52

Hyperlipidemias and Nutrient-Gene Interactions

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A variety of factors under genetic control are involved in the production and metabolism of serum lipids and lipoproteins (Table 52.1).[1,2] Nutrients in the diet may affect one or more steps of gene regulation of lipoproteins, resulting in abnormal lipid or lipoprotein levels and predisposition to atherosclerosis. The factors affected are listed in Table 52.1. Examples of effects of diet and lifestyle on genetic mechanisms are included in Table 52.2.[1]

Hyperlipidemias

These lipid disorders reflect abnormal increase in one or another serum lipid component and/or lipoprotein carrier (Tables 52.3, 52.4). The abnormalities often are inherited and are strongly influenced by the diet. Their management requires accurate diagnosis and evaluation, searching for other diseases that may induce secondary hyperlipidemia.[3] The dietary intervention, if unsuccessful, should be followed by appropriate medication that normalizes the lipids and lipoproteins in order to prevent complications of atherosclerotic disease (myocardial infarction, peripheral vascular disease) or pancreatitis.[4]

These subjects have lipid levels generally above the 90th percentile for their age and sex (Table 26.3). Blood samples should be obtained after a 12 to 14-hour fast in individuals ingesting their usual diet. At least three blood samples should be evaluated, two or three weeks apart. The lipid studies may need to be more elaborate than the usual lipid screen or profile (see Section 26). Ultracentrifugation of the plasma often is necessary, usually performed in a specialized lipid laboratory. These lipid disorders can be suspected from the patient's history, family history, and physical examination. First degree relatives should also be investigated in order to detect others with the disorder and to characterize the genetics.

Numerous mutations have been associated with the various types of familial hyperlipoproteinemias (Table 52.4).[5] In the future, nutrient modulation of gene expression may be used as therapy. More than half the variability in serum cholesterol (low density lipoprotein, LDL cholesterol) among individuals is attributable to genetic variation, presumably polygenic. Polymorphisms in apo-E or apo-B are examples. The remaining variability in cholesterol levels may be attributable to the diet, diet-gene interactions, or postulated genes that control variability of response to the environment. The prevalence of hyperlipidemias is increased in patients with premature coronary heart disease (CHD), i.e., <55 years of age.

TABLE 52.1

Factors Involved in the Formation and Metabolism of Lipoproteins

Type	Action
Apoproteins	
Apo A-I	Anti-atherogenic
Apo A-II	Apo A-II-containing lipoproteins are not effectively metabolized by lipoprotein lipase (defective lipolysis)
Apo B_{100}	Ligand for the LDL receptor
Apo C-I	Blocks apo E binding to receptors
Apo C-II	Activates lipoprotein lipase (LPL)
Apo C-III	Impairs TAG hydrolysis delaying clearance of remnants of chylomicrons; inhibits LPL; decreases LDL binding to receptors; displaces apo E from lipoprotein particles
Apo E	Ligand for the LDL receptor; interacts with the LDL receptor-related protein (LRP); enhances lipolysis
Enzymes	
Lipoprotein lipase (LPL)	Hydrolyzes TAGs to free fatty acids in chylomicrons and VLDL to form chylomicron remnants and IDL. Excess lipoprotein surface components are released to form HDL particles
Hepatic lipase (HL)	Functions as a phospholipase and TAG hydrolase. Important for conversion of IDL to LDL. Increased activity leads to LDL pattern B (small dense) and low HDL
Lecithin:cholesterol acyltransferase (LCAT)	Catalyzes the esterification of free cholesterol to cholesterol ester on plasma lipoproteins
Acyl CoA:cholesterol acyltransferase (ACAT)	Catalyzes cholesterol esterification
Carboxyl ester lipase (CEL)	
Receptors	
LDL receptor	Binds apo B-containing lipoproteins, such as LDL
LDL receptor-related protein (LRP)	Takes up chylomicron remnants
Scavenger receptor A (SR-A)	Binds LDL modified by oxidation
CD-36, a scavenger receptor on macrophages	Binds modified LDL
Scavenger receptor B1 (SR-B1)	Selectively removes cholesterol esters from HDL and apo B-containing lipoproteins
Peroxisome proliferator-activated receptor-α (PPARα)	Putative HDL receptor takes up HDL particles
VLDL receptor	
Transfer Proteins	
Cholesterol ester transfer protein (CETP)	Required for normal clearance of HDL. Transfers cholesterol esters synthesized in HDL to the apo B-containing lipoproteins in exchange for TAG
ATP-binding-cassette transporter 1 (ABC-1)	Actively transports free cholesterol out of cells and into HDL particles transforming lipid-poor A-I particles into nascent HDL particles
Microsomal triglyceride transfer protein (MTP)	Necessary to generate LDL (VLDL)

TABLE 52.2

Effects of Diet and Lifestyle on Gene Regulation of Lipoprotein Expression

Factor	Effect
Cholesterol	Decreases expression of the LDL receptor by suppressing transcription of its gene Regulates H:MG CoA reductase expression by controlling the stability of the HMG CoA reductase protein (post-translational level)
Polyunsaturated fatty acids	Block transcription of the fatty acid synthase gene
Fats	Excessive intake induces excessive secretion of apo-B containing lipoproteins by stabilizing the protein (post-translational) Affects LDL receptor expression Increases expression of LPL activity, inducing adipose tissue LPL activity and suppressing skeletal muscle LPL activity (perhaps via insulin). Post-translational regulation by glycosylation is possible.
Atherogenic diet	Decreases HDL Decreases the expression of the gene encoding paraoxonase, an enzyme that protects LDL from oxidation
Exercise	Increases muscle LPL activity pre-translationally
Glucose	Increases fatty acid synthesis by stabilizing the fatty acid synthase mRNA (post-transcriptional)
Other	Subjects with the E_3/E_4 phenotype respond to a low fat, low cholesterol diet intervention with a greater LDL decrease than those with the E_3/E_3 or E_3/E_2 phenotype

TABLE 52.3

Classification (Type) of Hyperlipidemia and the Underlying Lipoprotein Abnormality

Type	Lipoprotein Abnormality
I	Increased exogenous triacylglycerols (TAG) in the form of chylomicrons
IIa	Hypercholesterolemia with increase in LDL and normal TAG levels
Iib	Hypercholesterolemia combined with mild hypertriglyceridemia (increase in LDL and VLDL particle number, overproduction of apo-B)
III	Remnant hyperlipemia; hypercholesterolemia with hypertriglyceridemia and increase in IDL
IV	Mild to moderate endogenous hyperlipemia; increased VLDL with TAG 2.8-7.9 mmol/L or 250-700 mg/dl
V	Mixed hyperlipemia; moderate to severe hypertriglyceridemia (>11.3 mmol/L or 1000 mg/dl) with mixed VLDL and chylomicrons

Types of Hyperlipidemias

Chylomicronemia (Type I Hyperlipoproteinemia)[3-7]

Dietary TAGs that are transported as chylomicrons are increased in Type I. This rare disorder results from a defect in removal of chylomicrons from the blood due to the presence of a recessive gene that results in deficiency of lipoprotein lipase (LPL, Table 52.4).[6] A similar disorder results from the absence or abnormal function of the apo-C II activator of LPL,[7] or from the presence of a circulating inhibitor of LPL. Type I may present in infants and children. It does not usually predispose to vascular disease, but patients are at risk of recurrent severe pancreatitis. Signs of lipemia retinalis (Color Figure 52.1*), eruptive xanthomas (Color Figure 52.2), and hepatosplenomegaly may be present. The plasma shows a chylomicron creamy layer over a clear infranatant. Plasma TAG levels usually exceed 17 mmol/L.

TABLE 52.4

Genetic Basis of Familial Hyperlipidemias

Type	Abnormality	Mutation
Type I	Familial lipoprotein lipase deficiency	40 known missense and nonsense mutations of gene encoding enzyme
	Familial lipoprotein lipase inhibitor	
	Familial apo C-II deficiency	14 defects identified
	Familial hepatic lipase deficiency	
Type II	Familial hypercholesterolemia	400 deletions/point mutations in 5 classes of the LDL gene
	Familial defective apo B_{100}	Apo B 3500 mutation impairs binding to the LDL receptor
	Polygenic hypercholesterolemia	Apo A-I/C-III/A-IV gene clusters
Type Iib	Familial combined hyperlipidemia	Apo A-I/C-III/A-IV LCAT Mn superoxide dismutase linkage Partial LPL deficiency
Type III	Familial dysbetalipoproteinemia	Apo E gene polymorphism affects amino acid coding E_2/E_2 phenotype
Type IV	Familial hypertriglyceridemia (mild)	Apo A-I/C-III/A-IV ?Hepatic lipase deficiency
Type V	Familial hypertriglyceridemia (severe)	Apo A-I/C-III/A-IV
	Familial lipoprotein lipase deficiency	Apo A-II
	Apo C-II deficiency	

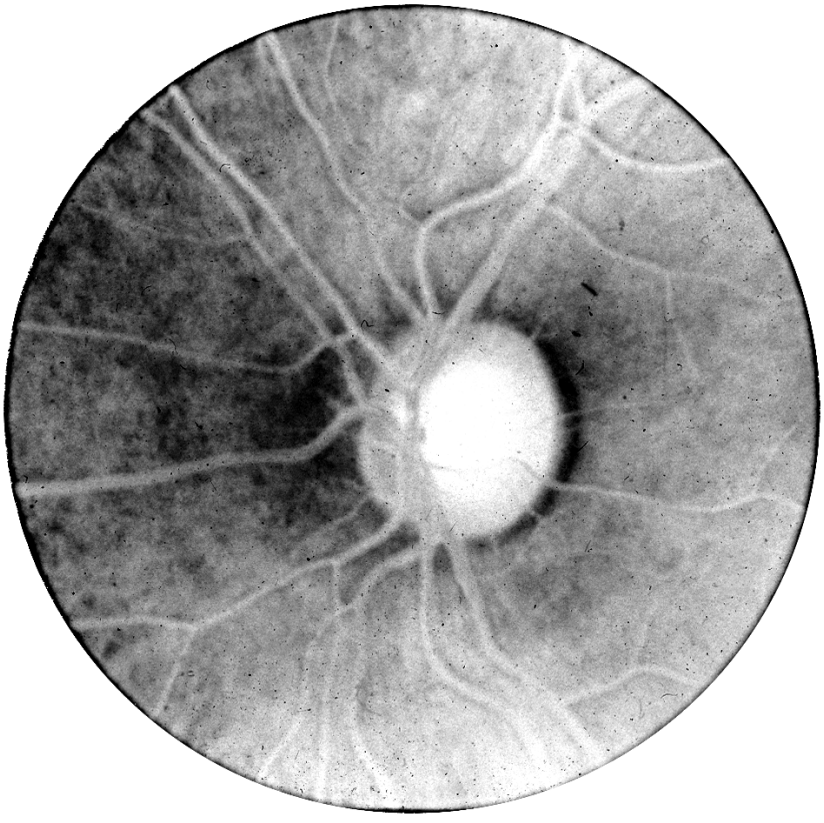

FIGURE 52.1

(See Color Figure 52.1) Lipemia retinalis visualized in the optical fundus of a patient with chylomicronemia with TAG levels exceeding 3000 mg/dl.

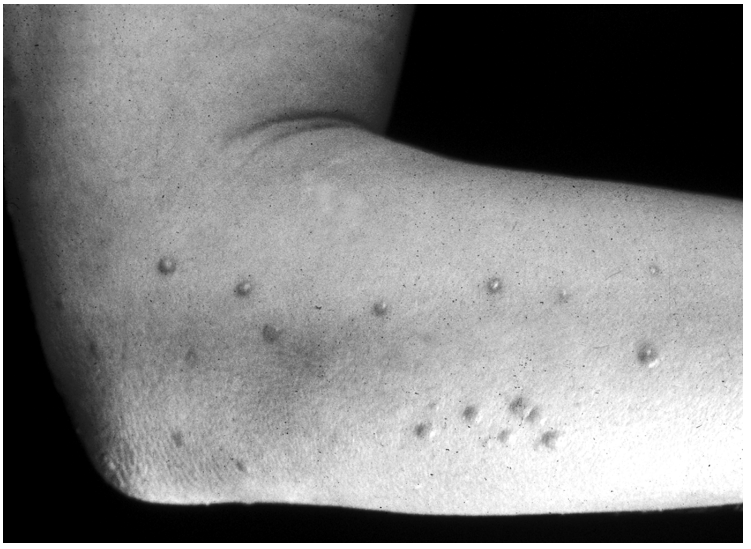

FIGURE 52.2
(See Color Figure 52.2) Eruptive xanthomas observed in a patient with chylomicronemia.

Hypercholesterolemia (Type IIa and Type IIb Hyperlipoproteinemias)[3,4,9]

In Type IIa hypercholesterolemia, increased LDL is present with normal levels of TAGs. Familial hypercholesterolemia (FH) is a single-gene defect of the cell surface receptor that binds circulating LDL and delivers cholesterol to cells.[8] To date, more than 400 mutations have been characterized in five classes.[5,9] In the heterozygote, receptor number or activity is about half normal. LDL cholesterol does not enter the cell and does not suppress the activity of hydroxymethylglutaryl coenzyme A (HMG CoA) reductase, the rate-limiting step in cholesterol synthesis. Cholesterol synthesis continues and esterified cholesterol accumulates in the cell, suppressing LDL receptor synthesis. The LDL cholesterol level in blood doubles (to about 9 mmol/L) and the fractional catabolic rate of LDL is halved. In the FH homozygote with no receptors, LDL production is greatly enhanced and removal severely decreased. LDL cholesterol levels average 19 mmol/L.

Signs of FH include lipid deposits such as eyelid xanthelasma (Color Figure 52.3), corneal arcus (Color Figure 52.4), and tendon and tuberous xanthomas of the skin (Color Figures 52.5, 52.6) that appear in the second or third decade of life. Hypercholesterolemia is present from birth.[10] FH homozygotes may have xanthomas in infancy or early childhood. The incidence of CHD is increased 25-fold in FH patients and occurs prematurely (before age 50). In FH homozygotes, CHD may be present in infancy and early childhood, with death occurring by age 21.

Patients with familial defective apo B (Table 52.4) may exhibit a phenotype identical to FH.[5] In Type IIb, hypercholesterolema is combined with hypertriglyceridemia, with LDL and very low density lipoprotein (VLDL) increased, and overproduction of apo-B. Familial combined hyperlipidemia (FCH) is the most common hyperlipidemic syndrome in patients with premature CHD. In this condition, small, dense LDL is overproduced, with increased levels of apo-B.[11-13]

Type III Hyperlipoproteinemia (Dysbetalipoproteinemia, Broad-beta or Floating-beta Disease)[14]

In this syndrome, hypercholesterolemia is combined with hypertriglyceridemia. Intermediate density lipoprotein (IDL) remnants are increased, at times mixed with chylomicrons.

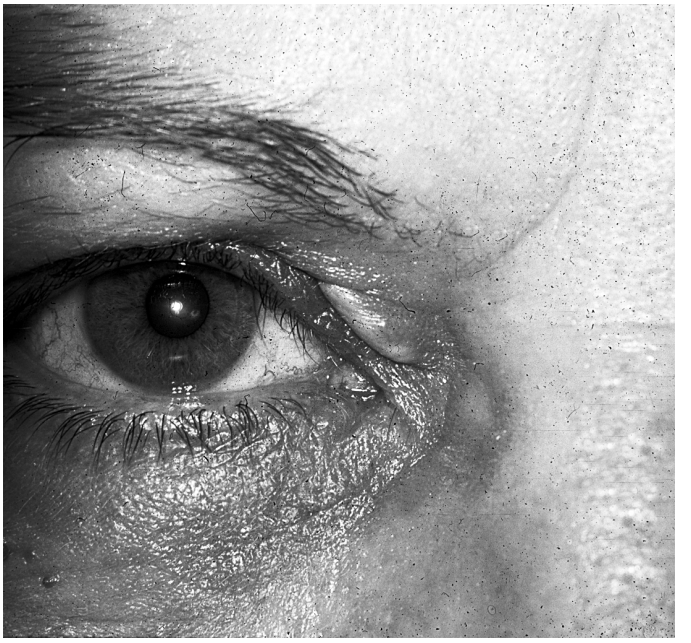

FIGURE 52.3
(See Color Figure 52.3) Eyelid xanthelasma from a woman with familial hypercholesterolemia.

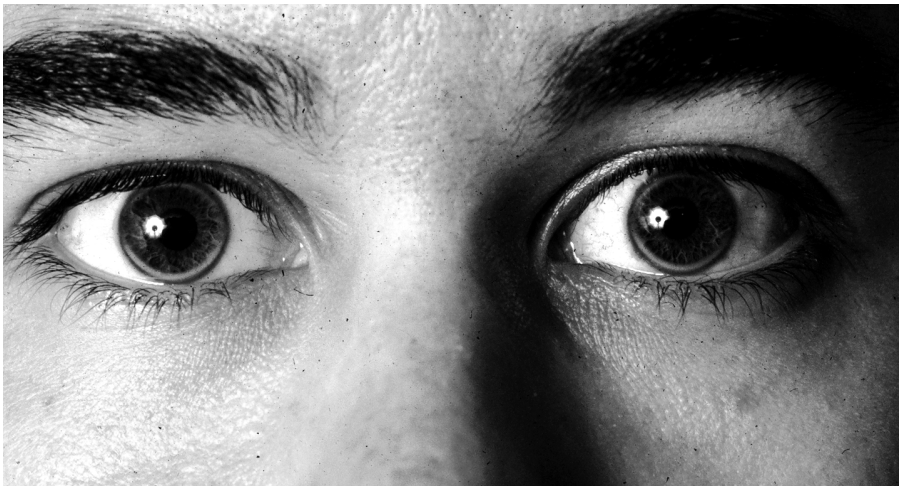

FIGURE 52.4
(See Color Figure 52.4) Corneal arcus observed in a 31-year-old man with familial hypercholesterolemia.

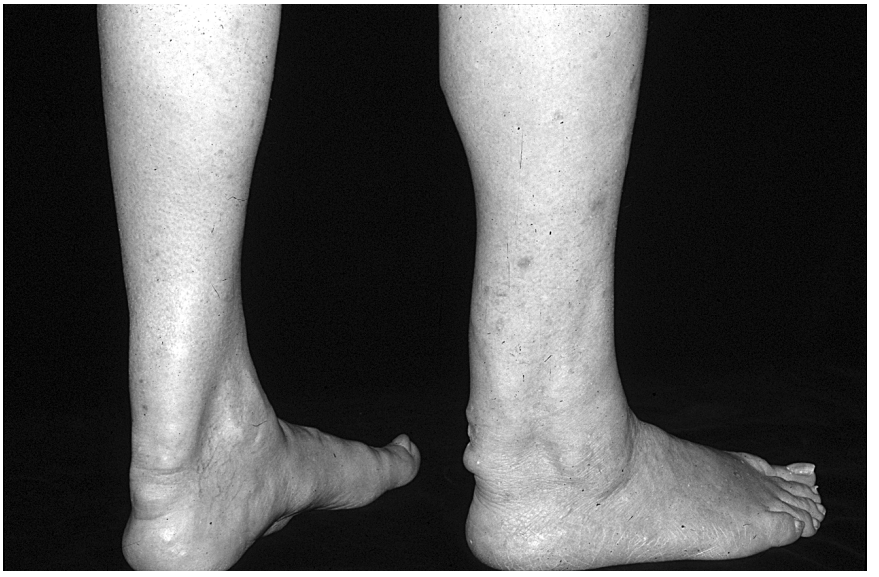

FIGURE 52.5
(See Color Figure 52.5) Xanthomas of the Achilles tendons of a patient with familial hypercholesterolemia.

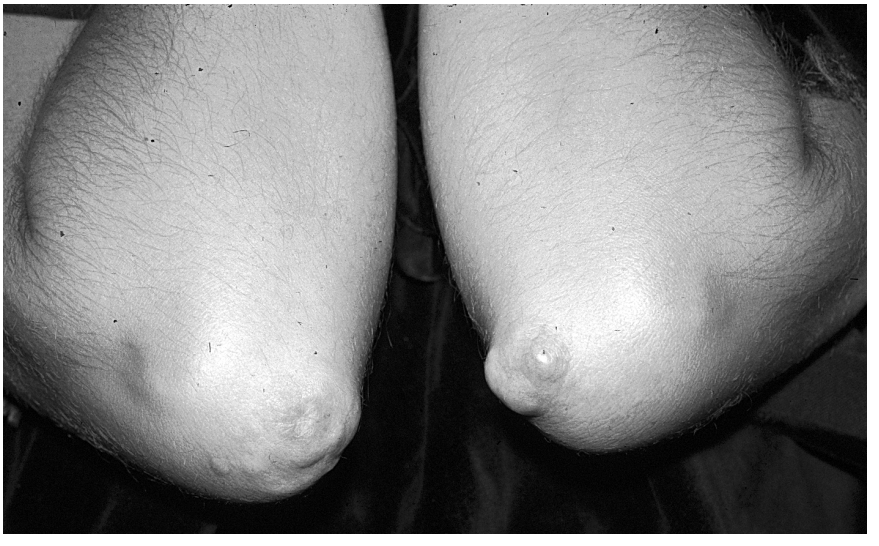

FIGURE 52.6
(See Color Figure 52.6) Tuberous xanthomas in the skin of the elbows of a teenage girl with familial hypercholesterolemia.

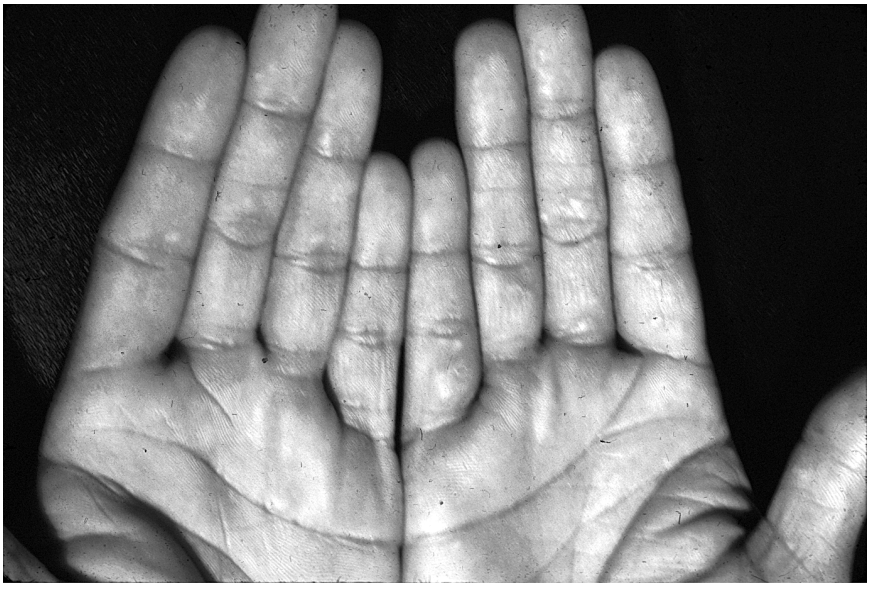

FIGURE 52.7
(See Color Figure 52.7) Yellow linear deposits in the creases of the fingers and palms of the hands of a 33-year-old man with Type III hyperlipoproteinemia.

The disorder is due to a genetic defect in the apo-E isoforms. The normal E_3 is replaced by one or two E_2 proteins that have defective receptor binding. This results in a lesser rate of removal and increases the circulating level of IDL. Preparative ultracentrifugation demonstrates increased cholesterol relative to TAG in the VLDL fraction, with more rapid migration of the lipoprotein on electrophoresis. Apo-E isoforms should be determined (E phenotype). Patients show planar xanthomas of the palms (Color Figure 52.7) and tuberous xanthomas as early as the third decade of life. Patients have premature peripheral vascular disease and CHD.[15]

Type IV Hyperlipoproteinemia[5]

Endogenous hypertriglyceridemia is characterized by mild to moderate increase in TAG levels (3 to 8 mmol/L, 250 to 700 mg/dl), with increase in VLDL.[16,17] Both overproduction and decreased removal of VLDL TAG may be responsible. LDL cholesterol levels are within the normal range. Usually HDL cholesterol is decreased. These subjects may be at increased risk of atherosclerosis, and hypertriglyceridemia per se may be an independent risk factor for cardiovascular disease (CVD).[16,17] Patients often have no signs or symptoms other than the abnormal lipid and lipoprotein values, and may present initially with cardiovascular events. Underlying mechanisms and genetic defects are multiple.[5] See also atherogenic dyslipidemia, below.

Type V Hyperlipoproteinemia

Moderate to severe increases in TAG levels exceeding 11.3 mmol/L or 1000 mg/dl characterize this disorder, often termed the chylomicronemia syndrome.[3,4,6,15] Chylomicrons appear along with increased levels of VLDL. Patients exhibit eruptive xanthomas and lipemia retinalis (TAG levels >34 mmol/L, 3000 mg/dl) (Color Figures 52.1, 52.2). They are at high risk for recurrent episodes of acute pancreatitis, at times resulting in pancreatic insufficiency. Fifty percent or more of these patients have diabetes mellitus that must be

TABLE 52.5

Metabolic Syndrome Risk Factors

Insulin resistance
Elevated Triaglycerides
Increased dense LDL
Low HDL
Hyperinsulinemia
Glucose intolerance
Hypertension
Prothrombotic state
Truncal obesity
Premature CVD

controlled to effectively lower TAG levels. Alcohol intake or estrogen treatment may convert a type IV patient to type V, or worsen type V and precipitate pancreatitis.[3] Underlying mechanisms and genetic defects are a mixture of those of Type I and Type IV (Table 52.4).

Dyslipoproteinemia (Atherogenic Dislipidemia)

Some lipidologists have proposed and prefer a simpler classification into subgroups of hypercholesterolemia, chylomicronemia, or atherogenic dyslipidemia.[4] This metabolic syndrome encompasses hypertriglyceridemia, small dense LDL, low HDL, insulin resistance, abdominal obesity, and hypertension (Table 52.5). These patients are at high risk of atherosclerosis.[1,7]

Evaluation of Patients with Hyperlipidemia

Table 52.6 enumerates the details of the history, physical examination, and laboratory tests used for the evaluation of subjects who may have one of the hyperlipidemic syndromes (Color Figure 52.8).

Dietary Management of Hyperlipidemias

Appropriate diet tailored to the lipid abnormality is the initial intervention. Treatment goals are to normalize lipids, or in patients with vascular disease, to lower these to optimal levels that promote regression of atherosclerotic disease and stabilize plaque. Lipid levels should be monitored at six- to eight-week intervals. After a three- to six-month trial of diet, depending on the response and the severity of the disease, appropriate cholesterol- and/or triglyceride-lowering medication should be added. The diet is continued (unless the response is adverse) so that medication dose can be lower, thereby minimizing side effects and cost. Treatment is lifelong.

Diets to Lower Serum Cholesterol and LDL Cholesterol[3,4]

Cholesterol lowering is achieved by a diet that regulates kcalories to achieve desirable weight, and includes an exercise regimen. Depending on the severity of hypercholesterolemia, total fat should be decreased to 30% or less of energy, with saturated fat reduced to <10% or <7% of kcalories depending on severity and response, and cholesterol intake should be 70 to 100 mg/1000 kcal. Consumption of plant based foods, complex carbohydrates, and dietary fiber should be increased.

TABLE 52.6

Evaluation of Patient for Hyperlipidemia

History of:

Vascular disease, angina, MI, angioplasty, bypass surgery, claudication
Abdominal pain
Diabetes
Thyroid, hepatic, renal, disease, gout
Smoking habits, exercise, medications
Body weight
Family history of vascular disease, diabetes, gout
Diet history: alcohol, supplement use, amount and type of fat and cholesterol, energy, protein, carbohydrate, sucrose intakes (best done by a dietitian)

Physical Examination:

Blood pressure, height, and weight
Corneal arcus, xanthelasma, retinopathy, lipemia retinalis
Xanthomas of skin and/or tendons
Dry skin, hair loss
Bruits, murmurs, absent pulses, arrhythmias
Liver, spleen size

Laboratory:

Blood, after 12-14 hour overnight fast, cholesterol, TAG, HDL cholesterol, glucose
Plasma turbidity
Apoproteins, ultracentrifugation, electrophoresis
Post-heparin lipolytic activity
Tests of renal, hepatic, and thyroid function
Electrocardiogram

FIGURE 52.8
(See Color Figure 52.8) The appearance of plasma, refrigerated overnight, from fasting patients. The tubes with plasma samples are taken from (left to right): a subject with normal lipid levels and clear plasma (similar to a patient with Type IIa); a patient with chylomicronemia (Type I) with a creamy top layer above a clear infranatant; a patient with hypercholesterolemia (Type IIa) with clear plasma; a patient with Type III hyperlipoproteinemia with diffusely turbid plasma; a patient with Type IV hyperlipoproteinemia also showing diffuse turbidity; and a patient with Type V hyperlipoproteinemia with plasma exhibiting a creamy top layer over a turbid infranatant.

TABLE 52.7

Guidelines of Food Choices and Menu Plans for Patients with Severe Hypercholesterolemia (FH)[a]

Very Low-Fat Diet-Meal Plan	Goal 10-15% Fat Kcals			
Food	Total Kcal	Fat (g)	Sat Fat (g)	Chol (mg)
Breakfast				
Orange juice, fresh, 6 fl. oz	84	0	0	0
Banana slices, 1/2 med	52	0.5	0	0
Shredded wheat, spoon size, 1 c	170	0.5	0	0
Milk, fat-free, 8 fl. oz	86	0.4	0.3	4
Breakfast subtotal	392	1.4	0.3	4
Lunch				
Turkey sandwich:				
Turkey breast, fat-free luncheon meat, 2 oz	52	0.4	0.2	23
Mayonnaise, light, 1 Tb	50	5	1	0
Whole wheat bread, 2 slices	130	2	0.4	0
Sliced tomato, 1/2 med	13	0.2	0	0
Apple, 1 med	81	0.5	0.1	0
Lunch subtotal	326	8.1	0.7	23
Dinner				
Pork tenderloin, marinated, 4 oz	140	4	1.5	65
Baked potato, w/skin, 8 oz	220	0.2	0.1	0
Fat-free sour cream, 2 Tb	35	0	0	5
Margarine, Promise Ultra fat free, 1 Tb	5	0	0	0
Broccoli, steamed, 1 c	44	0.6	0	0
Angel food cake, 1/12	130	0	0	0
Strawberries, fresh, 1/2 c	23	0.6	0	0
Whipped topping, fat-free, 2 Tb	15	0	0	0
Dinner subtotal	612	5.4	1.6	70
Snacks				
Non-fat vanilla yogurt, 8 fl oz	200	0	0	5
Honeydew melon, cubed pieces, 1c	60	0.2	0	0
Snacks subtotal	298	0.7	0	5
Daily Total	1628	15.6	2.6	102
		8.6%	1.4%	
19% Protein				
72% Carbohydrate				

[a] Prepared by Sandra Leonard, M.S., R.D.

See Table 52.7 for food choices and menu plans for patients with Type II hyperlipidemia or FH.[19,20] Compliance with and response to these changes may lower total and LDL cholesterol by 10 to 20%.

Diets to Lower Serum TAG[3,4]

TAG in VLDL are decreased when kcalories are restricted, especially the intake from refined carbohydrates and alcohol. N-3 fatty acids in fish and fish oils lower TAG.[21]

Chylomicron TAG are lowered by limiting fat intake severely to 50 g or less daily, or to less than 20% of kcalories. Patients with Type V who become pregnant may require

TABLE 52.8

Guidelines of Food Choices and Menu Plans for Patients with Severe Hypertriglyceridemia (Type V)[a]

Triglyceride-Lowering Meal Plan		Goals:	<30% Fat <10% Sat Fat low refined sugar low cholesterol		
Food	Total Kcal	Fat (g)	Sat Fat (g)	Sugar (g)	Cholesterol (mg)
Breakfast					
Cheerios, 1 1/2 c	165	3	0	1.5	0
Milk, 1%, 8 fl. oz	102	2.6	1.6	*N/A	10
Blackberries, fresh, 1/2 c	37	0.3	0	*N/A	0
Orange juice, 1/2 c	56	0.2	0	8	0
Breakfast subtotal	360	6.1	1.6	9.5	10
Lunch					
Ham and cheese sandwich					
Lean ham, 2 oz	69	2.2	0.8	1.8	29
Cheese, cheddar, lowfat, 1 oz	49	2	1.2	0	6
Mustard, 1 Tb	0	0	0	0	0
Whole wheat bread, 2 sl	130	2	0.4	4	0
Peach, fresh, 1 med	37	0.1	0	*N/A	0
Tea, w/sugar substitute	0	0	0	0	0
Lunch subtotal	285	6.3	2.4	5.8	35
Dinner					
Pink salmon, broiled, 6 oz	254	7.6	1.2	0	114
Salad:					
Romaine, 1 c	8	0.2	0	1.2	0
Tomato, 1/2 med	13	0.2	0	1.7	0
Ranch dressing, light, 2 Tb	100	8.0	1.0	1.0	5
Pasta, cooked, 1/2 c	100	0.5	0	0	0
Marinara sauce, 1/4 c	55	2.5	0.8	4.0	0
Asparagus, 6 spears	22	0.3	0.1	1.4	0
Lemon juice	0	0	0	0	0
Cherries, sweet, fresh, 10	49	0.7	0.1	*N/A	0
Dinner subtotal	601	20	3.2	9.3	119
Snacks					
Pear, raw, 1 med	98	0.7	0	*N/A	0
Triscuits, reduced fat, 8 wafers	130	3	0.5	0	0
Snacks subtotal	228	3.7	0.5	0	0
Daily Total	1474	36.1	7.7	24.6	164
		22%	4.7%		
19% Protein					
56% Carbohydrate					

* N/A = Not Available

[a] Provided by Sandra Leonard, M.S., R.D.

placement on diets with the fat content lowered to 20 g/day. Alcohol should be eliminated from the diet, which also controls kcalories and increases exercise to optimize weight. Table 52.8 indicates some food choices and menu plans for TAG lowering in patients with more severe forms of hypertriglyceridemia (Type V). [20] Patients may respond rapidly to withdrawal of dietary fat, with TAG levels falling by 50%/day.

Diet and Lp(a)[22]

The only effects of diet on levels of Lp(a) are the decrease observed with trans-fatty acids. Niacin is the only intervention that lowers Lp(a). Therefore, the advice to individuals with elevated Lp(a) is to aggressively treat any known risk factors for CHD, especially elevated levels of LDL cholesterol.

Drug Management of Hyperlipidemias[4,23-26]

Patients with severe hypercholesterolemia (FH) are unlikely to reach desirable levels in terms of CHD prevention with diet alone. Therefore the trial of diet should be shortened and medication added. The diet trial is worthwhile in order to ascertain whether the subject is diet responsive. Patients with CHD and hypercholesterolemia who are at higher risk also may be placed on medication after a shortened diet trial period. Drug treatment should be monitored for efficacy and safety, and medication needs to be taken throughout life.

Drugs to Lower Cholesterol[23,24]

Drugs that primarily lower total and LDL cholesterol include: the bile acid-binding resins cholestyramine and colestipol, niacin and the statins (lovastatin, pravastatin, simvastatin, atorvastatin, fluvastatin, cerivastatin). Relative efficacy of these classes of drugs is depicted in Figure 52.9. Niacin and statins also increase HDL cholesterol. Side effects with resins (constipation) and niacin (flushing, hepatotoxicity) are more common and serious than those encountered with statins (hepatotoxicity, myositis). Drugs may need to be used in combination in the management of severe hypercholesterolemia. Timing of medication and efficacy in combination with food vary among these drugs, so that the patient must be advised appropriately by health caregiver or pharmacist.

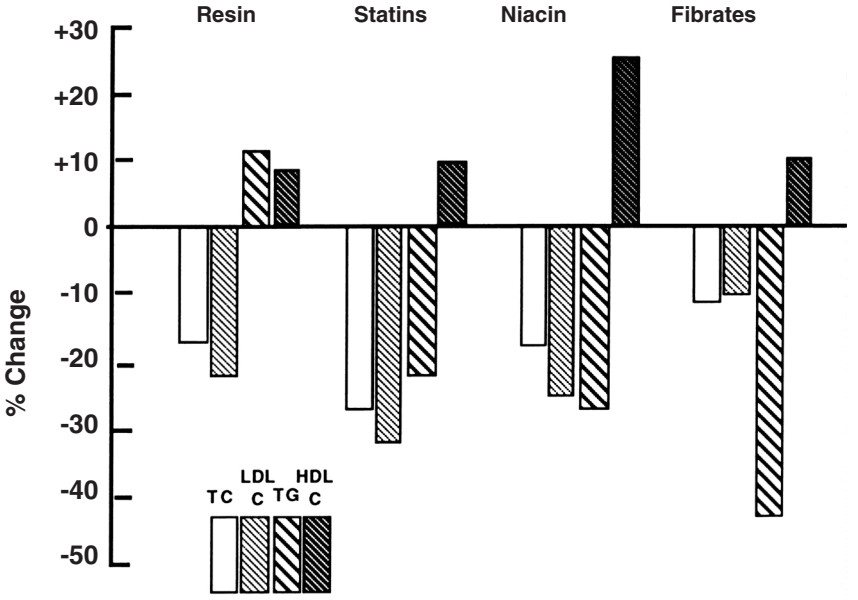

FIGURE 52.9
The efficacy of various lipid-lowering drugs in treating patients with hypercholesterolemia. Data represent the percent change in lipoprotein lipid levels from levels obtained from patients ingesting a baseline lipid-lowering diet.

Plasmapheresis has been used successfully for treating severe forms of FH that are poorly controlled with diet and multiple medications. Liver transplant may improve patients with homozygous FH.

Drugs Affecting TAG Levels[25,26]

Fibric acid derivatives (clofibrate, gemfibrozil, fenofibrate) and niacin are potent TAG-lowering medications that also increase HDL cholesterol. These medications should be added to the diet early in patients with Type V with severe elevations of TAG in order to prevent attacks of acute pancreatitis. At times the LDL levels will increase with fibric acid derivatives as VLDL and chylomicrons decrease, so that a statin may need to be combined with the initial agent. Side effects of fibric acid derivatives include lithogenic bile and gallstones, gastrointestinal distress, and myositis. Oral contraceptives, estrogens, or corticosteroids may raise triglycerides and worsen hypertriglyceridemia. TAG levels should be monitored carefully in patients with Type V using these drugs.

Additional relevant information may be found in Section 26, that addresses the laboratory assessment of lipids and lipoproteins and Section 51, that discusses the role of nutrition in preventing and modifying cardiovascular risk factors.

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