settings.

**Pathophysiology**

Understanding the pathophysiology of dyslipidemia elucidates the role of a spectrum of interconnected metabolic and cardiovascular disturbances. Dyslipidemia can cause inflammation, oxidative stress, cardiovascular diseases, and other metabolic dysfunctions by different mechanisms, such as:

**Inflammation**

Elevated levels of LDL and triglyceride-rich lipoproteins promote their retention in arterial walls; this can trigger an inflammatory response in the blood vessels, contributing to the development and progression of atherosclerosis.[15] Atherosclerosis is the accumulation of fatty plaques in the arterial walls, which can reduce blood flow and increase the risk of thrombosis. Dyslipidemia can activate inflammatory cells, such as macrophages and T cells, and inflammatory mediators, such as cytokines and chemokines--which can infiltrate and damage the endothelium (the inner lining of the blood vessels). Dyslipidemia can also increase the expression of adhesion molecules, such as intercellular adhesion molecule-1 and vascular cell adhesion molecule-1, which can facilitate the attachment and migration of inflammatory cells into the subendothelial space. Dyslipidemia can also modulate the function of endothelial progenitor cells (EPCs), which are involved in the repair and regeneration of the endothelium. Dyslipidemia can impair the number and activity of EPCs, which compromise endothelial integrity and function.

**Oxidative Stress**

LDL particles, when retained in arterial walls, undergo oxidative modifications. Oxidized LDL becomes pro-inflammatory and pro-atherogenic; this can increase the production of reactive oxygen species (ROS), unstable molecules that damage cells and tissues by oxidizing components such as lipids, proteins, and deoxyribonucleic acid. Dyslipidemia can also decrease the levels of antioxidants, which can neutralize ROS and protect the cells and tissues from oxidative damage.[16]

Dyslipidemia can induce oxidative stress by various mechanisms, such as:

- Oxidation of LDL cholesterol: LDL cholesterol is the primary carrier of cholesterol in the blood and the main target of oxidation by ROS. Oxidized LDL (oxLDL) is more atherogenic than native LDL, as it can stimulate cholesterol uptake by macrophages, leading to the formation of foam cells, which are the hallmark of atherosclerotic plaques. OxLDL can also induce the expression of inflammatory

mediators, such as tumor necrosis factor-alpha and interleukin-6, and the activation of nuclear factor-kappa B, a transcription factor that regulates the expression of genes involved in inflammation and immunity. OxLDL can also impair the function of endothelial nitric oxide synthase, an enzyme that produces nitric oxide, a vasodilator and anti-inflammatory molecule.

- Impairment of HDL cholesterol: HDL cholesterol is the main carrier of cholesterol from the peripheral tissues to the liver for excretion, and it has anti-inflammatory and antioxidant properties. Dyslipidemia can impair the function of HDL cholesterol by reducing its levels, altering its composition, or modifying its enzymes and receptors. Dyslipidemia can also increase the transfer of cholesterol esters from HDL to LDL and VLDL by using cholesteryl ester transfer protein, reducing HDL's ability to remove excess cholesterol from blood vessels. Dyslipidemia can impair the activity of paraoxonase-1, an enzyme associated with HDL that protects LDL from oxidation.[15]

**Cardiovascular Diseases**

Dyslipidemia can increase the risk of cardiovascular diseases, such as coronary artery disease, peripheral artery disease, stroke, and heart failure, by promoting atherosclerosis and its complications. Dyslipidemia can also affect the function of the heart and the blood vessels by impairing the production and availability of nitric oxide, a key regulator of vascular tone, blood pressure, and platelet aggregation. Dyslipidemia can induce endothelial dysfunction, the impairment of the ability of the endothelium to maintain vascular homeostasis and to respond to physiological stimuli. Dyslipidemia can also affect the structure and function of the cardiac muscle, leading to cardiac hypertrophy, fibrosis, and arrhythmias.

**Other Metabolic Dysfunctions**

Additional effects exist on the metabolism of other organs and systems, such as the liver, the pancreas, the adipose tissue, and the skeletal muscle, by altering lipid and glucose metabolism, insulin sensitivity, and inflammatory status. Dyslipidemia can also interact with other metabolic disorders, such as obesity, diabetes, and metabolic syndrome, and exacerbate complications.[17]

**History and Physical**

Understanding the signs and symptoms of dyslipidemia is crucial for timely intervention and preventing associated complications. As dyslipidemia often progresses silently, routine lipid screening (especially in high-risk populations) remains a cornerstone for early detection and effective management. Clinicians should consider the broader clinical

context, including family history and risk factors, to guide appropriate interventions and reduce the burden of cardiovascular diseases associated with dyslipidemia. Pertinent social history would include tobacco use or specific details about diet. Past medical history is vital in identifying patients needing primary prevention versus secondary prevention if statin therapy requires initiation. Lastly, family history is important to identify familial hypercholesterolemia.

Some patients with severe or untreated dyslipidemia may develop signs and symptoms related to the complications of dyslipidemia, such as atherosclerosis, coronary artery disease, peripheral artery disease, stroke, and heart failure. Some of the possible signs and symptoms of dyslipidemia are:

- **Xanthomas**: These are yellowish fat deposits visible on the skin of the eyelids (xanthelasma), palms, tendons, or other areas. They can form plaques or nodules and indicate high levels of cholesterol or triglycerides in the blood.
- **Arcus senilis**: This is a gray or white ring around the eye's cornea that is caused by cholesterol depositing in the corneal margin and indicates high cholesterol levels in the blood. This is more common in older people but can also occur in younger people with dyslipidemia.
- **Lipemia retinalis:** This condition produces a milky appearance in the retinal vessels due to high blood triglyceride levels. Lipemia retinalis is a rare condition that can cause blurred vision and may indicate severe hypertriglyceridemia.
- **Lower limb ischemia**: This type of ischemia is a common symptom of peripheral artery disease, caused by the narrowing or blockage of the arteries that supply blood to the legs due to atherosclerosis; this condition is usually characterized by pain or cramping during physical activity (walking or exercising) and improves with rest. Lower limb ischemia may indicate high levels of LDL, cholesterol, or triglycerides in the blood.
- **Angina**: This is a common symptom of coronary artery disease, caused by the narrowing or blockage of the arteries that supply blood to the heart due to atherosclerosis. The pain usually occurs when the heart needs more oxygen, such as during physical or emotional stress, and may radiate to the neck, jaw, shoulders, or back. Angina may indicate high levels of LDL cholesterol or triglycerides in the blood.
- **Transient ischemic attacks and strokes**: Dyslipidemia increases the risk of atherosclerosis in cerebral arteries, contributing to sudden interruption of blood

flow to the brain due to a clot or a bleed in weakened blood vessel walls. Symptoms may include sudden weakness, slurred speech, or visual disturbances.[18][19]

**Evaluation**

Dyslipidemia, a crucial risk factor for cardiovascular diseases, necessitates comprehensive diagnostic investigations for accurate assessment. The primary evaluation tool for dyslipidemia is a fasting lipid panel comprising total cholesterol, LDL, HDL, and triglycerides. Some debate is prevalent on the age at which dyslipidemia screening should start.

**Screening Guidelines and Tests**:

- The National Cholesterol Education Program provides the Adult Treatment Panel III—widely acknowledged guidelines for dyslipidemia screening. Guidelines recommend a fasting lipid panel every 5 years for adults 20 years and older.
- The US Preventive Services Task Force recommends lipid screening in men 35 years and older (as well as men who are high-risk, age 20 to 35) and women 45 years and older (as well as high-risk individuals between 20 and 45 years). Younger adults are advised to undergo screening if they have cardiovascular risk factors. Other recommendations suggest getting fasting lipid panels for all individuals who are between 20 to 78 at least every 5 years if no atherosclerotic disease is present.[20]
- The American Academy of Pediatrics recommends screening for dyslipidemia in children and adolescents aged 9 to 11 years and 17 to 21 years, regardless of risk factors, and selective screening for those aged 2 to 8 years and 12 to 16 years who have a family history of dyslipidemia or CVD, or other risk factors, such as obesity, diabetes, hypertension, or smoking.[21]
- The American Heart Association and American College of Cardiology recommendations for Cardiovascular Risk Assessment guidelines use a risk calculator to estimate the 10-year risk of atherosclerotic cardiovascular disease, which includes coronary heart disease, stroke, and peripheral artery disease. The risk calculator takes into account the age, sex, race, total cholesterol, HDL, systolic blood pressure, antihypertensive therapy, diabetes, and smoking status of the individual. The risk categories are: low risk (<5%), borderline risk (5% to 7.4%), intermediate risk (7.5% to 19.9%), and high risk (≥20%). These guidelines suggest routine lipid screening for patients between 40 and 75 years every 4 to 6 years. High-risk individuals, including those with diabetes or a history of cardiovascular disease, may require more frequent assessments.

- The National Institute of Health and Clinical Excellence provides comprehensive guidelines on lipid modification for cardiovascular risk reduction. The guideline uses the QRISK3 tool, which estimates the 10-year risk of cardiovascular disease, including coronary heart disease, stroke, and transient ischemic attack. The QRISK3 tool considers the age, sex, ethnicity, postcode, smoking status, body mass index, systolic blood pressure, cholesterol ratio, atrial fibrillation, diabetes, chronic kidney disease, rheumatoid arthritis, and family history of the individual. The risk categories are: low risk (<10%), moderate risk (10%-19%), and high risk (≥20%).

**Classification of Lipid Levels**

**Total cholesterol**

- Desirable: <200 mg/dL
- Borderline high: 200 mg/dL to 239 mg/dL
- High: ≥240 mg/dL

**Low-density lipoprotein cholesterol**

- Optimal: <100 mg/dL
- Near optimal/above optimal: 100 mg/dL to 129 mg/dL
- Borderline high: 130 mg/dL to 159 mg/dL
- High: 160 mg/dL to 189 mg/dL
- Very high: ≥190 mg/dL

**High-density lipoprotein cholesterol**

- Low: <40 mg/dL (men), <50 mg/dL (women)
- High: ≥60 mg/dL

**Triglycerides**

- Normal: <150 mg/dL
- Borderline high: 150 mg/dL to 199 mg/dL
- High: 200 mg/dL to 499 mg/dL
- Very high: ≥500 mg/dL

Classification of dyslipidemia is subdivided into 5 different categories, according to Frederickson phenotype:

- Phenotype I is an abnormality of chylomicrons and will result in triglycerides greater than 99 percentiles.
- Phenotype IIa consists mainly of LDL cholesterol abnormality and will have a total cholesterol concentration greater than 90 percentile and possibly apolipoprotein B greater than 90 percentile.
- Phenotype IIb consists of abnormality in LDL and VLDL cholesterol. This type will result in total cholesterol or triglycerides greater than the 90 percentile and apolipoprotein greater than the 90 percentile.
- Phenotype III is an abnormality in VLDL remnants and chylomicrons, which results in elevated total cholesterol and triglycerides greater than 90 percentile.
- Phenotype IV is mainly when VLDL is abnormal and results in total cholesterol greater than 90 percentile. This type can also present with triglycerides greater than 90 percentile and low HDL.
- Phenotype V is when chylomicrons and VLDL are abnormal and triglycerides are greater than 99 percentiles.[6][22]

**Treatment / Management**

Managing dyslipidemia initially involves lifestyle modifications, including those listed below.

**Dietary Modification**

Dietary changes include reducing the intake of saturated and trans fats, cholesterol, and refined carbohydrates and increasing the intake of unsaturated fats, fiber, plant sterols, and antioxidants. A healthy diet for dyslipidemia management should follow the principles of the Mediterranean diet, the Dietary Approaches to Stop Hypertension diet, or the Therapeutic Lifestyle Changes diet. These diets lower the LDL, triglyceride, and non-HDL levels, increase the HDL levels, and reduce blood pressure, inflammation, and oxidative stress.[23]

**Physical Activity**

Physical activity is an important component of lifestyle modification, as it can improve the lipid profile, lower blood pressure, enhance insulin sensitivity, and promote weight loss. Physical activity can also reduce cardiovascular risk by improving endothelial function,

reducing inflammation, and preventing thrombosis. The recommended amount and intensity of physical activity for dyslipidemia management vary depending on the patient's age, health status, and goals. The American Heart (AHA) Association suggests that adults should aim for at least 150 minutes of moderate-intensity aerobic exercise, 75 minutes of vigorous-intensity aerobic exercise per week, or a combination of both. Moderate-intensity aerobic exercise includes brisk walking, cycling, swimming, or dancing. Vigorous-intensity aerobic exercise includes running, jumping rope, or playing sports. In addition, the AHA recommends that adults should also perform muscle-strengthening exercises at least twice a week, involving all major muscle groups. Examples of muscle-strengthening exercises include lifting weights, doing push-ups, or using resistance bands. Patients with dyslipidemia should consult their clinician before starting or increasing physical activity and follow the appropriate safety precautions and guidelines.[24]

**Weight Management**

Weight management is another key aspect of lifestyle modification, as it can improve the lipid profile, lower blood pressure, and reduce the risk of diabetes and metabolic syndrome. Weight management involves achieving and maintaining a healthy body weight, defined as a body mass index of 18.5 to 24.9 $kg/m^2$. Patients with dyslipidemia who are overweight or obese should aim for a gradual and sustained weight loss of 5% to 10% of their initial body weight over 6 to 12 months, which can be achieved by reducing calorie intake and increasing physical activity.

**Smoking Cessation**

Smoking cessation can improve the lipid profile, lower blood pressure, and reduce the risk of CVD and other chronic diseases. Smoking can adversely affect the lipid profile by increasing the LDL, triglyceride, and non-HDL levels and decreasing the HDL level. Smoking can also increase the CVD risk by damaging the endothelium, increasing inflammation, promoting LDL oxidation, enhancing platelet aggregation, and inducing vasoconstriction. Quitting smoking can reverse these effects and improve the lipid profile and the CVD risk within weeks to months.

**Treatment Strategies**

The first-line treatment for dyslipidemia is statins that inhibit 3-hydroxy-3methylglutaryl-coenzyme A reductase. Patients with clinically significant atherosclerotic cardiovascular disease (ASCVD) (acute coronary syndromes, history of myocardial infarction, stable or unstable angina, arterial revascularization, and stroke) and are aged less than 75 should be prescribed a high-intensity statin. Patients 75 years or older with clinical ASCVD should be prescribed a moderate-intensity statin.

High-intensity statin therapy should start if the patient is aged 40 to 75, has LDL greater than or equal to 190 mg/dL, or has a history of diabetes and LDL between 70 to 189 mg/dL. Patients should be on a moderate or high-intensity statin if they are 40 to 75 years old, have LDL between 70 to 189 mg/dL, and have a 10-year ASCVD greater than or equal to 7.5%. The clinician-patient discussion should be undertaken to discuss the introduction of high or moderate-intensity statin in situations such as less than 5% to 7.5% 10-year ASCVD risk.[25]

For primary prevention, statin therapy should lower LDL by approximately 30% to less than 50% with a moderate-intensity statin and greater than or equal to 50% with a high-intensity statin. High-intensity statins are atorvastatin, 40 or 80 mg, and rosuvastatin, 20 mg. Some moderate-intensity statins are atorvastatin 10 mg, rosuvastatin 10 mg, simvastatin 20 or 40 mg, and pravastatin 10 mg.[26]

For secondary prevention, as defined by a patient with coronary artery disease, a target goal is set for LDL less than 70 mg/dL after being placed on a high-intensity statin for 6 weeks. If this goal is not met and LDL is significantly greater than 70, then combination therapy should be started in addition to high-intensity statin. The LDL goal should remain less than 70 mg/dL if the patient is not high-risk. If the patient is high risk (eg, had acute coronary syndrome in the last year, familial hypercholesterolemia, diabetes, chronic kidney disease stage 3 or 4, atherosclerotic cardiovascular disease event, or the need for revascularization while on a statin), the LDL goal is less than 50 mg/dL, and another agent is added.

Currently, 2 classes of medications are recommended with statin therapy because they decrease cardiovascular outcomes. One of these is ezetimibe, which inhibits the absorption of cholesterol. Combined with statin therapy, this drug can lower LDL by 25%. Another category targets proprotein convertase subtilisin/kexin type 9 (PCSK9), which regulates the LDL receptor. An increase in PSCK9 decreases LDL receptors and increases LDL levels in the blood. PCSK9 inhibitors are monoclonal antibodies that bind PCSK9 and decrease LDL levels. The new agent, inclisiran, is an interfering ribonucleic acid drug that stops the production of PCSK9 with twice-yearly dosing.[27] This agent is beneficial in patients who are intolerant of LDL-lowering medications. Icosapent ethyl is a Food and Drug Administration-approved medication that reduces cardiovascular risk in patients with elevated triglycerides in addition to maximal statin therapy. Bempedoic acid is another drug that is an option for people intolerant to statins in combination with ezetimibe. This drug works by inhibiting adenosine triphosphate citrate lyase, which increases cholesterol in the liver and decreases levels. Many new medications are being researched to help lower cholesterol levels and prevent cardiovascular events.

Other categories of treatment not shown to reduce cardiovascular events but have been useful in dyslipidemia therapy are bile acid sequestrants such as cholestyramine, colestipol, and colesevelam, which decrease bile acid reabsorption, therefore increasing clearance of LDL. Fibric acid derivatives (fibrates) are peroxisome proliferator-activated receptor agonists. These increase HDL and reduce triglycerides. However, in combination with statins, they can increase the risk of myopathy and rhabdomyolysis, which can cause generalized muscle pain. Current guidelines recommend against the use of statins and gemfibrozil. Niacin increases HDL and reduces VLDL, decreasing LDL but with a significant side effect profile. Aspirin can decrease the occurrence of this side effect.[28][29][30][31][32][33]

Different guidelines are available that provide recommendations and targets for the pharmacological treatment of dyslipidemia, such as the U.S. Department of Veterans Affairs and Department of Defense, the European Society of Cardiology and European Atherosclerosis Society, the Canadian Cardiovascular Society, the American College of Cardiology and American Heart Association.[34]

Different guidelines have been developed to provide recommendations and targets for the pharmacological treatment of dyslipidemia (see **Table.** Recommendations and Targets for Pharmacologically Treating Dyslipidemia), such as the U.S. Department of Veterans Affairs and Department of Defense (VA/DoD), the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS), the Canadian Cardiovascular Society (CCS), and the American College of Cardiology (ACC) and American Heart Association (AHA).[34]

**Differential Diagnosis**

The differential diagnosis should include the following:

- Nephrotic syndrome [35]
- Biliary obstruction
- Hypothyroidism
- Pregnancy
- Drugs (oral estrogens, glucocorticoids, tamoxifen, thiazides)[29]

**Prognosis**

The prognosis of dyslipidemia depends on several factors, such as the type and severity of the lipid disorder, the presence of other cardiovascular risk factors, adherence to lifestyle modification and pharmacotherapy, and the occurrence of complications. Some types of dyslipidemia are more serious and require more aggressive intervention than others. For

example, familial hypercholesterolemia is a genetic form of dyslipidemia that causes very high levels of LDL cholesterol and increases the risk of early and severe cardiovascular events. Patients with this condition need to start pharmacotherapy, usually with statins, ezetimibe, or PCSK9 inhibitors, as early as possible and may also require other treatments, such as apheresis or gene therapy.

Environmental or behavioral factors, such as diet, obesity, physical inactivity, smoking, alcohol consumption, or the use of certain medications, influence other types of dyslipidemia. These types of dyslipidemia are improved by modifying these factors and adopting a healthier lifestyle. Some types of dyslipidemia are associated with other medical conditions, such as diabetes, hypothyroidism, chronic kidney disease, liver disease, or pancreatitis. These types of dyslipidemia are improved by treating the underlying condition and managing complications.[36]

**Complications**

The most significant complication of dyslipidemia is cardiovascular disease. Complications include sudden cardiac death, acute myocardial infarction, or stroke. Multiple studies have demonstrated that statin and appropriate dyslipidemia treatment has significantly reduced the risk of all-cause mortality, cardiovascular events, and cardiovascular mortality.[37]

**Deterrence and Patient Education**

As discussed above, patients must recognize and adhere to specific health behaviors that can maintain and lower lipid levels. These include, but are not limited to, weight control, which consists of a heart-healthy diet and exercise, as well as avoidance of tobacco. As stated above, patients should also talk with their primary care clinicians about when to start getting screened or initiate treatment. Herbs, red yeast extract, turmeric and curcumin, garlic, and other herbs are some of the natural supplements that may benefit the lipid profile and cardiovascular risk. However, the evidence for their efficacy and safety is inconclusive, and they may interact with some medications or cause adverse effects.

**Enhancing Healthcare Team Outcomes**

Enhancing healthcare outcomes for patients with dyslipidemia requires a multidisciplinary treatment team, including cardiologists or endocrinologists, nurses, pharmacists, dietitians, and educators. A multidisciplinary team approach can offer several benefits in managing dyslipidemia, such as improving the diagnosis of lipid conditions like familial hypercholesterolemia, hypertriglyceridemia, and mixed dyslipidemia through appropriate screening and testing methods. Providing individualized and evidence-based treatment plans, including lifestyle modifications and pharmacological interventions, based on the

patient's cardiovascular risk profile, comorbidities, preferences, and goals, is imperative. Enhancing adherence to lipid-lowering therapies and evaluating the outcomes and effectiveness of dyslipidemia management are both essential. Clinicians must know up-to-date guidelines on lipid screening, treatment indications, and LDL level goals.

**Review Questions**

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**Tables**

**Table. Recommendations and Targets for Pharmacologically Treating Dyslipidemia**

| | LDL Target (mg/dL) | Non-HDL Target (mg/dL) | First-line Treatment | Add-on Treatm |
|---|---|---|---|---|
| **VA/DoD** | <100 for patients with CVD or diabetes, <130 for patients without CVD or diabetes | <130 for patients with CVD or diabetes or <160 for patients without CVD or diabetes | Moderate-dose statins for all patients | High-dose stat ezetimibe, or P inhibitors for h patients |
| **ESC/EAS** | <55 for patients at very high risk, <70 for patients at high risk, <100 for patients at moderate risk, <115 for patients at low risk | <80 for patients at very high risk, <100 for patients at high risk, <130 for patients at moderate risk, <145 for patients at low risk | High-intensity statins for patients at very high or high risk or Moderate-intensity statins for patients at moderate or low risk | Ezetimibe or P inhibitors for p who have not a their LDL targe intolerant to st fibrates, niacin omega-3 fatty a specific indica |

| | | | | |
|---|---|---|---|---|
| **CCS** | <50% reduction in LDL-C from baseline in patients at high risk or <30% reduction in LDL from baseline in patients at intermediate risk | <50% reduction in non-HDL-C from baseline in patients at high risk or < 30% reduction in non-HDL from baseline in patients at intermediate risk | Moderate- or high-intensity statins for patients at high or intermediate risk, depending on the baseline LDL level and the presence of risk-enhancing factors | Ezetimibe or P inhibitors for p who have not a their LDL targe intolerant to st fibrates, niacin omega-3 fatty a specific indica |
| **ACC/AHA** | <70 for patients with CVD or diabetes or <100 for patients without CVD or diabetes | <100 for patients with CVD or diabetes or <130 for patients without CVD or diabetes | Moderate-intensity statins for all patients | High-intensity ezetimibe, or P inhibitors for h patients or tho risk-enhancing |



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