Hyperlipidemia

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Background

Hyperlipidemia is caused by increased plasma triglycerides, cholesterol, or both and is a normal postprandial finding; within 0.5 to 2 hours of consuming dietary fat, chylomicrons appear and remain in the blood for 6 to 10 hours. In a fasted (>12 hours) sample, hyperlipidemia is caused by a disturbance in the metabolism of the lipoprotein responsible for carrying hydrophobic fat to and from tissue (eg, intestine, muscle, adipose, liver).[1] Therefore, *hyperlipoproteinemia* has been used interchangeably with *hyperlipidemia* when an abnormally high plasma lipoprotein is identified.

Increased fasted lipoprotein blood levels are associated with either an overproduction or decreased removal of the specific lipoprotein and the type of fat it carries. High blood concentrations of chylomicrons and very-low-density lipoprotein (VLDL) will appear as high plasma triglyceride levels, whereas high concentrations of high-density lipoprotein (HDL) and/or low-density lipoprotein (LDL) raise plasma cholesterol levels. Hypertriglyceridemia is more clinically relevant than hypercholesterolemia.

Primary lipoprotein metabolism disorders are relatively uncommon and associated with specific breeds (eg, miniature schnauzer, Shetland sheepdog, briard, rough collie, Doberman, rottweiler).[2] Secondary hypertriglyceridemia is clinically more common and caused by several primary disorders. Endocrine disease (eg, diabetes mellitus [DM], hypothyroidism, hyperadrenocorticism), pancreatitis, obesity, protein-losing nephropathy (PLN), and cholestasis are known to cause or be associated with secondary hypertriglyceridemia.[2]

How I Treat Hyperlipidemia

- ❑ Treat hypertriglyceridemia (>500 mg/dL) present in a 12- to 18-hour fasted sample.
- ❑ Feed a low-fat (≤30 g/Mcal*) diet with reevaluation in 6–8 weeks.
- ❑ Consider individual diet history.
- ❑ Consider concurrent diseases.
- ❑ Consider supplementing with fish oil containing EPA and DHA.
- ❑ Consider other possible treatments for lowering VLDLs.

Clinical Signs

Common, mild presentations of hypertriglyceridemia include intermittent episodes of vomiting, diarrhea, and abdominal pain or discomfort. The more severe presentations are pancreatitis (as a secondary or primary disorder), lipemia retinalis, cutaneous xanthomas, seizures, peripheral nerve paralysis (eg, tibial, radial, Horner syndrome), and behavioral changes. Less common presentations include splenomegaly, lipid keratopathy, anemia, and xanthelasma. Signs of DM, hypothyroidism, hyperadrenocorticism, pancreatitis, obesity, PLN, and/or cholestasis are also likely.

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DHA = docosahexaenoic acid, DM = diabetes mellitus, EPA = eicosapentaenoic acid, HDL = high-density lipoprotein, LDL = low-density lipoprotein, PLN = protein-losing nephropathy, VLDL = very-low-density lipoprotein

*1 Mcal (megacalorie) = 1000 kcal

How I Diagnose Hyperlipidemia

12- to 18-hour fasted lipemic serum sample is suggestive of hypertriglyceridemia.[2]

- Clear serum contains <200 mg/dL (2.26 mmol/L).
- Turbid serum begins at 200–300 mg/dL (2.26–3.39 mmol/L).
- Lactescent (milk-like) serum indicates ~1000 mg/dL (11.3 mmol/L).
- Hypercholesterolemia does not cause an increase in serum turbidity because LDL and HDL do not refract light.

Refrigerate sample for 12 hours to determine if the hypertriglyceridemia was caused by chylomicrons or VLDL.

- Chylomicrons float to the top (ie, as a creamy layer).
- VLDL results in a uniformly turbid sample.
- A creamy layer over a cloudy serum layer indicates both are present.

Perform a heparin release test to assess activity level of lipoprotein lipase.

- A defect in endothelium lipoprotein lipase is suspected if there is no difference in the pre- and postheparin sample triglyceride concentration (heparin releases lipoprotein lipase and stimulates triglyceride hydrolysis).[1]

Consider lipoprotein electrophoresis and ultracentrifugation to identify and quantify the lipoproteins, respectively.

- These are not routine.
- Normal ranges are not well defined.

How I Treat Hyperlipidemia

Treat hypertriglyceridemia (>500 mg/dL) present in a 12- to 18-hour fasted sample.

- Secondary hypertriglyceridemia typically improves with correction of the primary metabolic disorder (eg, pancreatitis, DM, PLN).
- Maintain a fasted triglyceride level of <400 mg/dL to minimize signs and complications.

Feed a low-fat (≤30 g/Mcal) diet; reevaluate in 6–8 weeks.

- Fat content of low-fat diets expressed as a percentage of dry matter may not coincide with grams of fat/Mcal.
- Compare products on a caloric basis (**Tables 1** and **2**).

Consider individual diet history in diet selection.

- If the patient currently eats a high-fat diet, recommend 20–30 g/Mcal diet initially.
- If the patient is already on a fat-restricted diet (≤30 g/Mcal), recommend changing to an ultra-low-fat diet (<10 g/Mcal) formulated by a nutritionist.

Consider concurrent diseases.

- For diabetic dogs and overweight diabetic cats, consider low-fat/high-fiber therapeutic diets.
- For hyperlipidemic, underweight diabetics and PLN cases, commercial diet options are limited but highly specialized diets can be tailored by a nutritionist.

Consider supplementing with fish oil containing EPA and DHA, as hypertriglyceridemia caused by disturbances in the metabolism of endogenous VLDL lipoproteins may not fully respond to a low-fat diet.

- For dogs, the recommended omega-3 dose (70–100 mg/kg body weight) may be increased as needed up to the National Research Council safe upper limit (200 mg/kg body weight); no safe upper limit has been determined for cats.[3]
- Pet foods may include omega-3 fatty acids; however, those using flaxseed meal or oil contain only ALA, and ALA–EPA conversion in dogs and cats is thought to be low (<10%).

MORE ▶

ALA = alphalinolenic acid, DHA = docosahexaenoic acid, DM = diabetes mellitus, DMB = dry matter basis, EPA = eicosapentaenoic acid, PLN = protein-losing nephropathy, VLDL = very-low-density lipoprotein

Table 1 Canine Foods by Fat*

Product	*Fat g/Mcal*	*Fat % DMB*
Rayne Clinical Nutrition Low Fat Kangaroo (wet)	18.4	6.1
Royal Canin Veterinary Diet GI Low Fat (canned)	19	6.5
Hill's Pet Nutrition i/d Low Fat (dry)	20	7.4
Royal Canin Veterinary Diet GI Low Fat (dry)	20.1	7.1
Iam's Weight Loss Mobility Plus (dry)	22.6	8.3
Hill's Pet Nutrition i/d Low Fat (canned)	23	8.5
Purina Veterinary Diets OM Overweight Management (dry)	24	7.2
Hill's Pet Nutrition r/d (dry)	25	8.2
Hill's Pet Nutrition w/d (dry)	26	8.7
Purina Veterinary Diets HA (dry)	26	10.5
Hill's Pet Nutrition r/d (canned)	29	8.6
Purina Veterinary Diets EN (dry)	30	12.4
Purina Veterinary Diets OM Overweight Management (canned)	34	10.5
Hill's Pet Nutrition w/d (canned)	36	12.7
Iam's Weight Loss Mobility Plus (canned)	38.1	16.09
Rayne Clinical Nutrition Moderate Protein Cod (wet)	42.6	17.05
Purina Veterinary Diets EN (canned)	41.3	17.8

*Sorted based on fat-per-calorie basis

Table 2 Feline Foods by Fat*

Product	*Fat g/Mcal*	*Fat % DMB*
Iam's Weight Loss Mobility Plus (canned)	24.8	16.3
Purina Veterinary Diets OM Overweight Management (dry)	25	8.5
Hill's Pet Nutrition r/d (dry)	26	8.7
Rayne Clinical Nutrition Low Fat Kangaroo (wet)	26.5	8.9
Hill's Pet Nutrition w/d (dry)	27	9.1
Iam's Weight Loss Mobility Plus (dry)	28.2	10.4
Royal Canin Veterinary Diet Calorie Control (dry)	29.5	10.6
Hill's Pet Nutrition r/d (canned)	30	9.2
Royal Canin Veterinary Satiety Support (dry)	30.6	9.5
Royal Canin Veterinary Diet Calorie Control (3 oz canned)	31.3	11.2
Royal Canin Veterinary Diet GI Moderate Calorie (dry)	37.4	13.8
Royal Canin Veterinary Diet Calorie Control (5.8 oz canned)	37.5	13.7
Purina Veterinary Diets OM Overweight Management (canned)	38	13.1
Royal Canin Veterinary Diet GI Moderate Calorie (canned)	39.4	15.1
Royal Canin Veterinary Diet GI Fiber Response HF	40.7	15.9
Rayne Clinical Nutrition Cod and Sweet Potato (wet)	43	17.1
Hill's Pet Nutrition w/d (canned)	48	16.6

*Sorted based on fat-per-calorie basis

- Pet foods containing fish oil contain EPA and DHA but typically at low levels.
  - Supplementing with concentrated fish oil containing EPA and DHA is necessary for therapy.

Consider other possible treatments for lowering VLDLs.

- Consider niacin (dogs, 100 mg PO q24h) and gemfibrozil (dogs, 7.5 mg/kg body weight PO q12h; cats, 10 mg/kg body weight PO q12h).[1]
  - Both have adverse effects and should be considered only when diet cannot maintain serum triglyceride <500 mg/dL.

The Take-Home

- Hyperlipidemia is common in blood sampled within 12 hours of a meal.
- Hypertriglyceridemia is more clinically common than hypercholesterolemia.
- Hypertriglyceridemia is caused by disturbances in the metabolism of the chylomicron and/or VLDL lipoprotein.
- The disturbance in chylomicron and/or VLDL lipoprotein metabolism is more likely secondary to another ongoing disease process rather than a primary disorder, except in certain breeds.
- Clinical signs can be intermittent and not specific to hyperlipidemia.
- More severe presentations are more likely to be associated with well-described diseases (eg, endocrine disorders, pancreatitis, obesity, PLN, cholestasis).
- Feeding a low-fat diet (≤20–30 g/Mcal) for 6–8 weeks is the first line of treatment with a fasted serum triglyceride goal <400 mg/dL.
- Homemade diets with ultra-low-fat content (<10 g/Mcal) can be formulated on an individual basis by a nutritionist.
- Supplementing with fatty acids (70–100 mg/kg) may be needed in cases of hyper-VLDL production. ■ cb

See **Aids & Resources**, back page, for references & suggested reading.

DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, PLN = protein-losing nephropathy, VLDL = very-low-density lipoprotein