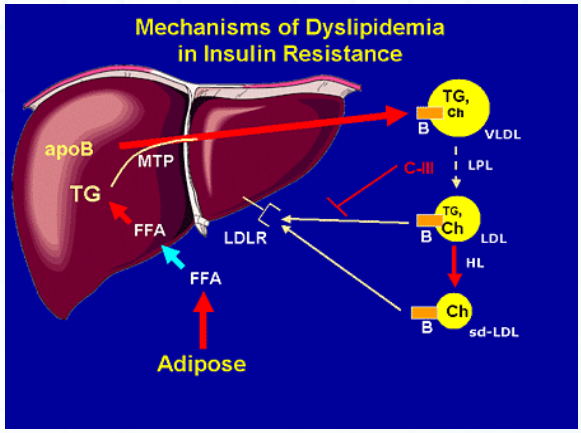
Dyslipidemia



Dyslipidemia is the elevation of plasma cholesterol, triglycerides (TGs), or both, or a low high-density lipoprotein level that contributes to the development of atherosclerosis. Causes may be primary (genetic) or secondary. Diagnosis is by measuring plasma levels of total cholesterol, TGs, and individual lipoproteins. Treatment involves dietary changes, exercise, and lipid-lowering drugs.

There is no natural cutoff between normal and abnormal lipid levels because lipid measurements are continuous. A linear relation probably exists between lipid levels and cardiovascular risk, so many people with “normal” cholesterol levels benefit from achieving still lower levels. Consequently, there are no numeric definitions of dyslipidemia; the term is applied to lipid levels for which treatment has proven beneficial. Proof of benefit is strongest for lowering elevated low-density lipoprotein (LDL) levels. In the overall population, evidence is less strong for a benefit from lowering elevated TG and increasing low high-density lipoprotein (HDL) levels.

HDL levels do not always predict cardiovascular risk. For example, high HDL levels caused by some genetic disorders may not protect against cardiovascular disorders, and low HDL levels caused by some genetic disorders may not increase the risk of cardiovascular disorders. Although HDL levels predict cardiovascular risk in the overall population, the increased risk may be caused by other factors, such as accompanying lipid and metabolic abnormalities, rather than the HDL level itself.

Classification

Dyslipidemias were traditionally classified by patterns of elevation in lipids and lipoproteins (Fredrickson phenotype—Lipoprotein Patterns (Fredrickson Phenotypes)). A more practical system categorizes dyslipidemias as primary or secondary and characterizes them by increases in cholesterol only (pure or isolated hypercholesterolemia), increases in TGs only (pure or isolated hypertriglyceridemia), or increases in both cholesterol and TGs (mixed or combined hyperlipidemias). This system does not take into account specific lipoprotein abnormalities (eg, low HDL or high LDL) that may contribute to disease despite normal cholesterol and TG levels.

Etiology

Primary (genetic) causes and secondary (lifestyle and other) causes contribute to dyslipidemias in varying degrees. For example, in familial combined hyperlipidemia, expression may occur only in the presence of significant secondary causes.

Primary causes

The primary causes are single or multiple gene mutations that result in either overproduction or defective clearance of TG and LDL cholesterol, or in underproduction or excessive clearance of HDL (Genetic (Primary) Dyslipidemias). The names of many primary disorders reflect an old nomenclature in which lipoproteins were detected and distinguished by how they separated into α (HDL) and β (LDL) bands on electrophoretic gels.

Secondary causes

Secondary causes contribute to many cases of dyslipidemia in adults. The most important secondary cause in developed countries is a sedentary lifestyle with excessive dietary intake of saturated fat, cholesterol, and trans fats. Trans fats are polyunsaturated or monounsaturated fatty acids to which hydrogen atoms have been added; they are commonly used in many processed foods and are as atherogenic as saturated fat. Other common secondary causes include diabetes

mellitus, alcohol overuse, chronic kidney disease, hypothyroidism, primary biliary cirrhosis and other cholestatic liver diseases, and drugs, such as thiazides, β-blockers, retinoids, highly active antiretroviral agents, cyclosporine, tacrolimus, estrogen and progestins, and glucocorticoids. Secondary causes of low levels of HDL cholesterol include cigarette smoking, anabolic steroids, HIV infection, and nephrotic syndrome.

Diabetes is an especially significant secondary cause because patients tend to have an atherogenic combination of high TGs; high small, dense LDL fractions; and low HDL (diabetic dyslipidemia, hypertriglyceridemic hyperapo B). Patients with type 2 diabetes are especially at risk. The combination may be a consequence of obesity, poor control of diabetes, or both, which may increase circulating free fatty acids (FFAs), leading to increased hepatic very-low-density lipoprotein (VLDL) production. TG-rich VLDL then transfers TG and cholesterol to LDL and HDL, promoting formation of TG-rich, small, dense LDL and clearance of TG-rich HDL. Diabetic dyslipidemia is often exacerbated by the increased caloric intake and physical inactivity that characterize the lifestyles of some patients with type 2 diabetes. Women with diabetes may be at special risk of cardiac disease from this form.

Symptoms and Signs

Dyslipidemia itself usually causes no symptoms but can lead to symptomatic vascular disease, including coronary artery disease (CAD), stroke, and peripheral arterial disease. High levels of TGs (> 1000 mg/dL [> 11.3 mmol/L]) can cause acute pancreatitis. High levels of LDL can cause Arcus corneae and tendinous Xanthomas of the Achilles, elbow, and knee tendons and over metacarpophalangeal joints. Patients with the homozygous form of familial hypercholesterolemia may have the above findings plus planar or tuberous xanthomas. Planar Xanthomas are flat or slightly raised, yellowish patches. Tuberous xanthomas are painless, firm nodules typically located over extensor surfaces of joints. Patients with severe elevations of TGs can have eruptive Xanthomas over the trunk, back, elbows, buttocks, knees, hands, and feet.

Patients with the rare dysbetalipoproteinemia can have palmar and tuberous xanthomas.

Severe hypertriglyceridemia (> 2000 mg/dL [> 22.6 mmol/L]) can give retinal arteries and veins a creamy white appearance (lipemia retinalis). Extremely high lipid levels also give a lactescent (milky) appearance to blood plasma. Symptoms can include paresthesias, dypsnea, and confusion

Diagnosis

Serum lipid profile (measured total cholesterol, TG, and HDL cholesterol and calculated LDL cholesterol and VLDL)

Dyslipidemia is suspected in patients with characteristic physical findings or complications of dyslipidemia (eg, atherosclerotic disease). Primary lipid disorders are suspected when patients have physical signs of dyslipidemia, onset of premature atherosclerotic disease (at < 60 yr), a family history of atherosclerotic disease, or serum cholesterol > 240 mg/dL (> 6.2 mmol/L). Dyslipidemia is diagnosed by measuring serum lipids. Routine measurements (lipid profile) include total cholesterol (TC), TGs, HDL cholesterol, and LDL cholesterol.

Lipid profile measurement

TC, TGs, and HDL cholesterol are measured directly. TC and TG values reflect cholesterol and TGs in all circulating lipoproteins, including chylomicrons, VLDL, intermediate-density lipoprotein (IDL), LDL, and HDL. TC values can vary by 10% and TGs by up to 25% day-to-day even in the absence of a disorder. TC and HDL cholesterol can be measured in the nonfasting state, but most patients should have all lipids measured while fasting (usually for 12 h) for maximum accuracy and consistency.

Testing should be postponed until after resolution of acute illness because TG and lipoprotein(a) levels increase and cholesterol levels decrease in inflammatory states. Lipid profiles can vary for about 30 days after an acute MI; however,

results obtained within 24 h after MI are usually reliable enough to guide initial lipid-lowering therapy.

Clinical Calculator: Very Low Density Lipoprotein (VLDL)

LDL cholesterol values are most often calculated as the amount of cholesterol not contained in HDL and VLDL. VLDL is estimated by TG ÷ 5 because the cholesterol concentration in VLDL particles is usually one fifth of the total lipid in the particle.

This calculation is valid only when TGs are < 400 mg/dL and patients are fasting, because eating increases TGs. The calculated LDL cholesterol value incorporates measures of all non-HDL, nonchylomicron cholesterol, including that in IDL and lipoprotein (a) [Lp(a)]. LDL can also be measured directly using plasma ultracentrifugation, which separates chylomicrons and VLDL fractions from HDL and LDL, and by an immunoassay method. Direct measurement may be useful in some patients with elevated TGs, but these direct measurements are not routinely necessary. The role of APO B testing is under study because values reflect all non-HDL cholesterol (in VLDL, VLDL remnants, IDL, and LDL) and may be more predictive of CAD risk than LDL cholesterol. Non-HDL cholesterol (TC - HDL cholesterol) may also be more predictive of CAD risk than LDL cholesterol.

Clinical Calculator: Friedewald Equation for Low Density Lipoprotein (LDL-C SI units)

Other tests

Patients with premature atherosclerotic cardiovascular disease, cardiovascular disease with normal or near-normal lipid levels, or high LDL levels refractory to drug therapy should probably have Lp(a) levels measured. Lp(a) levels may also be directly measured in patients with borderline high LDL cholesterol levels to

determine whether drug therapy is warranted. C-reactive protein may be considered in the same populations. Measurements of LDL particle number or apoprotein B-100 (APO B) may be useful in patients with elevated TGs and the metabolic syndrome. Apo B provides similar information to LDL particle number because there is one APO B molecule for each LDL particle. APO B measurement includes all atherogenic particles, including remnants and LP (a).

Secondary causes

Tests for secondary causes of dyslipidemia—including measurements of fasting glucose, liver enzymes, creatinine, thyroid-stimulating hormone (TSH), and urinary protein—should be done in most patients with newly diagnosed dyslipidemia and when a component of the lipid profile has inexplicably changed for the worse.

Screening

Universal screening using a fasting lipid profile (TC, TGs, HDL cholesterol, and calculated LDL cholesterol) should be done in all children between age 9 and 11 (or at age 2 if children have a family history of severe hyperlipidemia or premature CAD). Adults are screened at age 20 yr and every 5 yr thereafter. Lipid measurement should be accompanied by assessment of other cardiovascular risk factors, defined as

- Diabetes mellitus
- Cigarette use
- Hypertension

Family history of CAD in a male 1st-degree relative before age 55 or a female 1st-degree relative before age 65

A definite age after which patients no longer require screening has not been established, but evidence supports screening of patients into their 80s, especially in the presence of atherosclerotic cardiovascular disease.

Patients with an extensive family history of heart disease should also be screened by measuring Lp(a) levels.

Treatment

Risk assessment by explicit criteria

Lifestyle changes (eg, exercise, dietary modification)

For high LDL cholesterol, statins, sometimes bile acid sequestrants, ezetimibe, niacin, and other measures

For high TG, niacin, fibrates, omega-3 fatty acids, and sometimes other measures

General principles

Treatment is indicated for all patients with cardiovascular disease (secondary prevention) and for some without (primary prevention). The National Institutes of Health's National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) guidelines are the most common reference for deciding which adults should be treated (National Cholesterol Education Program Adult Treatment Panel III Approach to Dyslipidemias and see Table: NCEP Adult Treatment Panel III Guidelines for Treatment of Hyperlipidemia). The guidelines focus primarily on reducing elevated LDL cholesterol levels and secondarily on treating high TGs, low HDL, and metabolic syndrome (seeMetabolic Syndrome). New guidelines have just been published by the American Heart Association (late November 2013; see ACC/AHA Guideline on the Treatment of Blood Cholesterol) and will be available on this page shortly.

Treatment of children is controversial; dietary changes may be difficult to implement, and no data suggest that lowering lipid levels in childhood effectively prevents heart disease in adulthood. Moreover, the safety and effectiveness of long-term lipid-lowering treatment are questionable. Nevertheless, the American Academy of Pediatrics (AAP) recommends treatment for some children who have elevated LDL cholesterol levels. Children with heterozygous familial hypercholesterolemia should be treated beginning at age 10. Children with homozygous familial hypercholesterolemia require diet, medications, and often

LDL apheresis to prevent premature death; treatment is begun when diagnosis is made.

Treatment options depend on the specific lipid abnormality, although different lipid abnormalities often coexist. In some patients, a single abnormality may require several therapies; in others, a single treatment may be adequate for several abnormalities. Treatment should always include treatment of hypertension and diabetes, smoking cessation, and in patients with a 10-yr risk of MI or death from CAD of ≥ 10% (as determined from the NHLBI NHLBI Cardiac Risk **Calculator or Framingham tables—** Framingham Risk Tables for Men and see Table: Framingham Risk Tables for Women), low-dose daily aspirin. In general, treatment options for men and women are the same.

Elevated LDL cholesterol

In adults , ATPIII guidelines recommend treatment for those with any of the following:

Elevated LDL cholesterol levels and a history of CAD

Conditions that confer a risk of future cardiac events similar to that of CAD itself (CAD equivalents, defined as diabetes mellitus, abdominal aortic aneurysm, peripheral arterial disease, and symptomatic carotid artery disease)

≥ 2 CAD risk factors

ATPIII guidelines recommend that these patients have LDL cholesterol levels lowered to < 100 mg/dL, but accumulating evidence suggests that this target may be too high and a target LDL cholesterol < 70 mg/dL is an option for patients at very high risk (eg, patients with known CAD and diabetes, other poorly controlled risk factors, metabolic syndrome, or acute coronary syndrome). When drugs are used, a dose providing at least a 30 to 40% decrease in LDL cholesterol is desirable (Lipid–Lowering Drugs).

For children , the AAP recommends dietary treatment for children with LDL cholesterol > 110 mg/dL (> 2.8 mmol/L). Drug therapy is recommended for children > 8 yr and with either of the following:

Poor response to dietary therapy, LDL cholesterol ≥ 190 mg/dL (≥ 4.9 mmol/L), and no family history of premature cardiovascular disease

LDL cholesterol ≥ 160 mg/dL (> 4.13 mmol/L) and a family history of premature cardiovascular disease or ≥ 2 risk factors for premature cardiovascular disease

Childhood risk factors besides family history and diabetes include cigarette smoking, hypertension, low HDL cholesterol (< 35 mg/dL), obesity, and physical inactivity.

Treatment options to lower LDL cholesterol in all age groups include lifestyle changes (diet and exercise), drugs, dietary supplements, procedural interventions, and experimental therapies. Many of these options are also effective for treating other lipid abnormalities. Exercise lowers LDL cholesterol in some people; it is also essential to maintain ideal body weight. Dietary changes and exercise should be the initial approach whenever feasible.

Lifestyle changes can involve diet and exercise. Dietary changes include decreasing intake of saturated fats and cholesterol; increasing the proportion of dietary fiber, and complex carbohydrates; and maintaining ideal body weight. Referral to a dietitian is often useful, especially for older people. The length of time for which lifestyle changes should be attempted before beginning lipid-lowering drugs is controversial. In patients at average or low cardiovascular risk, 3 to 6 mo is reasonable. Generally, 2 to 3 visits with a patient over 2 to 3 mo are sufficient to assess motivation and adherence.

Drugs are the next step when lifestyle changes are not effective. However, for patients with extremely elevated LDL cholesterol (≥ 190 mg/dL [≥ 4.9 mmol/L]) and those at high cardiovascular risk, drug therapy should accompany diet and exercise from the start.

Statins are the drugs and possibly treatment of choice for LDL cholesterol reduction; they demonstrably reduce cardiovascular mortality. Statins inhibit hydroxymethylglutaryl CoA reductase, a key enzyme in cholesterol synthesis, leading to up-regulation of LDL receptors and increased LDL clearance. They reduce LDL cholesterol by up to 60% and produce small increases in HDL and

modest decreases in TGs. Statins also appear to decrease intra-arterial inflammation, systemic inflammation, or both by stimulating production of endothelial nitric oxide and may have other beneficial effects. Adverse effects are uncommon but include liver enzyme elevations and myositis or rhabdomyolysis. Liver enzyme elevations are uncommon, and serious liver toxicity is extremely rare. Muscle problems occur in up to 10% of patients taking statins and may be dose-dependent in many patients. Muscle symptoms can occur without enzyme elevation. Adverse effects are more common among older patients, patients with several disorders, and patients taking several drugs. In some patients, changing from one statin to another or lowering the dose relieves the problem. Muscle toxicity seems to be most common when some of the statins are used with drugs that inhibit cytochrome P3A4 (eg, macrolide antibiotics, azole antifungals, cyclosporine) and with fibrates, especially gemfibrozil. Properties of statins differ slightly by drug, and the choice of drug should be based on patient characteristics, LDL cholesterol level, and provider discretion (Lipid–Lowering Drugs). Statins are contraindicated during pregnancy and lactation.

Bile acid sequestrants block intestinal bile acid reabsorption, forcing up-regulation of hepatic LDL receptors to recruit circulating cholesterol for bile synthesis. They are proved to reduce cardiovascular mortality. Bile acid sequestrants are usually used with statins or with nicotinic acid (see Lipid Disorders:Low HDL) to augment LDL cholesterol reduction and are the drugs of choice for women who are or are planning to become pregnant. Bile acid sequestrants are safe, but their use is limited by adverse effects of bloating, nausea, cramping, and constipation. They may also increase TGs, so their use is contraindicated in patients with hypertriglyceridemia. Cholestyramine and colestipol, but not usually colesevelam, interfere with absorption of other drugs—notably thiazides, β-blockers, warfarin, digoxin, and thyroxine—an effect that can be decreased by administration 4 h before or 1 h after other drugs. Bile acid sequestrants should be given with meals to increase their efficacy.

Cholesterol absorption inhibitors , such as ezetimibe, inhibit intestinal absorption of cholesterol and phytosterol. Ezetimibe usually lowers LDL cholesterol by 15 to 20% and causes small increases in HDL and a mild decrease in TGs.Ezetimibe can

be used as monotherapy in patients intolerant to statins or added to statins for patients on maximum doses with persistent LDL cholesterol elevation. Adverse effects are infrequent.

Dietary supplements that lower LDL cholesterol levels include fiber supplements and commercially available margarines and other products containing plant sterols (sitosterol and campesterol) or stanols. The latter reduce LDL cholesterol by up to 10% without affecting HDL or TGs by competitively displacing cholesterol from intestinal micelles.

Drugs for homozygous familial hypercholesterolemia include mipomersen and lomitapide. Mipomersen is an apo B antisense oligonucleotide that decreases synthesis of apo B in liver cells and decreases levels of LDL, apo B, and Lp(a). It is given by subcutaneous injection and can cause injection site reactions, flu-like symptoms, and increased hepatic fat and liver enzyme elevations. Lomitapide is an inhibitor of microsomal triglyceride transfer protein inhibitor that interferes with the secretion of TG-rich lipoproteins in the liver and intestine. Dose is begun low and gradually titrated up about every 2 wk. Patients must follow a diet with less than 20% of calories from fat. Lomitapide can cause GI adverse effects (eg, diarrhea, increased hepatic fat, elevated liver enzymes).

Procedural approaches are reserved for patients with severe hyperlipidemia (LDL cholesterol > 300 mg/dL (> 7.74 mmol/L) in patients without vascular disease, and for LDL apheresis, LDL cholesterol > 200 mg/dL (> 5.16 mmol/L) in patients with vascular disease) that is refractory to conventional therapy, such as occurs with familial hypercholesterolemia. Options include LDL apheresis (in which LDL is removed by extracorporeal plasma exchange) and rarely, ileal bypass (to block reabsorption of bile acids), liver transplantation (which transplants LDL receptors), and portocaval shunting (which decreases LDL production by unknown mechanisms). LDL apheresis is the procedure of choice in most instances when maximally tolerated therapy fails to lower LDL adequately. Apheresis is also the usual therapy in patients with the homozygous form of familial hypercholesterolemia who have limited or no response to drug therapy.

Future therapies to reduce LDL include peroxisome proliferator–activated receptor agonists that have thiazolidinedione-like and fibrate-like properties, LDL-receptor activators, LPL activators, and recombinant apo E. Cholesterol vaccination (to induce anti-LDL antibodies and hasten LDL clearance from serum) and gene transfer are conceptually appealing therapies that are under study but years away from being available for use. Injectable monoclonal antibodies that inhibit the function of PCSK9 and substantially lower LDL cholesterol are in clinical trials.

Elevated TGs

Although it is unclear whether elevated TGs independently contribute to cardiovascular disease, they are associated with multiple metabolic abnormalities that contribute to CAD (eg, diabetes, metabolic syndrome). Consensus is emerging that lowering elevated TGs is beneficial (National Cholesterol Education Program Adult Treatment Panel III Approach to Dyslipidemias). No target goals exist, but levels < 150 mg/dL (< 1.7 mmol/L) are generally considered desirable. No guidelines specifically address treatment of elevated TGs in children.

The overall treatment strategy is to first implement lifestyle changes, including exercise, weight loss, and avoidance of concentrated dietary sugar and alcohol. Intake of 2 to 4 servings/wk of marine fish high in ω-3 fatty acids may be effective, but the amount of ω-3 fatty acids is often lower than needed; supplements may be helpful. In patients with diabetes, glucose levels should be tightly controlled. If these measures are ineffective, lipid-lowering drugs should be considered. Patients with very high TGs may need to begin drug therapy at diagnosis to more quickly reduce the risk of acute pancreatitis.

Fibrates reduce TGs by about 50%. They appear to stimulate endothelial LPL, leading to increased fatty acid oxidation in the liver and muscle and decreased hepatic VLDL synthesis. They also increase HDL by up to 20%. Fibrates can cause GI adverse effects, including dyspepsia, abdominal pain, and elevated liver enzymes. They uncommonly cause cholelithiasis. Fibrates may potentiate muscle toxicity when used with statins and potentiate the effects of warfarin.

Statins can be used in patients with TGs < 500 mg/dL (< 5.65 mmol/L) if LDL cholesterol elevations are also present; statins may reduce both LDL cholesterol and TGs through reduction of VLDL. If only TGs are elevated, fibrates are the drug of choice.

Omega-3 fatty acids in high doses (1 to 6 g/day of eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) can be effective in reducing TGs. The ω-3 fatty acids EPA and DHA are the active ingredients in marine fish oil or ω-3 capsules. Adverse effects include eructation and diarrhea. These may be decreased by giving the fish oil capsules with meals in divided doses (eg, bid or tid). Omega-3 fatty acids can be a useful adjunct to other therapies.

Low HDL

Although higher HDL levels are associated with lower cardiovascular risk, it is not clear whether treatments to increase HDL cholesterol levels decrease risk of death. ATPIII guidelines define low HDL cholesterol as < 40 mg/dL [<1.04 mmol/L]; the guidelines do not specify an HDL cholesterol target level and recommend interventions to raise HDL cholesterol only after LDL cholesterol targets have been reached. Treatments for LDL cholesterol and TG reduction often increase HDL cholesterol, and the 3 objectives can sometimes be achieved simultaneously. No guidelines specifically address treatment of low HDL cholesterol in children.

Treatment includes lifestyle changes such as an increase in exercise and weight loss. Alcohol raises HDL cholesterol but is not routinely recommended as a therapy because of its many other adverse effects. Drugs may be successful in raising levels when lifestyle changes alone are insufficient, but it is uncertain whether raising HDL levels reduces mortality.

Nicotinic acid (niacin) is the most effective drug for increasing HDL. Its mechanism of action is unknown, but it appears to both increase HDL production and inhibit HDL clearance; it may also mobilize cholesterol from macrophages. Niacin also decreases TGs and, in doses of 1500 to 2000 mg/day, reduces LDL cholesterol. Niacincauses flushing, pruritus, and nausea; premedication with low-dose aspirin

may prevent these adverse effects. Extended-release preparations cause flushing less often. However, most OTC slow-release preparations are not recommended; an exception is polygel controlled-release niacin. Niacin can cause liver enzyme elevations and occasionally liver failure, insulin resistance, and hyperuricemia and gout. It may also increase homocysteine levels. The combination of high doses of niacin with statins may increase the risk of myopathy. In patients with average LDL cholesterol and below-average HDL cholesterol levels, niacin combined with statin treatment may be effective in preventing cardiovascular disorders. In patients treated with statins to lower LDL cholesterol to < 70 mg/dL (< 1.8 mmol/L), niacin does not appear to have added benefit.

Fibrates increase HDL. Fibrates may decrease cardiovascular risk in patients with TGs > 200 mg/dL (< 2.26 mmol/L) and HDL cholesterol < 40 mg/dL (< 1.04 mmol/L).Infusion of recombinant HDL (eg, apoprotein A-1 Milano, an HDL variant in which a cysteine is substituted for an arginine at position 173 allowing for dimer formation) appears promising as a treatment for atherosclerosis but requires further study.

Elevated Lp(a)

The upper limit of normal for Lp(a) is about 30 mg/dL (0.8 mmol/L), but values in African Americans run higher. Few data exist to guide the treatment of elevated Lp(a) or to establish treatment efficacy. Niacin is the only drug that directly decreases Lp(a); it can lower Lp(a) by ≤ 20% at higher doses. The usual approach in patients with elevated Lp(a) is to lower LDL cholesterol aggressively. LDL apheresis has been used to lower Lp(a) in patients with high Lp(a) levels and progressive vascular disease.

Secondary causes

Treatment of diabetic dyslipidemia should always involve lifestyle changes and statins to reduce LDL cholesterol. To decrease the risk of pancreatitis, fibrates can be used to decrease TGs when levels are > 500 mg/dL (> 5.65 mmol/L). Metformin lowers TGs, which may be a reason to choose it over other oral antihyperglycemic drugs when treating diabetes. Some thiazolidinediones (TZDs) increase both HDL

cholesterol and LDL cholesterol. Some TZDs also decrease TGs. These antihyperglycemic drugs should not be chosen over lipid-lowering drugs to treat lipid abnormalities in diabetic patients but may be useful adjuncts. Patients with very high TG levels and less than optimally controlled diabetes may have better response to insulin than to oral antihyperglycemic drugs.

Treatment of dyslipidemia in patients with hypothyroidism, renal disease, liver disease, or a combination of these disorders involves treating the underlying disorders primarily and lipid abnormalities secondarily. Abnormal lipid levels in patients with low-normal thyroid function (high-normal TSH levels) improve with hormone replacement. Reducing the dosage of or stopping drugs that cause lipid abnormalities should be considered.

Monitoring treatment

Lipid levels should be monitored periodically after starting treatment. No data support specific monitoring intervals, but measuring lipid levels 2 to 3 mo after starting or changing therapies and once or twice yearly after lipid levels are stabilized is common practice.

Despite the low incidence of liver and severe muscle toxicity with statin use (0.5 to 2% of all users), current recommendations are for baseline measurements of liver and muscle enzyme levels at the beginning of treatment. Routine monitoring of liver enzyme levels is not necessary, and routine measurement of CK is not useful to predict the onset of rhabdomyolysis. Muscle enzyme levels need not be checked regularly unless patients develop myalgias or other muscle symptoms. If statin-induced muscle damage is suspected, statin use is stopped and CK may be measured. When muscle symptoms subside, a lower dose or a different statin can be tried.

Refereces:

Eruptive Xanthoma
Tuberous Xanthoma

Tendinous Xanthoma
Lipoprotein Patterns (Fredrickson Phenotypes)
Genetic (Primary) Dyslipidemias
National Cholesterol Education Program Adult Treatment Panel III Approach to Dyslipidemias
NCEP Adult Treatment Panel III Guidelines for Treatment of Hyperlipidemia
Framingham Risk Tables for Men
Framingham Risk Tables for Women
Lipid–Lowering Drugs
https://www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/lipid-disorders/dyslipidemia