HYPERTRIGLYCERIDEMIA (FASTING TG ≥500 mg/dL)

TRIGLYCERIDES (TG) contain three fatty acids attached to a glycerol backbone. They form a white fatty substance known as fat that is important for the storage of energy in the body. Triglycerides are obtained from fat in the diet and can also be made in the body. They are carried in the bloodstream on lipoprotein particles made in the intestine known as chylomicrons and on lipoprotein particles made in the liver known as very low-density lipoproteins (VLDL). Normally the triglyceride on these lipoproteins is rapidly broken down in the bloodstream by the enzyme lipoprotein lipase (LPL), forming chylomicron remnant lipoproteins from chylomicrons or low-density lipoproteins (LDL) from VLDL. Chylomicron remnants are removed from the bloodstream by the liver via receptors that bind apolipoprotein (apo) B-100 and/or apoE. The triglyceride is taken up by various tissues, especially fat and muscle cells. Moderate increases in serum triglyceride levels, between 150 and 500 mg/dL, are often associated with a sedentary lifestyle, obesity, and diabetes. They may also be caused by a variety of common gene variants.[1,2]

SEVERE HYPERTRIGLYCERIDEMIA, with fasting triglyceride levels ≥500 mg/dL, is associated with an increased risk of pancreatitis and heart disease.[3] The risk of pancreatitis is especially increased in patients with fasting triglyceride values ≥ 2,000 mg/dL.[3] Pancreatitis is a disease causing significant recurrent and intermittent abdominal pain, which may be due to gallstones, excess alcohol intake, or trauma. In the setting of severe hypertriglyceridemia, pancreatitis results from the release of lipases that cause autodigestion of pancreatic cells, marked inflammation, and necrosis of tissue. When the pancreatitis is chronic and recurrent, it can lead to significant disability and even mortality. Markedly high triglyceride levels can also result from excess alcohol intake, uncontrolled diabetes, or certain medications like oral cortisol or oral estrogen.[3]

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose disorders associated with severe hypertriglyceridemia. The test menu includes a fasting lipid profile, a standard metabolic profile that measures fasting glucose, and measurement of liver enzymes, which can rule out secondary causes of hypertriglyceridemia.[1,2] The LipidSeq panel can then be used to identify potential genetic variants underlying severe hypertriglyceridemia.[2-4] LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1, ABCG5*, *ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.

HYPERTRIGLYCERIDEMIA, with fasting serum triglyceride levels ≥500 mg/dL in the absence of excess alcohol intake, uncontrolled diabetes, or oral cortisol or oral estrogen therapy, is found in about 1% of the population. These patients may have eruptive xanthomas. They are at a markedly increased risk of developing recurrent pancreatitis unless they are treated. **Genetics:** Hypertriglyceridemic patients are unable to breakdown the triglycerides in their bloodstream due to defects either in the lipases which metabolize triglycerides (especially lipoprotein lipase) or in the activator and or binding proteins that are involved in this process. The genes that encode for these enzymes and proteins include *APOA5*, *APOC2*, *GPIHBP1*, and *LPL*. Knowing the precise genetic defect may allow for optimal therapy with lifestyle modification and medication to prevent recurrent pancreatitis and premature ASCVD.[2-4] **Treatment:** The goal of therapy is to reduce fasting triglyceride levels to <150 mg/dL, using dietary fat and sugar restriction, fenofibrate therapy (200 mg/day), omega-3 fatty acids supplementation (3 capsules twice daily), and, if necessary, statin therapy which will not only lower triglycerides but also optimize LDL-C levels. Optimization of diabetes control is also critical if diabetes is present.

DYSBETALIPOPROTEINEMIA, with fasting triglyceride levels ≥ 500 mg/dL, is a variant of hypertriglyceridemia. **Genetics:** These patients have a defect in the removal of chylomicrons and VLDL remnant particles from the bloodstream due to defects in the *APOE* gene. As a result, they have increased plasma levels of remnant lipoprotein cholesterol (RLP-C). They usually have VLDL-C values ≥ 50 mg/dL (normal < 30 mg/dL) and a VLDL-C/TG ratio >0.3. Such patients may develop tubo-eruptive xanthomas and premature ASCVD. They may be homozygous for the *APOE* ε*2*/ε*2* genotype or have other *APOE* defects causing abnormal apoE or apoE deficiency. **Treatment:** The goal of therapy is to reduce fasting triglyceride levels to <150 mg/dL, using dietary fat and sugar restriction, fenofibrate therapy (200 mg/day), omega-3 fatty acids (3 capsules twice daily), and, if necessary, statin therapy which will not only lower triglycerides but also optimize RLP-C and LDL-C levels. Optimization of diabetes control is also critical if diabetes is present.[1,5-7]

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SITOSTEROLEMIA and CEREBROTENDINOUS XANTHOMATOSIS

CHOLESTEROL is a waxy substance in the body that is important for the function of all cells. It is primarily made in the body but is also obtained from the diet in foods of animal origin. The body uses cholesterol to make male and female sex hormones, cortisol (a hormone necessary for life), vitamin D (important for bones), and bile acids (important for absorbing fat in the intestine). Cholesterol is carried in the bloodstream on lipoprotein particles, mainly on low-density lipoprotein or LDL.[1]

LOW DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) levels ≥160 mg/dL in the bloodstream are an important risk factor for early heart disease and stroke, known collectively as atherosclerotic cardiovascular disease (ASCVD). A high LDL-C level may result from excess consumption of dietary animal and trans fats, an underactive thyroid, kidney disease, or liver disease.[2,3] It may also be due to defects in genes involved in cholesterol metabolism that can elevate blood sterol levels as well as LDL-C.

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose disorders associated with high LDL-C and/or high sterol levels. The test menu includes a fasting lipid profile, the Cholesterol Balance® Test, and liver and thyroid tests, which can rule out secondary causes of high LDL-C and high sterol levels.[1] The LipidSeq panel can then be used to identify potential genetic defects underlying these biochemical abnormalities. LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1, ABCG5*, *ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.[3,4]

SITOSTEROLEMIA is a rare autosomal recessive disorder found in about 4% of patients with LDL-C levels ≥ 190 mg/dL and is associated with a high risk of premature ASCVD. These patients have very high levels of β-sitosterol (≥10.0 mg/L), which is found in foods of plant origin. **Genetics:** The disease is caused by defects in the *ABCG5* and *ABCG8* genes. As a result, patients have marked overabsorption of β-sitosterol and cholesterol from the diet. They may have β-sitosterol and cholesterol deposits in their tendons and the corneas of their eyes. **Treatment:** Restriction of dietary cholesterol and plant sterols and treatment with ezetimibe and statins can prevent early ASCVD.[5] Patients with heterozygous *ABCG5* and *ABCG8* defects may have a milder form of the disease.

CEREBROTENDINOUS XANTHOMATOSIS (CTX) is a very rare autosomal recessive condition associated with cholestanol levels ≥10.0 mg/L. **Genetics:** The disease is due to defects in the *CYP27A1* gene which encodes for sterol 27-hydroxylase, a key enzyme in the production of bile acid from cholesterol. The defects prevent the formation of the bile acid chenodeoxycholic acid (CDCA) and increase cholestanol levels. These patients present with chronic diarrhea and learning disabilities in childhood, premature cataracts in adolescence, and neurologic disease and often large tendon xanthomas in their tendons in their twenties and thirties. **Treatment:** CDCA therapy, 250 mg given orally three times daily, can prevent the neurologic disease, provided the diagnosis is made early, ideally prior to age 30 years.[6]

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HYPERCHOLESTEROLEMIA

CHOLESTEROL is a waxy substance in the body that is important for the function of all cells. It is primarily made in the body but is also obtained from the diet in foods of animal origin. The body uses cholesterol to make male and female sex hormones, cortisol (a hormone necessary for life), vitamin D (important for bones), and bile acids (important for absorbing fat in the intestine). Cholesterol is carried in the bloodstream on lipoprotein particles, mainly on low-density lipoprotein or LDL.[1]

LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) levels ≥160 mg/dL in the bloodstream are an important risk factor for early heart disease and stroke, known collectively as atherosclerotic cardiovascular disease (ASCVD). A high LDL-C level may result from an excess consumption of dietary animal and trans fats, an underactive thyroid, or kidney or liver disease.[2,3] It may also be due to extremely high levels of lipoprotein(a) or Lp(a).[4] This lipoprotein particle which is genetically determined is a major risk factor for ASCVD.[3] Another common cause of high LDL-C is familial combined hyperlipidemia or FCH, a disorder found in about 15% of families with early ASCVD. FCH, which is associated with overproduction of cholesterol in the body (high plasma lathosterol level), is due to a number of common genetic variants.[5,6] These patients respond very well to statin therapy.

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose disorders associated with elevated LDL-C. The test menu includes a fasting lipid profile, the Cholesterol Balance® Test, and liver and thyroid tests, which can rule out uncontrolled diabetes, thyroid disease, and other secondary causes of high LDL-C.[1-6] The LipidSeq panel can then be used to identify potential genetic defects underlying high LDL-C values. LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1*, *ABCG5*, *ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.[7,8]

FAMILIAL HYPERCHOLESTEROLEMIA (FH) is a less common familial condition found in about 1% of patients with early ASCVD and in about 1:250 in the general population. These patients have LDL-C levels ≥190 mg/dL, but no kidney, thyroid, or liver disease.[7-9] They may have cholesterol deposits in their tendons (tendinous xanthomas) and the corneas of their eyes (arcus). They have a very high risk of developing early ASCVD, often prior to age 45 years if untreated. **Genetics:** FH patients usually have heterozygous defects at the *LDLR* (LDL receptor), *LDLRAP1, APOB, PCSK9,* or *STAP1* gene loci.[3,8,9] These genes are all very important for making receptors and proteins in the body that lead to the normal breakdown of LDL in the bloodstream. When these receptors and proteins are defective, LDL is not efficiently removed from the bloodstream and the resultant high levels in the bloodstream lead to early heart disease. Patients with homozygous or compound heterozygous FH usually have LDL-C values >500 mg/dL, tubo-eruptive xanthomas, and very premature ASCVD. **Treatment:** With early detection and treatment with effective statins, ezetimibe, and, if necessary, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, ASCVD can be prevented; and these patients can have a normal lifespan.[3,7] Those patients that do not respond to statins, ezetimibe, anion-exchange resins, and/or PCSK9 inhibitors may require incliseran and/or LDL apheresis.

LYSOSOMAL ACID LIPASE DEFICIENCY, also known as cholesteryl ester storage disease, is a very rare condition associated with very high levels of LDL-C (usually ≥190 mg/dL) and early liver disease associated with elevated liver transaminase levels. **Genetics:** Cholesteryl ester (a form of cholesterol) is deposited in the liver and other organs and cannot be broken down because of lack of the enzyme lysosomal acid lipase (LAL), due to defects in the *LIPA* gene. **Treatment:** If not diagnosed and treated with enzyme replacement (now available and known as sebelipase), the patient will develop liver failure.[10]

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HIGH-DENSITY LIPOPROTEIN DEFICIENCY

HIGH-DENSITY LIPOPROTEINS (HDL) are protein-rich particles that also carry cholesterol in the bloodstream. Unlike low-density lipoprotein (LDL) particles which deposit cholesterol in the artery wall, HDL particles remove cholesterol from the artery wall and other tissues. Therefore, HDL protects patients from developing heart disease. HDL cholesterol (HDL-C) values <40 mg/dL in men and <50 mg/dL in women have been defined as low and being associated with an increased risk of heart disease and stroke, known collectively as atherosclerotic cardiovascular disease (ASCVD). Low levels of HDL-C may be associated with high triglyceride levels, obesity, cigarette smoking, a sedentary lifestyle, diabetes, inflammation, and use of anabolic steroids.[1-4]

HDL particles contain apolipoprotein A-I (apoA-I) as their major protein. They vary in size and function. Very small preβ-1 HDL particles pick up cholesterol from cells via ATP binding cassette transporter A1 or ABCA1 and are then converted to small α-4 HDL particles. These particles in turn are acted upon by an enzyme known as lecithin:cholesterol acyltransferase or LCAT, which converts free cholesterol to cholesteryl ester, forming medium α-3 HDL. Medium α-3 HDL particles pick up more cholesterol from cells to form large α-2 HDL and very large α-1 HDL particles. These particles can either transfer the cholesteryl ester to triglyceride-rich lipoproteins via the cholesteryl ester transfer protein (CETP), or they can deliver cholesterol to the liver via scavenger receptor-B1 (SR-B1). Once HDL particles have transferred cholesterol to the liver or other lipoproteins, they can be converted back into smaller HDL particles.[5-7] Patients with high levels of α-1 and α-2 HDL particles are generally protected from premature ASCVD.[2]

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose disorders associated with HDL deficiency. The test menu includes the proprietary HDL Map® Test that measures the amount of apoA-I in the five major HDL particles, as well as a fasting lipid profile, a standard metabolic profile that includes fasting glucose, and measurement of kidney function, liver enzymes, C-reactive protein, and myeloperoxidase. These tests can rule out secondary causes of HDL deficiency.[4] The LipidSeq panel can then be used to identify potential genetic defects underlying HDL deficiency.[8,9] LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1, ABCG5*, *ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.

MARKED HIGH-DENSITY LIPOPROTEIN DEFICIENCY of genetic origin has been defined as an HDL-C value of <25 mg/dL in men and <30 mg/dL in women. It may be associated with premature ASCVD, neurologic disease, kidney disease, and cloudy corneas, depending on the underlying disorder, as described below.[3]

Apolipoprotein A-I Deficiency patients have undetectable or very low levels of HDL particles and apoA-I due to defects in the *APOA1* gene. They often develop premature ASCVD. The treatment of choice is statin therapy to optimize LDL-C to < 50 mg/dL.[3,4,10-13] Milder forms exist with heterozygous defects.[4]

Tangier Disease patients usually have only very small preβ-1 HDL particles, since they cannot remove cholesterol from the artery wall and other tissues due to defects in the *ABCA1* gene. They may have an enlarged liver or spleen due to cholesterol deposition and may have premature ASCVD. The treatment of choice is statin therapy to optimize LDL-C to <50 mg/dL.[3,4,14] Milder heterozygous forms also exist.[4]

LCAT Deficiency patients cannot esterify cholesterol (i.e., add a fatty acid to cholesterol) on lipoprotein particles due to defects in the *LCAT* gene.[17,18] These patients often have only preβ-1 and α-4 HDL particles, very low direct LDL-C values (<40 mg/dL), cloudy corneas, anemia, and an enlarged spleen. They can develop kidney failure. The therapy of choice is to optimize the kidney disease risk factors: lower blood glucose levels and blood pressure and monitor kidney function. In the future, enzyme replacement therapy will potentially become available for this disease.[3,4.16,17]

Fish-Eye Disease patients, with normal or elevated LDL-C values, have a variant of LCAT Deficiency. These patients lack only α-LCAT enzyme activity which affects HDL. They do not develop kidney disease but may develop early heart disease. Therefore, their LDL-C levels should be optimized with lifestyle and statin treatment. Milder heterozygous forms of both types of LCAT deficiency also exist.[4,18]

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HIGH-DENSITY LIPOPROTEIN EXCESS AND PREMATURE ASCVD

HIGH-DENSITY LIPOPROTEINS (HDL) are protein-rich particles that also carry cholesterol in the bloodstream. Unlike low-density lipoprotein (LDL) particles which deposit cholesterol in the artery wall, HDL particles remove cholesterol from the artery wall and other tissues. Therefore, they protect patients from developing heart disease. An HDL cholesterol (HDL-C) <40 mg/dL in men and <50 mg/dL in women is associated with an increased risk of heart disease and stroke, known collectively as atherosclerotic cardiovascular disease (ASCVD).[1] There are also some rare circumstances where high levels of HDL-C may cause premature ASCVD.[2,3]

HDL particles contain apolipoprotein A-I (apoA-I) as their major protein. They vary in size and function. Very small preβ-1 HDL particles pick up cholesterol from cells via the ATP binding cassette transporter A1 (ABCA1) and are converted to small α-4 HDL particles. These particles in turn are acted upon by an enzyme known as lecithin:cholesterol acyltransferase (LCAT), which converts free cholesterol to cholesteryl ester, forming medium α-3 HDL. Medium α-3 HDL particles pick up more cholesterol from cells to form large α-2 HDL and very large α-1 HDL particles. These particles can either transfer their cholesteryl ester to triglyceride-rich lipoproteins via the cholesteryl ester transfer protein (CETP), or they can deliver their cholesterol to the liver via scavenger receptor-B1 (SR-B1). Once HDL particles have transferred cholesterol to the liver or other lipoproteins, they can be converted back into smaller HDL particles.[5-7] Patients with high levels of α-1 and α-2 HDL particles are generally protected from premature ASCVD.[2]

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose the rare disorders associated with high levels of HDL-C that cause premature ASCVD. The test menu includes the proprietary HDL Map® Test that measures the amount of apoA-I in the five major HDL particles, as well as a fasting lipid profile, a metabolic profile that includes fasting glucose and measurement of liver enzymes, C-reactive protein, and myeloperoxidase. These tests can rule out secondary causes of HDL excess.[1-8] The LipidSeq panel can then be used to identify potential genetic variants underlying abnormalities associated with elevated HDL-C that cause premature ASCVD.[2-9] LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1, ABCG5, ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.

MARKED HIGH-DENSITY LIPOPROTEIN EXCESS is defined as a HDL-C value ≥100 mg/dL in men and ≥120 mg/dL in women and is usually associated with very low ASCVD risk. In rare circumstances, it may be associated with premature ASCVD.

Hepatic Lipase Deficiency patients have very high levels of apoA-I in very large α-1 HDL, but decreased levels of apoA-I in large α-2 HDL. They often have fasting triglycerides levels >300 mg/dL and decreased hepatic lipase activity due to defects in the *LIPC* gene. The treatment of choice is to optimize triglyceride and LDL-C levels with fenofibrate, omega-3 fatty acids, and statins.[10]

Scavenger Receptor-B1 (SR-B1) Deficiency patients have markedly elevated levels of apoA-I in α-1 and α-2 HDL particles due to defects in *SCARB1*, the gene which encodes for SR-B1. These patients are unable to deliver cholesterol from HDL to the liver and, as a result, often develop premature ASCVD. The treatment of choice is to optimize all other ASCVD risk factors including LDL-C levels.[11]

Cholesteryl Ester Transfer Protein (CETP) Deficiency patients have very high levels of HDL-C (usually >150 mg/dL), an inability to transfer cholesteryl ester from HDL to other lipoproteins, and exceptionally large abnormal HDL particles, due to defects in the *CETP* gene. Since this disorder is not usually associated with premature ASCVD, no treatment is required.[12]

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HYPOCHOLESTEROLEMIA

CHOLESTEROL is a waxy substance in the body that is important for the function of all cells. It is primarily made in the body but is also obtained from the diet in foods of animal origin. The body uses cholesterol to make male and female sex hormones, cortisol (a hormone necessary for life), vitamin D (important for bones), and bile acids (important for absorbing fat in the intestine). Cholesterol is carried in the bloodstream on lipoprotein particles, mainly on low-density lipoprotein (LDL).[1]

LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) levels <10 mg/dL in the bloodstream may be associated with neurologic disease or fatty liver disease depending on the underlying cause. A very low LDL-C level may be caused by aggressive lipid-lowering therapy with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor or the statin-ezetimibe combination; or it can be due to chronic illness, liver failure, severe intestinal malabsorption, or marked hyperthyroidism.[1-4] The treatment for these latter conditions may include correcting the underlying causes.[1,2]

BOSTON HEART TESTING, along with a well-documented patient history, can be used to diagnose disorders associated with low LDL-C. The test menu includes a fasting lipid profile, the Cholesterol Balance® Test, the Fatty Acid Balance™ Test, and liver and thyroid tests, which can rule out secondary causes of low LDL-C. The LipidSeq panel can then be used to identify potential genetic variants underlying low LDL-C values.[2,3] LipidSeq sequences 23 genes linked to disorders associated with abnormalities in lipid metabolism: *ABCA1, ABCG5*, *ABCG8*, *APOA1*, *APOA5*, *APOB*, *APOC2*, *APOC3*, *APOE*, *CETP*, *CYP27A1*, *GPIHBP1*, *LCAT*, *LDLR*, *LDLRAP1*, *LIPA*, *LIPC*, *LIPG*, *LPL*, *MTTP*, *PCSK9*, *SCARB1,* and *STAP1*.

HYPOBETALIPOPROTEINMEMIA is a rare condition caused by defects in apolipoprotein (apo) B, the major protein of LDL. **Genetics:** Some defects in the *APOB* gene cause a shortened form of apoB to be made and decrease the formation of apoB-containing lipoproteins. These patients usually have LDL-C levels <10 mg/dL, low fasting triglycerides levels, and normal high-density lipoprotein cholesterol (HDL-C) levels. They often have low levels of plasma fat soluble vitamins A, D, E, and K, co-enzyme Q10, and essential fatty acids, especially the omega-3 fatty acids (α-linolenic acid or ALA; eicosapentaenoic acid or EPA; docosahexaenoic acid or DHA). **Treatment:** Supplementation with fat soluble vitamins, co-enzyme Q10 (300 mg/day), and omega-3 fatty acids (4 grams/day) will prevent the muscle aches and other symptoms that these patients often have.[1-4]

ABETALIPOPROTEINEMIA is a very rare condition associated with undetectable serum apoB levels, very low levels of LDL-C (<10 mg/dL) and fasting triglycerides (<40 mg/dL), and normal HDL-C levels. **Genetics:** The disease is caused by an inability to form and secrete apoB-containing lipoproteins in either the intestine or the liver due to defects in the microsomal triglyceride transfer protein (*MTTP*) gene. These patients have very low levels of plasma co-enzyme Q10, fat soluble vitamins A, D, E, and K, and essential fatty acids, especially the omega-3 fatty acids (ALA, EPA, and DHA). These patients often present with anemia, abnormal red blood cells, and fat malabsorption in childhood. If undiagnosed, they may present in adolescence with abnormal retinal pigmentation and neurologic disease with ataxia. **Treatment:** Supplementation with co-enzyme Q10, all the fat-soluble vitamins (A, D, E, and K), and omega-3 fatty acids (fish oil capsules, 4 grams/day) will often prevent the complications of this disease. Treatment with vitamin E, at least 800 units per day, is essential to prevent the neurologic disease that these patients develop.[4]

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