

Disorders of Lipid Metabolism

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"It is a scientific fact that your body will not absorb cholesterol if you take it from another person's plate."

Dave Barry

CLINICAL IMPORTANCE

Hyperlipidemia (also called hyperlipoproteinemia) refers to a disturbance of lipid metabolism that results in an elevated concentration of blood lipids, particularly triglycerides, cholesterol or both. In the fasted state, hyperlipidemia is an abnormal laboratory finding that represents either accelerated synthesis or retarded degradation of lipoproteins (Brown and Goldstein, 1987). Among dogs and cats, the most common, clinically important type of hyperlipidemia is characterized by an excess concentration of triglycerides in blood, a condition referred to as hypertriglyceridemia (Ford, 1993, 1996). The serum and plasma of affected animals typically appear milky white and turbid, or lipemic. In cases of extreme hypertriglyceridemia, the patient's serum can be so lipemic that it is opaque, or lactescent (Figure 28-1).

Hypercholesterolemia is an excess concentration of cholesterol in blood. Most of the circulating cholesterol in dogs and cats is carried on high-density lipoprotein (HDL), the smallest lipoprotein (Ford, 1996; Mahley and Weisgraber, 1974; Mahley et al, 1974). Because HDL particles are small and do not refract light, patients with extreme cholesterol elevations will not have lipemic serum unless the triglyceride concentration is also elevated.

The clinical importance of hyperlipidemia in companion animal medicine centers around four facts: 1) lipemic serum may positively or negatively interfere with quantitative analyses of

other serum analytes, 2) hyperlipidemia in fasted (>12 hours) dogs or cats is abnormal and should be addressed as a significant clinical finding, 3) hyperlipidemic patients are at risk for developing significant clinical illness, including acute pancreatitis and 4) specific dietary and/or drug intervention can eliminate or at least diminish the morbidity associated with hyperlipidemia.

PATIENT ASSESSMENT

History and Physical Examination

The major clinical manifestations of hyperlipidemia include intermittent vomiting, diarrhea and abdominal discomfort and seizures in dogs; cutaneous xanthomata (Figure 28-2) and peripheral neuropathy in cats and lipid keratopathies (Figure 28-3) and lipemia retinalis in both species (Figure 28-4). Some hyperlipidemic dogs and cats do not manifest clinical signs but are considered to be at risk for developing overt signs in the future. Atherosclerosis is a rare manifestation of hyperlipidemia in dogs and cats as opposed to people.

Dogs with Hyperlipidemia

Table 28-1 lists the clinical signs associated with hypertriglyceridemia in dogs. The most common presenting complaints are vague and intermittent but usually center around vomiting and diarrhea. Accompanying signs include non-localizing abdominal discomfort and occasional pain, accompanied by a transient

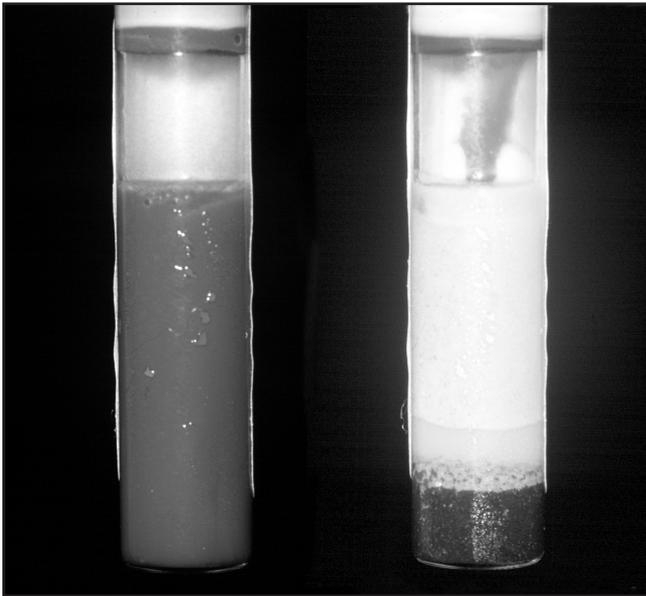


Figure 28-1. Blood samples from a Doberman pinscher with hypothyroidism and severe lipemia. The picture on the left was taken immediately after the sample was drawn. Note that the lipid content is so high that even in black and white photography the blood has a “tomato soup” appearance. The blood sample on the right was allowed to separate forming a “cream layer” of triglyceride-rich chylomicrons on top.

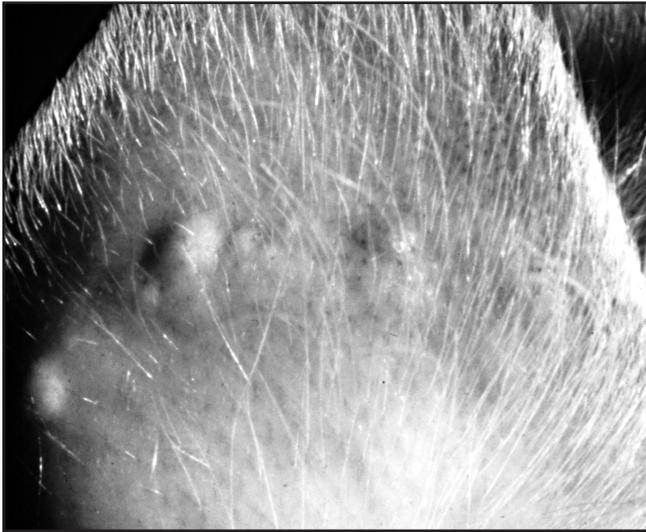


Figure 28-2. Xanthomas on the pinna of a cat with hyperlipidemia. Xanthomas are tumors composed of lipid-laden foam cells, which are histiocytes containing cytoplasmic lipid material. These lesions resolved with use of a low-fat, high-fiber food.

decrease in appetite. The owner may report episodic signs, lasting a few hours to a few days that may resolve spontaneously with fasting. Abdominal distention is occasionally reported. There appears to be no gender predilection. Affected dogs are usually four years of age and older although younger dogs may be affected.

On physical examination, dogs may appear lethargic and may or may not manifest abdominal pain. Clinical signs and

history are compatible with acute pancreatitis; however, abdominal radiographs, ultrasound and laboratory evidence supporting a diagnosis of pancreatitis are typically lacking. The term pseudopancreatitis has been used to describe the clinical manifestations associated with hypertriglyceridemia (Ford, 1993, 1996).

Lipemia retinalis, a condition characterized by pale pink retinal arterioles and venules, is an incidental finding seen on fundoscopic examination of lipemic dogs and cats (Figure 28-4). This condition does not affect vision. Laboratory analysis of affected animals will verify extreme hypertriglyceridemia, typically greater than 1,000 mg/dl.

Sustained hypertriglyceridemia is a principal risk factor among people and dogs for developing acute pancreatitis (Brown and Goldstein, 1987; Ford, 1993; Armstrong and Ford, 1989; DeBowes, 1987; Sanfey and Cameron, 1985; Whitney et al, 1987; Williams, 1995). Dogs with acute abdominal pain and vomiting should be evaluated for hyperchylomicronemia at the time of presentation and during the recovery phase when food intake is restored.

Hypertriglyceridemia should be considered in patients presenting with a history of seizures. A small number of patients, many of them miniature schnauzers, diagnosed with idiopathic epilepsy have elevated fasting triglyceride concentrations and lipemic serum (Rogers et al, 1975, 1975a). In some dogs, dietary therapy has successfully reduced blood triglyceride levels and eliminated seizures without concomitant use of anticonvulsant drugs. Interestingly, seizures associated with hyperlipidemia are not necessarily associated with other signs typically attributed to hyperlipidemia (e.g., vomiting and diarrhea).

Although owners of hypertriglyceridemic dogs rarely express concern about their pet’s inactivity or lethargy at the time of initial presentation, owners often remark that the pet’s activity level increased as a result of lowering circulating triglyceride levels.^a

Cats with Hyperlipidemia

Clinical signs in hyperlipidemic cats are different than those reported to occur in dogs (Table 28-1). The most common clinical finding in affected cats is cutaneous xanthoma, a painless, raised lesion caused by accumulation of lipid-laden macrophages or foam cells in the skin (Figure 28-2) (Jones and Watson, 1995; Jones et al, 1983; Jones, 1995). Xanthomas are most likely to occur over bony prominences and areas of skin subject to chronic pressure or direct injury.

Xanthomata may also occur in other tissues such as liver, spleen, kidney, heart, skeletal muscle and intestines. Uniquely, xanthomata can form at the point where spinal nerves emerge through the vertebral foramina (Jones, 1993), the point at which nerves and vascular tissue are subject to mild injury associated with the movement of adjacent vertebrae. Peripheral neuropathy caused by neuronal xanthoma is characterized by motor paralysis. Signs vary depending on the specific nerves involved. Horner’s syndrome, tibial nerve paralysis and radial nerve paralysis have been reported most often (Jones, 1993, 1995). In cases in which mixed motor and

sensory nerves have been affected, sensation to painful stimuli was retained.

Lipemia retinalis is more common in cats than dogs (Figure 28-4). Other ocular manifestations of hyperchylomicronemia in cats are uncommon but include iridocyclitis, arcus lipoides corneae and lipemic aqueous and lipid keratopathy (Figure 28-3). These lesions are thought to occur subsequent to existing ocular disease in lipemic cats (Jones, 1995; Crispin, 1993).

Laboratory Evaluation

Veterinarians assessing a dog or cat for hyperlipidemia should submit serum or plasma rather than whole blood (Box 28-1). Plasma or serum samples for cholesterol and triglyceride determinations can be refrigerated or frozen for several days without significant effect.

The presence of excess triglycerides, particularly if associated with retention of chylomicrons, is an important source of either positive (falsely increased) or negative (falsely decreased) interference for analytes determined by colorimetric methods (Whitney et al, 1987). The effect of lipemia on individual analytes is variable and depends on the degree of lipemia, the analyte being measured and the analytic method used. Lipemia also causes *in vitro* hemolysis, a phenomenon induced by the effect of lipid on erythrocyte membrane fragility, which may also induce interference when performing laboratory profiles (Allerman, 1990). The extent to which *in vitro* hemolysis affects determination of hemoglobin and hematocrit values has not been established. The amount of red-cell hemolysis appears to be proportional to the length of time red cells are in contact with the lipemic serum and the degree of lipemia. The type and extent of interference induced by lipemia varies from one laboratory to another, depending on the analytical instrumentation and methodologies used. Visual inspection of the patient's serum provides valuable physical evidence about the presence or absence of an excessive concentration of triglycerides. In fasting patients (i.e., 24-hour fast or longer), lipemia or lactescent serum denotes hypertriglyceridemia and is usually associated with triglyceride concentrations in excess of 2,000 mg/dl (canine normal = 50 to 150 mg/dl, feline normal = 50 to 100 mg/dl). A diagnosis of hypertriglyceridemia should be based on laboratory determination of serum triglycerides in unclarified serum. By laboratory methods used in North America, serum triglyceride concentrations greater than 500 mg/dl are abnormal for fasted dogs and cats. Although a correlation has not been observed between triglyceride concentrations and the severity of clinical signs, dogs with a triglyceride concentration of 1,000 mg/dl or higher are at risk for developing clinical signs and, as such, are candidates for dietary intervention (Armstrong and Ford, 1989; Rogers et al, 1975a; Chapman, 1980). Maintaining triglyceride levels less than 500 mg/dl in lipemic (familial) patients may be difficult with nutritional management alone. A more reasonable target range for dietary control is 500 to 1,000 mg/dl postprandially. Furthermore, clinical signs of hypertriglyceridemia appear to be uncommon in patients with postprandial triglyceride levels less than 1,000 mg/dl.



Figure 28-3. Lipid keratopathy in a rabbit. Note the white lipid accumulation in the corneal stroma. Corneal vascularization may precede or follow lipid deposition. Lipid keratopathy has been described in several species including human beings, rabbits, cats and dogs.

Table 28-1. Clinical signs and diseases associated with hypertriglyceridemia in dogs and cats.

Dogs

- Abdominal discomfort*
- Acute pancreatitis
- Behavior (lethargy, inactivity)
- Crystalline stromal dystrophy (especially cavalier King Charles spaniels)
- Cushing's syndrome
- Fasting lipemia (six to 12 hours)
- Intermittent diarrhea*
- Intermittent vomiting*
- Lipemia retinalis
- Lipemic aqueous
- Lipid corneal dystrophy/arcus lipoides corneae
- Seizures

Cats

- Cutaneous xanthomata
- Lipemia retinalis
- Lipid keratopathy
- Peripheral nerve paralysis
 - Horner's syndrome
 - Tibial nerve paralysis
 - Radial nerve paralysis
- Splenomegaly

*These clinical signs may occur concomitantly in the same patient. The collective term used to describe these signs is "pseudopancreatitis."

Significant hyperlipidemia characterized by lipemic serum and hypertriglyceridemia has been observed as an incidental finding in fasted adult dogs and cats. The absence of clinical signs at the time of presentation does not justify ignoring the significance of the lipemia. Because of the risks associated with hypertriglyceridemia, patients that behave normally but have persistent lipemia should be managed in the same manner as



Figure 28-4. Lipemia retinalis in a cat with hyperlipidemia. Note the white, milky appearance of the retinal blood vessels.

Box 28-1. Handling Lipemic Samples.

Submission of lipemic blood to a commercial laboratory necessitates knowing how the sample will be processed. Because of the interference induced by lipemia, some laboratories will simply reject lipemic samples. Many laboratories, however, will attempt to clear lipemic serum (by removing chylomicrons) before performing any biochemical assays. Unfortunately, there is neither a standardized method for clearing lipemic serum nor do commercial laboratories consistently report whether or not an attempt was made to clear the sample. For veterinarians, however, knowledge of the fact that a lipemic sample was cleared before determining the triglyceride concentration is critical in making reasonable interpretations. Although clearing a lipemic sample eliminates interference associated with chylomicrons, it effectively eliminates a critical element of clinical information (i.e., that the patient is hypertriglyceridemic).

Ideally, two aliquots of a serum sample from a lipemic patient should be submitted simultaneously. One sample, if effectively cleared, can be used to perform routine biochemical testing, including triglyceride levels. Determining triglyceride concentrations in the second, lipemic (uncleared) sample documents the true extent of triglyceride excess, serves as an important baseline value for assessing response to therapy and can, when compared to the triglyceride value in the cleared sample, characterize the nature of the hyperlipidemia.

those presenting with clinical signs.

Hyperchylomicronemia is confirmed in fasted dogs with lipemic serum, hypertriglyceridemia (in uncleared serum) greater than 500 mg/dl and a positive chylomicron test. Clinical signs are not prerequisite for diagnosis nor for recommending therapeutic intervention. However, therapy in dogs that do not have associated signs is generally reserved for those having fasting hypertriglyceridemia on two consecutive samples two to four weeks apart.

Chylomicrons will normally appear in the serum of dogs and cats within 30 minutes to one hour after ingestion of a meal containing fat. This finding is associated with a transient (i.e., six to 12 hours) increase in serum triglycerides after which triglyceride levels rapidly return to baseline values. Physiologic hyperlipidemia is easily excluded from consideration if the patient is known to have fasted throughout the 12-hour period before blood collection. In normal, postprandial animals, serum turbidity is associated with a modest elevation of serum triglycerides (from 150 to 400 mg/dl) that typically returns to normal within 10 hours.

Lipoprotein Electrophoresis

Lipoprotein electrophoresis (LPE) has been used as a means of characterizing abnormalities in lipid metabolism (Ford, 1993; Armstrong and Ford, 1989; Whitney, 1992). The value of LPE has been in question in human medicine for several years and is justifiably questioned in veterinary medicine. Compared to the quantitative assays currently available, LPE appears to have limited value in the clinical evaluation of lipid disorders in dogs and cats.

The Chylomicron Test

Knowing that the patient has fasting lipemia provides immediate evidence of hypertriglyceridemia. The lipid disorder may be further characterized by performing a simple, in-hospital test for the presence of chylomicrons. The lipemic serum, separated from red cells, is refrigerated and allowed to stand undisturbed for six to 12 hours. Chylomicrons, if present, will float to the surface of the sample forming an opaque “cream layer” over a clear infranatant (Figure 28-5). This finding suggests a disorder of chylomicron metabolism, the most common form of hyperlipidemia in dogs. If the sample remains turbid, but doesn’t form a cream layer, retention of very low-density lipoproteins (VLDL), rather than chylomicrons, is suggested. This finding also suggests that the hyperlipidemia is secondary to an underlying disorder. In some dogs, particularly poorly regulated diabetics, a cream layer may form over turbid, lipemic serum suggesting retention of chylomicrons and VLDL (Armstrong and Ford, 1989; Chapman, 1980).

Risk Factors

Familial (primary) hyperchylomicronemia in cats has been reported as an autosomal recessive trait limited to certain lines of cats. The trait is thought to be present in mixed-breed cats throughout much of the world; therefore, clinically affected cats appear sporadically. Certain dog breeds, most notably

miniature schnauzers, are also at increased risk of clinical illness associated with hypertriglyceridemia characterized by the inability to degrade chylomicrons. Though not definitively proven, familial traits are thought to cause these disorders. Results of a limited survey of healthy adult dogs suggested that primary hypercholesterolemia might occur within some families of Doberman pinschers, rottweilers,³ Shetland sheepdogs (Sato et al, 2000), rough collies (Jeusette et al, 2004) and briards (Watson et al, 1993).

Secondary risk factors (i.e., particularly endocrine disorders, certain drugs and possibly certain diets leading to hyperlipidemia) are known to occur but have not been well studied. For example, profound fasting hypertriglyceridemia occurs inconsistently in dogs with unregulated diabetes mellitus. Clinical signs associated with excess triglyceride concentrations typically include vomiting, diarrhea and abdominal discomfort. Approximately 30% of untreated hypothyroid dogs and from 25 to 30% of untreated dogs with pituitary-dependent hyperadrenocorticism have excess serum cholesterol concentrations. However, the relationship between clinical signs, if any, and the hyperlipidemia has not been established.

Obesity is known to cause abnormalities of lipid metabolism in people. Experimentally induced chronic obesity in otherwise normal dogs fed a complete and balanced maintenance food resulted in significantly higher concentrations of cholesterol in total plasma (+41%) and in VLDL (+125%), HDL (+45%) and low-density lipoprotein (LDL) (+58%) fractions and significantly higher concentrations of triglycerides in total plasma (+75%) and in the VLDL (+118%). When switched to a low-energy, high-fiber diet that resulted in overall decreased energy intake, plasma lipid values decreased (Jeusette et al, 2005).

In some animals, drugs are known to either decrease lipoprotein degradation or increase lipoprotein production, thereby causing hyperlipidemia. For example, dogs receiving long-term phenobarbital therapy for regulation of idiopathic epilepsy may develop hypercholesterolemia. The clinical significance is unknown and may, in fact, be related to thyroid-hormone production or activity. Cats receiving megestrol acetate may secondarily develop diabetes mellitus, which may culminate in altered lipoprotein lipase activity and hyperchylomicronemia.

Etiopathogenesis

Normal Lipid Metabolism

LIPOPROTEINS

Cholesterol and triglycerides are hydrophobic molecules; therefore, they cannot circulate in the aqueous milieu of blood without being incorporated into complex, spherical macromolecules called lipoproteins (Brown and Goldstein, 1987; Chapman, 1980; Schaefer and Levy, 1985; Weinberg, 1987; Watson and Barrie, 1993). The water-soluble outer coat of the lipoprotein is comprised of phospholipids, nonesterified (free) cholesterol and several unique proteins called apolipoproteins (Figure 28-6). Cholesterol, in the form of cholesterol esters, and triglycerides are carried within the nonpolar core of spherical lipoprotein macromolecules. Abnormally high concentra-

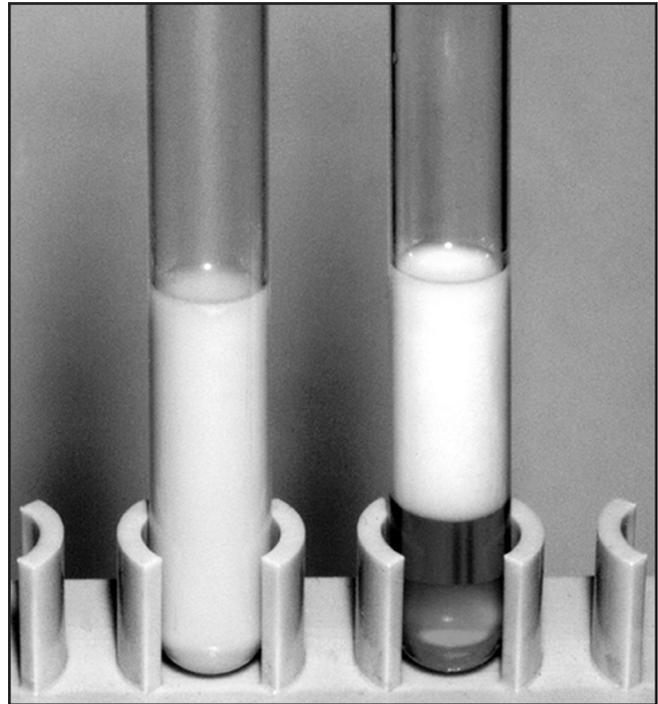


Figure 28-5. The positive chylomicron test. The lactescent serum in both tubes was obtained from a dog with hypertriglyceridemia. The sample on the left is the serum immediately after separation from the red blood cells whereas the sample on the right was allowed to stand undisturbed for 10 hours. The so-called “cream layer” is comprised of triglyceride-rich chylomicrons. (Reprinted with permission from Ford RB. Canine hyperlipidemia. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine, 4th ed. Philadelphia, PA: WB Saunders Co, 1995; 1417.)

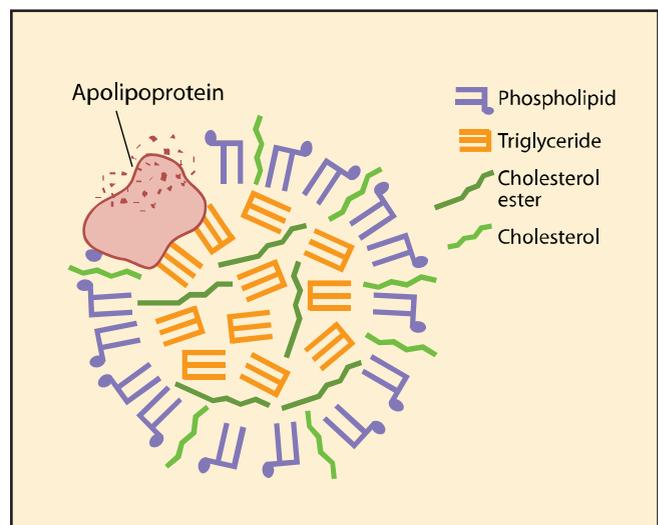


Figure 28-6. Diagram illustrating the composition and structure of lipoproteins. Cholesterol and triglycerides comprise much of the lipoprotein core and are present in varying proportions. (Adapted from Brody T, ed. Nutritional Biochemistry. New York, NY: Academic Press Inc, 1994; 276.)

tions of cholesterol or triglycerides, as measured in routine biochemical assays, actually reflect increased synthesis or decreased degradation of lipoproteins.

APOLIPOPROTEINS

It is well recognized that the apolipoproteins (commonly referred to as apoproteins), contained within the outer coat of lipoproteins, bind to specific enzymes or transport proteins on cell membranes (Brown and Goldstein, 1987; Chapman, 1980; Naito, 1986). Thus, they are responsible for directing the lipoprotein to various sites of metabolism. Several apoproteins have been recognized in dogs and cats. Abnormalities or deficiencies in specific apoproteins are likely to be responsible for altered lipoprotein metabolism that culminates in hyperlipidemia.

Apoprotein C-II (also called apo C-II) (Figure 28-6) activates lipoprotein lipase and is very much involved in triglyceride metabolism during the postprandial period. An inherited deficiency in apo C-II is one of the proposed mechanisms responsible for hyperchylomicronemia in dogs.

Classes of Lipoproteins

Four major lipoprotein classes in dogs and cats can be separated by preparative nonionic precipitation and ultracentrifugation: 1) chylomicrons, 2) VLDL, 3) LDL and 4) HDL (Mahley et al, 1974; Armstrong and Ford, 1989; Barrie et al, 1993). A comprehensive lipoprotein profile consists of determining the concentration (mg/dl) of triglycerides and cholesterol in each lipoprotein class. Through lipoprotein profiling, it is possible to categorize hyperlipidemic patients according to lipoprotein phenotype, facilitate diagnosis of primary and secondary lipid disorders and even prescribe therapy. Unfortunately, uniform standards for performing lipoprotein profiles are not commercially available. Alternatively, laboratory determinations of total cholesterol and triglycerides are routinely available and can be used to make good diagnostic and therapeutic decisions.

CHYLOMICRONS

The largest and least dense lipoprotein particles are chylomicrons. These large, triglyceride-rich lipoprotein complexes transport dietary fat (triglycerides) from the small intestine via the lymphatics and general circulation to various sites of metabolism. Appearing in plasma within one hour after consumption of a fat-containing meal, chylomicrons can be visually confirmed as turbid or cloudy serum, a finding that corresponds to a transient (i.e., six to 12 hours postprandial), physiologic hypertriglyceridemia. A cream layer comprised of chylomicrons may form over a clear infranatant if serum is allowed to stand undisturbed for six to 10 hours.

In dogs, and probably cats, only about 10% of the lipid contained in chylomicrons is cholesterol (cholesterol ester). After a meal, hypertriglyceridemia is associated with transient increases in serum cholesterol that may exceed the normal reference range.

Chylomicrons transport fat to the capillaries of adipose tissue and skeletal muscle where they are exposed to the enzyme lipoprotein lipase. The enzyme, once activated by apo C-II,

hydrolyzes triglycerides into glycerol and free fatty acids. What remains of the chylomicron is a remnant particle, rich in cholesteryl esters, that subsequently delivers cholesterol to the liver (Schaefer and Levy, 1985; Weinberg, 1987; Gotto, 1988; Eckel, 1989). Chylomicron hydrolysis is normally complete within six to 12 hours following a meal, after which the plasma will again become clear. Fasting hyperchylomicronemia is an abnormal condition resulting from decreased clearance of chylomicrons in the circulation. It is recognized in dogs, cats and people. Although clinical manifestations recognized in dogs are quite different from those in cats, hyperchylomicronemia is the most common lipid disorder recognized in companion animals.

VERY LOW-DENSITY LIPOPROTEINS

Produced in the liver and containing a predominance of triglycerides, VLDL are transported to tissue capillaries where they are catabolized by lipoprotein lipase in the same manner as chylomicrons (Brown and Goldstein, 1987; Eckel, 1989). Retention of VLDL, and the resulting hypertriglyceridemia, occurs frequently in dogs with insulin-dependent diabetes mellitus. Although serum turbidity is manifest in the fasted patient, a cream layer will not separate when the sample is left undisturbed, even when refrigerated.

LOW-DENSITY LIPOPROTEINS

Like VLDL, LDL is responsible for transporting endogenously synthesized lipids (especially cholesterol) from the liver to target tissues. Subsequent to the hydrolysis of VLDL and the removal of triglycerides from its core, a short-lived intermediate-density lipoprotein is ultimately processed by hepatic lipase to form LDL. Delivery of LDL to peripheral tissues is facilitated by the interaction of the structural protein of LDL with a specific receptor, called the LDL receptor. In people, approximately 70% of total cholesterol is carried within LDL, which is sometimes referred to as the atherogenic lipoprotein (Mahley et al, 1974). However, most cholesterol in dogs and cats is carried on HDL.

HIGH-DENSITY LIPOPROTEINS

Newly formed HDL, secreted by the liver and the intestine, binds with unesterified cholesterol released from peripheral tissues during normal cellular turnover (Brown and Goldstein, 1987; Barrie et al, 1993; Gotto, 1988; Eckel, 1989). The conversion process from nascent HDL to mature, spherical HDL particles is mediated by the enzyme lecithin-cholesterol acyltransferase (LCAT) (Brown and Goldstein, 1987; Gotto, 1988). As members of the antiatherogenic lipoprotein family, HDL is recognized for its ability to remove excess cholesterol from tissues and transport it to the liver.

A number of subgroups of HDL have been recognized in people (HDL₂ and HDL₃) (Brown and Goldstein, 1987) and dogs (HDL₁ and HDL₂) (Mahley et al, 1974; Rogers et al, 1975, 1975a). In both dogs and cats, a large HDL molecule (HDL₁) is formed as HDL acquires free cholesterol and expands under the influence of LCAT. However, the actual role of HDL subgroups in predicting or diagnosing disease in ani-

mals has not been defined. Because commercial laboratories do not routinely isolate HDL subgroups, subgroup analyses in veterinary medicine have not been found to have immediate application in clinical practice.

Classification of Hyperlipidemic States

Hyperlipidemic states can be classified as postprandial, familial or acquired. Familial hyperlipidemia, also called primary hyperlipidemia, refers to those defects in lipoprotein metabolism that are known or suspected to be inherited. Fasting lipemia is frequently recognized in miniature schnauzers and is possibly linked to a familial defect in chylomicron metabolism. Feline hyperchylomicronemia is the only hyperlipidemic state proven to be familial (Jones and Watson, 1995; Jones et al, 1983; Jones, 1993, 1995).

Acquired hyperlipidemia, also called secondary hyperlipidemia, refers to an excess concentration of lipid in blood resulting from an underlying disease in which normal lipoprotein metabolism is markedly altered. Several endocrine diseases alter lipid metabolism leading to secondary hyperlipidemia. For example, insulin-deficient states alter carbohydrate and lipid metabolism. Animals with insulin-dependent diabetes mellitus may have either hypertriglyceridemia or hypercholesterolemia. Hyperadrenocorticism, renal disease and hypothyroidism are variably associated with secondary hyperlipidemia (Ford, 1996; DeBowes, 1987; Whitney, 1992; Barrie et al, 1993; Rogers, 1977; Zerbe, 1986).

In clinical practice, it is not unusual to encounter a patient with both primary and secondary hyperlipidemia. A miniature schnauzer presented with diabetes mellitus is likely to have extreme elevations in serum triglycerides and lactescent serum. From the clinician's perspective, hyperlipidemia, whether primary or secondary, can be associated with undesirable clinical effects. The ability to recognize the signs associated with hyperlipidemia and to make appropriate dietary or therapeutic recommendations becomes fundamental to the management of these cases.

Postprandial Hyperlipidemia

Triglycerides are the predominant dietary fat in pet food. Subsequent to consuming a meal, dogs and cats will experience transient, physiologic hyperlipidemia characterized by increased triglyceride concentration (circulating chylomicrons) and, depending on the amount of fat consumed, serum turbidity (lipemia). However, postprandial hyperlipidemia does not necessarily imply that a disorder of lipid or lipoprotein metabolism exists. In normal dogs and cats, postprandial hyperlipidemia normally persists from six to 12 hours after a meal. Even when a high-fat food is consumed, serum triglyceride levels are not expected to exceed 500 mg/dl in normal animals. In dogs and cats, hyperlipidemia associated with serum triglyceride levels greater than 1,000 mg/dl, whether fasted or not, is likely to result from an underlying disorder of lipid metabolism (Ford, 1996). Because chylomicrons carry only a fraction of circulating cholesterol, consumption of a meal has little impact on cholesterol during the six- to 12-hour postprandial period.

Postprandial hyperlipidemia, although physiologic, must be

distinguished from intrinsic causes (primary or secondary). Confirming that a hyperlipidemic patient has fasted for 10 to 12 hours before collection of blood effectively excludes a recent meal as the cause for increased blood lipids and, therefore, justifies further evaluation in an attempt to determine the source of the hyperlipidemic state.

Canine Familial Hyperchylomicronemia

Hypertriglyceridemia, particularly that associated with retention of chylomicrons, is the most prevalent lipid disorder recognized in dogs and cats and is associated with the greatest health risk (Ford, 1993, 1995). In dogs, the precise mechanism has not been elucidated; however, this disorder of lipoprotein metabolism is believed to be caused by either the lack of lipoprotein lipase activity or the absence of apo C-II (Brown and Goldstein, 1987; Schaefer and Levy, 1985; Gotto, 1988; Zerbe, 1986). Several reports have been published suggesting that miniature schnauzers are predisposed to primary or familial hyperlipidemia (Ford, 1993, 1995, 1996; Rogers et al, 1975; Rogers, 1975a). Although it is not definitively known that hyperlipidemia is an inherited disorder of miniature schnauzers, there appears to be a higher than expected prevalence of hypertriglyceridemia in the breed (Ford, 1993).^a Several other purebred and mixed-breed dogs have been identified as having fasting hyperchylomicronemia with significant clinical illness, but have no detectable underlying disease.

Canine Idiopathic Hypercholesterolemia

Results of a limited survey of healthy, adult dogs suggested that primary hypercholesterolemia might occur within some families of Doberman pinschers and rottweilers (Armstrong and Ford, 1989). A relationship between the presence of peripheral corneal dystrophy, regarded by some ophthalmologists as containing cholesterol, and excess serum cholesterol concentration (>300 mg/dl) is of noteworthy interest. Lipoprotein profiles of affected dogs demonstrate elevations of LDL-cholesterol.^a To date, no studies have demonstrated whether or not administration of cholesterol lowering drugs (e.g., fibrates, statins) would either decrease the cholesterol concentration of hypercholesterolemic dogs or cause regression of the corneal dystrophy. Dietary management with a low-fat veterinary therapeutic food was successful in treatment of bilateral lipid keratopathy in one dog (Linton et al, 1994). In a family of rough collies, treatment with a low-fat, energy-restricted food had no effect on serum total cholesterol or corneal lipidosis. The addition of short-chain fructooligosaccharides resulted in regression of corneal lipidosis, but had a variable and transient effect on total serum cholesterol (Jeusette et al, 2004).

Occasionally, extreme elevations of cholesterol will be discovered incidentally in healthy, adult dogs with normal triglyceride values. The clinician is justified in evaluating the patient for evidence of an underlying disorder, such as diabetes mellitus or hyperadrenocorticism. However, in some dogs, hypercholesterolemia cannot be explained. Unless clear evidence of underlying disease exists, treatment specifically intended to lower serum cholesterol does not appear warranted.

Table 28-2. Key nutritional factors for hyperlipidemia.

Disorder	Factor	Dietary recommendations
Hyperlipidemia	Triglycerides	<p>Feed a food that reduces serum triglycerides</p> <p>Restrict dietary fat (<12% dry matter [DM])</p> <p>Feed a food that reduces serum triglycerides and binds cholesterol and bile acids</p> <p>Increase dietary fiber: Dogs: ≥10% DM Cats: ≥7% DM</p> <p>Add lipid-reducing drugs (fibrates) if dietary management alone is unsuccessful in controlling hyperlipidemia</p>

Feline Inherited Hyperchylomicronemia

A primary, genetic disorder of young cats was found to alter chylomicron metabolism (Jones et al, 1983). Cats that had inherited this disorder developed a form of hyperlipidemia similar to that reported to occur in miniature schnauzers.

Secondary Disorders of Lipid Metabolism

Considering the prevalence of metabolic diseases that affect lipid metabolism, it is possible that secondary hyperlipidemia affects more animals than primary hyperlipidemia. Several endocrine diseases, as well as renal and hepatic diseases, variably alter lipoprotein metabolism resulting in either hypertriglyceridemia or hypercholesterolemia.

DIABETES MELLITUS

Hyperlipidemia secondary to diabetes mellitus in dogs and cats may be characterized by hypertriglyceridemia and moderate hypercholesterolemia (Ford, 1996; Armstrong and Ford, 1989; Barrie et al, 1993). In insulin-deficient states, clearance of chylomicrons is impaired due to insufficient activation of lipoprotein lipase in vascular endothelial cells by insulin (Brown and Goldstein, 1987). Examination of lipid profiles of diabetic dogs reveals lipemia, an increase in chylomicrons and VLDL and a corresponding increase in triglyceride concentration. In some diabetic dogs, excess serum cholesterol concentrations will be present independent of hypertriglyceridemia. In one study, diabetic dogs did not have cholesterol levels significantly different from those of a control population (Barrie et al, 1993). LDL-cholesterol, on the other hand, was increased presumably as a result of increased LDL synthesis. The clinical significance of this finding is unknown.

Although a relationship between the quality of glucose regulation and serum triglyceride levels has been recognized in people, it is unknown whether a similar relationship exists in dogs and cats. Lipemia retinalis in dogs and cutaneous xanthomatosis in cats are associated clinical findings that may be apparent among insulin-dependent diabetics, particularly those with severe hypertriglyceridemia. The hyperlipidemia associated

with diabetes mellitus usually improves or resolves as glycemic control is achieved.

Diabetic dogs with excess serum triglyceride concentrations appear to be at risk for developing acute pancreatitis or pseudopancreatitis. Dietary fat restriction can be expected to lower the serum triglyceride concentration and may facilitate glycemic regulation in dogs receiving insulin.

PROTEIN-LOSING NEPHROPATHY

Hyperlipidemia, characterized by increased serum cholesterol or triglyceride levels, may be detected in patients with proteinuria due to glomerulonephritis or amyloidosis. An inverse relationship between elevated blood lipids/lipoproteins and decreased plasma albumin concentration has been reported to occur in patients with nephrotic syndrome. The actual pathogenesis whereby the hyperlipidemia develops is complex and appears to be due to a combination of factors involving altered metabolism of lipoproteins (Bernard, 1982). Hypercholesterolemia occurs inconsistently in dogs with heavy proteinuria. The lipoprotein profile of dogs and cats with nephrotic syndrome has not yet been characterized. The influence of hyperlipidemia on morbidity and mortality in nephrotic syndrome is unknown.

HYPERADRENOCORTICISM

Hypercholesterolemia has been recognized in dogs with hyperadrenocorticism (Cushing's syndrome) without concomitant diabetes mellitus (Armstrong and Ford, 1989; DeBowes, 1987; Barrie et al, 1993). Affected dogs have clear serum, increased plasma cholesterol and LDL-cholesterol levels, but no discrete clinical signs specifically attributable to excess cholesterol. In a limited study of adult dogs confirmed to have hyperadrenocorticism, only 30% were hypercholesterolemic.^a There appears to be little diagnostic value to performing lipid determinations in dogs suspected of having endogenous cortisol excess. However, monitoring changes in a given patient's cholesterol profile may have prognostic value in dogs undergoing treatment.

HYPOTHYROIDISM

Hypercholesterolemia is present in up to two-thirds of hypothyroid dogs and is believed to result from impaired LDL clearance from the general circulation. It has been suggested that an absolute triiodothyronine deficiency may lead to an increased hepatic cholesterol pool. In turn, LDL-receptor activity is down regulated preventing excess sterol accumulation in the liver (Barrie et al, 1993). Atherosclerotic-type arterial lesions have occasionally been reported (DeBowes, 1987). This finding has led to the suggestion that cholesterol be included in an initial diagnostic screening for hypothyroidism. However, superior laboratory tests are available for evaluating thyroid disease in cats and dogs and should be considered before serum cholesterol evaluation. Therapy should be directed towards correcting the thyroid-hormone deficiency. Although hypothyroid people may experience decreased cholesterol levels after thyroid-replacement therapy is started, there is no apparent value in monitoring cholesterol in affected dogs.

Table 28-3. Selected commercial foods used in dogs with hyperlipidemia compared to recommended levels of key nutritional factors.*

Dry foods	Energy density (kcal/cup)**	Fat (%)	Crude fiber (%)
Recommended levels	-	<12	≥10
Hill's Prescription Diet r/d Canine	242	8.2	13.5
Hill's Prescription Diet r/d with Chicken Canine	241	8.8	13.6
Iams Veterinary Formula Weight Loss/Restricted Calorie	217	9.1	2.4
Purina Veterinary Diets EN GastroENteric Formula	397	12.6	1.5
Purina Veterinary Diets HA HypoAllergenic Formula	311	10.5	1.6
Purina Veterinary Diets OM Overweight Management Formula	266	7.2	10.3
Royal Canin Veterinary Diets Digestive Low Fat LF	226	6.6	2.3
Moist foods	Energy density (kcal/can)**	Fat (%)	Crude fiber (%)
Recommended levels	-	<12	≥10
Hill's Prescription Diet r/d Canine	257 (12.3-oz. can)	8.6	21.2
Iams Veterinary Formula Weight Loss/Restricted Calorie	397 (14-oz. can)	14.9	3.2
Purina Veterinary Diets EN GastroENteric Formula	423 (12.5-oz. can)	13.8	0.9
Purina Veterinary Diets OM Overweight Management Formula	189 (12.5-oz. can)	8.4	19.2
Royal Canin Veterinary Diets Digestive Low Fat LF	442 (13.6-oz. can)	6.9	3.0

*From manufacturers' published information; all values expressed on a dry matter basis unless otherwise stated.

**Energy density values are listed on an as fed basis and are useful for determining the amount to feed (the amount to feed = the daily energy requirement ÷ the energy density [kcal/cup or can]); cup = 8-oz. measuring cup. To convert to kJ, multiply kcal by 4.184.

Key Nutritional Factors

Fat

Chylomicrons are exclusively of dietary origin; therefore, the amount and type of dietary fat is of primary importance. Foods containing less than 12% dry matter (DM) fat are most commonly recommended (Table 28-2).

Marine fish oils are rich in omega-3 (n-3) fatty acids, which effectively decrease production of triglyceride-rich VLDL. Marine fish oils have been recommended as the first line of medical treatment for idiopathic hypertriglyceridemia in dogs. Suggested doses range from 10 to 30 mg/kg to 200 mg/kg body weight. Experience with marine fish oils is limited and most reported successes are based on anecdotal reports.

Fiber

Many low-fat foods also have increased levels of dietary fiber. The contribution of fiber in low-fat foods and fiber's ability to reduce serum lipids is unclear. At this time, no studies have been done in animals to evaluate the effects of dietary fiber type or amount on reducing serum triglyceride levels. Multiple studies in people have shown that dietary fiber, regardless of type or amount, has no significant effect on serum triglyceride levels. Increasing dietary fiber, however, can lower serum cholesterol levels. Furthermore, primarily soluble fibers of differing types have been evaluated. Psyllium, oat bran, guar gum and pectin are a few that effectively reduce cholesterol in people. Reports have shown cholesterol reductions with fiber range from 3 to 10%, depending on fiber type and amount (Hunninghake et al, 1994; Anderson et al, 2000). In some studies, the amount of dietary fiber was high and patient compliance may have been reduced due to increased gastrointestinal side effects (i.e., diarrhea, flatulence, abdominal distention).

Several mechanisms have been suggested for the cholesterol-reducing effects of soluble fiber. Fiber binds dietary cholesterol in the intestine thereby reducing absorption and binds bile acids in the intestine resulting in increased gastrointestinal excretion and increased cholesterol usage to synthesize more

bile acids (Marlett, 1997). Some investigators suggest that the cholesterol-lowering effect is due to the substitution of dietary fiber for higher fat content foods (Swain et al, 1990). Studies with prebiotic fibers have shown similar cholesterol-reducing effects (Maki et al, 2003; Behall et al, 2004). Similar effects may occur in animals. Short-chain fructooligosaccharides are reportedly effective in reducing serum cholesterol concentrations and treating corneal lipidosis (Diez et al, 2000); however, when used to treat long-term corneal lipidosis in a rough collie dog the serum cholesterol-lowering effects were transient although the corneal lipidosis resolved (Jeusette, 2004).

Several low-fat veterinary therapeutic foods that have been used successfully to treat hyperlipemic dogs and cats also include increased levels of dietary fiber. The effect of fiber in low-fat foods on further reduction of serum lipids is unclear. However, responses of hyperlipemic patients to dietary intervention with low-fat, high-fiber foods have been positive, including significant decreases in serum triglycerides (Case 28-1) (Jeusette et al, 2005; Linton et al, 1994; Rogers et al, 1975). Therefore, based on the lipid-lowering effects observed clinically when commercial low-fat, high-fiber foods have been used, including knowledge of the fiber content of these foods, fiber levels of at least 10% DM are recommended for dogs and at least 7% are recommended for cats.

FEEDING PLAN

Assess and Select the Food

Long-term dietary management of dogs and cats with lipemia caused by primary hypertriglyceridemia is indicated only after secondary causes of hypertriglyceridemia have been ruled out. Food is the single most important element in managing primary hyperlipidemia, particularly in hypertriglyceridemic patients. Tables 28-3 and 28-4 list commercially available foods marketed for the management of primary hyperlipidemia for dogs and cats, respectively, and compare their key nutritional

Table 28-4. Selected commercial foods used in cats with hyperlipidemia compared to recommended levels of key nutritional factors.*

Dry foods	Energy density (kcal/cup)**	Fat (%)	Crude fiber (%)
Recommended levels	-	<12	≥7
Hill's Prescription Diet r/d Feline	263	9.3	13.6
Hill's Prescription Diet r/d with Chicken Feline	266	9.8	13.8
Purina Veterinary Diets OM Overweight Management Formula	321	8.5	5.6
Moist foods	Energy density (kcal/can)**	Fat (%)	Crude fiber (%)
Recommended levels	-	<12	≥7
Hill's Prescription Diet r/d with Liver & Chicken Feline	114 (5.5-oz. can)	9.2	15.4
Purina Veterinary Diets OM Overweight Management Formula	150 (5.5-oz. can)	14.6	10.2

*From manufacturers' published information; all values expressed on a dry matter basis unless otherwise stated.

**Energy density values are listed on an as fed basis and are useful for determining the amount to feed (the amount to feed = the daily energy requirement ÷ the energy density [kcal/cup or can]); cup = 8-oz. measuring cup. To convert to kJ, multiply kcal by 4.184.

factor content with the recommended levels of key nutritional factors (Table 28-2). The patient's current food should be compared to the foods in Tables 28-3 and 28-4 and a new food selected if the key nutritional factors in the patient's current food do not closely match the levels recommended in the tables. Selection of a new food should be made on the basis of the closest match to the recommended key nutritional factors.

The approach to treating any patient with secondary hypertriglyceridemia includes managing the underlying disease; an appropriate response to the medication should include resolution of the lipemia. Concurrent disorders may also influence the key nutritional factors and lead to other food and feeding method choices. Depending on their underlying disease, dogs and cats with secondary hyperlipidemia may benefit from foods listed in Tables 28-3 and 28-4. However, there may be other nutritional factors to consider in some diseases, for example, key nutritional factors important for patients with protein-losing nephropathy should also be considered when making food selections (Chapter 37).

Assess and Determine the Feeding Method

The method of feeding is often not altered in the nutritional management of lipid disorders. If a new food is fed, the amount to feed can be determined from the product label or other supporting materials. The food dosage may need to be changed if the fat level in the food is reduced, because the caloric density of the new food will probably differ from that of the previous food (i.e., the caloric density will usually be lower). The patient's body condition score (BCS) and body weight should be recorded before initiating dietary management because these become important parameters to monitor during reassessment. If body weight and BCS are optimal initially, the dosage of the new food should reflect the amount of energy (kcal or kJ) consumed by the animal previously.

Dogs and cats with hyperlipidemia due to diabetes mellitus may benefit from a feeding protocol that matches their insulin therapy (Chapter 29). Good compliance is necessary for effective clinical nutrition. Enabling compliance includes limiting access to other foods and knowing who feeds the animal. If the dog or cat comes from a household with multiple pets, access to other pets' food should be denied.

MEDICAL MANAGEMENT OF SECONDARY HYPERLIPIDEMIC STATES

Hyperlipidemic states associated with a primary underlying disorder (e.g., diabetes mellitus or hyperadrenocorticism) can cause clinical signs in dogs and cats indistinguishable from those caused by primary hyperlipidemic states. Accurate diagnosis and treatment of the underlying disorder should resolve the hyperlipidemia and any associated signs. However, dietary therapy as outlined above should still be implemented. Dogs and cats with clinical signs associated with persistent hyperlipidemia, whether primary or secondary, should benefit from appropriate dietary therapy (Tables 28-3 and 28-4) as long as optimal weight is maintained.

REASSESSMENT

The effect of dietary therapy on hyperlipidemic patients is best determined three to four weeks after the feeding plan is initiated. Reassessment includes reviewing the client's assessment of the patient's response, documenting body weight and condition and evaluating the extent outward manifestations (i.e., ocular or cutaneous lesions) have resolved. Laboratory assessment involves: 1) collecting a blood sample from a fasted animal (10 to 12 hours), 2) evaluating the appearance of the serum for lipemia, 3) determining the triglyceride level in unclered serum and 4) performing a chylomicron test. The veterinary health care team should assess the client's compliance with the outlined feeding plan. Feeding high-fat snacks and treats and access to other pet foods, even infrequently, can markedly increase circulating triglyceride levels in affected patients.

The goals of dietary therapy are to achieve: 1) a clear serum sample, 2) a total triglyceride concentration less than 500 mg/dL, 3) a negative chylomicron test, and, most importantly 4) amelioration or elimination of clinical signs. Amelioration or elimination of clinical signs can be expected within two weeks (dogs with pseudopancreatitis) to as long as three months (cats with cutaneous xanthomata) after initiation of appropriate dietary therapy.

Most dogs and cats with primary hyperlipidemia will experience a marked reduction in serum triglyceride and cholesterol concentrations if appropriate dietary management is employed

Box 28-2. Medical Management of Primary Hyperlipidemia.

Although dietary therapy is recommended as the initial means of managing primary hypertriglyceridemia, up to 10% of dogs with idiopathic hyperlipidemia are unresponsive to dietary fat restriction and may require pharmacologic supplementation. A variety of medical treatments for reducing lipid levels in dogs and cats have been recommended. However, the efficacy and pharmacokinetics of these treatments in animals have not been well researched. Furthermore, cost, dosage and toxicity are factors that must be considered when recommending long-term drug therapy to manage primary hyperlipidemic states.

FIBRATES

Gemfibrozil is the most commonly recommended drug to lower serum triglyceride levels in dogs and cats when dietary management fails. The drug is administered to dogs at doses ranging from 200 mg/day, orally, to 150 to 300 mg every 12 hours. The dosage of gemfibrozil for cats is 7.5 to 10 mg/kg body weight every 12 hours. Side effects in cats and dogs appear to be minimal; however, reports have suggested a long-term cancer risk associated with its use in people.

DIETARY SUPPLEMENTS

Massive doses of nicotinic acid (niacin) have also been recommended for reducing serum cholesterol concentrations in people and thereby reducing the risk of coronary artery disease. There is no known value in using nicotinic acid to manage primary hyperlipidemic states in dogs and cats.

Dietary supplementation with aged garlic extract has beneficial effects on the lipid profile and blood pressure of moderately hypercholesterolemic human patients. The effect of garlic extracts on hyperlipidemic animals has not been investigated.

STATINS

The 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors, commonly referred to as "statins," effectively reduce hepatic cholesterol synthesis and enhance excretion of LDL-cholesterol from the circulation. Because of their ability to reduce the

risk of coronary artery disease, the HMG CoA reductase inhibitors are the preferred class of drug prescribed to manage hypercholesterolemia in people. Although these drugs are generally well tolerated by dogs, the actual therapeutic advantage associated with lowering circulating levels of LDL-cholesterol is unknown. Dogs and cats normally have very low levels of LDL-cholesterol. Specific dosages for dogs and cats have not been reported.

CHOLESTEROL ABSORPTION INHIBITORS

Drugs such as ezetimibe inhibit dietary cholesterol and bile acid cholesterol uptake in the intestine and have been an effective tool for reducing serum cholesterol levels. In people, the use of statin drugs markedly reduces cholesterol production; however, there is a resultant increase in cholesterol uptake from the gastrointestinal tract. Similar compensatory mechanisms have been demonstrated in dogs. Combining statins with drugs that selectively inhibit cholesterol uptake from the digestive tract is more effective than statins alone at lowering serum cholesterol concentrations. Safety and similar synergistic effects have been shown in normal dogs. The application and dosages of these combination drugs in clinical patients have not been evaluated. Because these drugs (especially statins) can have serious side effects, their use is currently not recommended.

BILE ACID SEQUESTRANTS

The bile acid sequestrants, categorized as ion exchange resins, effectively reduce serum cholesterol concentrations through their ability to reduce enterohepatic circulation of bile salts and enhance cholesterol excretion. Cholestyramine has been recommended for dogs with persistent idiopathic hypercholesterolemia at dosages of 1 to 2 g every 12 hours. However, the associated side effects, principally gastrointestinal discomfort and diarrhea, combined with the fact that actually reducing serum cholesterol levels may not resolve clinical signs, limits the clinical value of these drugs.

The Bibliography for **Box 28-2** can be found at www.markmorris.org.

and rigorously followed. A reasonably acceptable goal is slight serum turbidity, a triglyceride concentration less than 1,000 mg/dl and an incomplete cream layer at the top of the sample.

Unless weight loss is desired, the patient's body weight and BCS should be the same as it was before the feeding plan was initiated.

For reasons currently unknown, some patients remain profoundly hyperlipidemic despite excellent owner compliance in feeding an appropriate food. However, these animals should continue to receive the appropriate low-fat food; human table food should not be fed. The patient should be reassessed in one to two months. If a demonstrable reduction in fasting serum triglyceride concentrations still hasn't occurred, drug therapy should be added to the dietary therapy. Drug therapy for patients with primary hypertriglyceridemia has included clofibrate, niacin, gemfibrozil and dietary supplementation with omega-3 fatty acids from fish oils (**Box 28-2**) (Logas et al, 1991; Levy, 1988; Schaefer, 1988; Watson, 1996).

Patients that lose a significant amount of weight (more than 1% of body weight per week) should receive gradually increasing amounts of the recommended food until desired weight can be maintained. In these cases, caloric intake may be inadequate.

ENDNOTE

a. Ford RB. Unpublished observation. April 1994.

REFERENCES

The references for **Chapter 28** can be found at www.markmorris.org.

CASE 28-1**Episodic Diarrhea in a Mixed-Breed Dog**

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Patient Assessment

A seven-year-old, female, mixed-breed dog was initially examined for a four-month history of episodic diarrhea accompanied by lethargy and a decreased appetite. The owner reported that the frequency of the episodes had gradually increased to once weekly over the last two months. Clinical signs would spontaneously resolve within 24 to 48 hours.

The initial physical examination revealed an active, alert dog. Abdominal palpation was unremarkable and well tolerated. The dog weighed 11.8 kg and appeared thin (body condition score 2/5) although the owner had not reported weight loss.

A presumptive diagnosis of dietary intolerance was made and empiric treatment with a veterinary therapeutic food for management of gastrointestinal (GI) disease was initiated. Ten days later the dog was examined for significant lethargy and abdominal discomfort. The owner indicated that the dog had eaten nothing during the past 24 hours but did drink water. Soft feces were noted occasionally. Abdominal palpation was associated with discomfort; however, the source of the abdominal pain could not be localized.

Results of an abdominal radiograph, urinalysis and fecal flotation for intestinal parasites were normal. Blood collected for analysis was profoundly lipemic and moderately hemolyzed. Test results were obtained from a commercial laboratory on the following day. Results of a complete blood count were normal. Abnormal serum biochemistry profile results included hypocalcemia (8.5 mg/dl, normal 9.2 to 11.2). Serum cholesterol (278 mg/dl) and triglyceride (96 mg/dl) concentrations were normal.

Assess the Food and Feeding Method

The dog was normally fed a combination of dry and moist commercial grocery store brand foods with occasional snacks. The food was offered once daily. The dog's diet had been consistent for several years until the change 10 days ago to a moist veterinary therapeutic food (Prescription Diet i/d Canine^a) designed for the management of GI disorders.

Questions

1. Why is the serum triglyceride concentration normal in a patient with lipemia?
2. What is the tentative diagnosis in this patient?
3. What is an appropriate feeding plan (food and feeding method) for this dog?

Answers and Discussion

1. In an attempt to avoid lipid interference with other biochemical assays, many commercial laboratories will use ultracentrifugation to clear chylomicrons before performing any tests on a lipemic serum sample. This process removes excess triglycerides before testing. Thus, the triglyceride concentration reported by the laboratory may be normal. Simply observing a lipemic sample in a fasted (six to 12 hours) animal is sufficient clinical evidence to document hypertriglyceridemia. The low serum calcium concentration was probably an artifact due to interference from the lipemia.
2. The predominant cause of hyperlipidemia in dogs is excess concentrations of triglyceride-rich chylomicrons. Thus, canine hyperchylomicronemia (hypertriglyceridemia) is the most likely diagnosis, after the clinician has observed the serum sample and confirmed the presence of lipemia (i.e., a cream layer denoting hyperchylomicronemia) or measured triglyceride levels (i.e., levels exceeding 500 mg/dl). Fasting lipemia can be a significant clinical problem associated with episodic diarrhea, inappetence, abdominal discomfort and occasional vomiting. The collective term to describe this syndrome is "pseudopancreatitis." The rapid worsening of clinical signs justifies expanding the differential diagnosis to include pancreatitis, hypoadrenocorticism, neoplasia and primary intestinal disease (e.g., inflammatory bowel disease, etc.). Additional endocrine testing may be indicated to rule out secondary causes of hyperlipidemia.
3. For any patient with fasting hyperlipidemia, regardless of the cause, food with a fat content less than 12% dry matter is recommended. Foods designed for empiric management of GI disorders often have a fat content that exceeds this recommendation. Multiple small meals rather than one large meal per day may be helpful in patients with GI signs.

Progress Notes

After fasting hypertriglyceridemia (hyperchylomicronemia) was confirmed, the initial treatment prescribed was limited to dietary intervention with low-fat, high-fiber food. Prescription Diet w/d Canine^a dry was recommended because of its palatability, low-fat content (approximately 9.0% dry matter [DM]) and high-fiber level (17.6% DM). The owner was advised that: 1) dietary manage-

ment is the most reasonable, economical means of controlling this potentially serious condition, 2) dietary fat restriction would be a life-long requirement, if treatment were successful and 3) even a single high-fat meal (e.g., eating from the trash) could acutely exacerbate clinical signs and cause pancreatitis.

The patient was reexamined after consuming the veterinary therapeutic food for three weeks to assess dietary compliance and serum triglyceride levels. A fasting (overnight) blood sample was collected. The serum triglyceride (uncleared) concentration was determined and compared to that obtained during the initial examination (Table 1).

Results suggested excellent dietary control of the hyperlipidemic state and good dietary compliance. Specific drug intervention was deemed unnecessary at the time the patient was rechecked. However, the owner was advised that although the risk of serious illness (pancreatitis) had been markedly reduced, follow-up examinations twice yearly, including fasting triglyceride measurements, would be a prudent course to follow.

Endnote

a. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

Bibliography

Ford RB. Canine hyperlipidemia. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine, 4th ed. Philadelphia, PA: WB Saunders Co, 1995; 1414-1419.

Table 1. Serum triglyceride levels before and after three weeks of treatment with a low-fat, high-fiber veterinary therapeutic food.*

Initial level	2,350 mg/dl**
Three-week level	477 mg/dl**

*Prescription Diet w/d Canine. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

**Uncleared specimen.