METROPOLITAN VETERINARY ASSOCIATES
NEWSLETTER
VOLUME 12 ISSUE 1 • 2022 SPRING EDITION

THE ELEPHANT IN THE ROOM: HYPERLIPIDEMIA IN DOGS

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Why care about hyperlipidemia?

In our increasingly busy lives as clinicians, one could be easily forgiven for ignoring a high cholesterol or triglyceride value on an otherwise picture perfect chemistry profile. It is even easier to fall into the habit of not even including these values when selecting your chemistry profile. While hyperlipidemia might seem easy to pass off as unimportant, it is closely linked to far-from-obscure conditions that most veterinarians would agree are tremendously important to our patients. Think pancreatitis, biliary mucocele and protein-losing nephropathy just to name a few.

Understanding the lingo

Hyperlipidemia is defined as the increased concentration of lipids in the blood, whether that includes triglycerides (hypertriglyceridemia), cholesterol (hypercholesterolemia) or a combination of both. Lipemia refers to the presence of grossly turbid or lactescent serum or plasma samples. Lipemia only occurs during hypertriglyceridemia (but not hypercholesterolemia), and a lipemic blood sample can be a useful tip-off that a patient has at least moderately elevated triglycerides (>200-300mg/dL). On the other hand, a patient may have completely clear or only slightly hazy-appearing serum, and be experiencing severe hypercholesterolemia.

See Table 1 (Page 2). Severity categorizations of hypertriglyceridemia and hypercholesterolemia.

Measuring lipids

The first step in detecting hyperlipidemia is making sure to select a chemistry panel that includes cholesterol and/or triglyceride levels. While cholesterol is common in many in-house and send-out chemistry bundles, measurement of triglycerides often requires a more intentional decision. Triglycerides can be added on as a standalone test or included in a variety of different reference lab chemistry bundles (eg. Antech Superchem or IDEXX Total Health with Triglycerides). This is an added expense to owners and might not be indicated in young or healthy patients, so measurement of triglycerides should be prioritized for i) patients whose serum samples are grossly lipemic, ii) in breeds associated with familial hyperlipidemias (eg. Miniature Schnauzers), or iii) where documentation of hyperlipidemia will strengthen clinical suspicion of a related secondary condition (eg. hypothyroidism, protein-losing nephropathy, or cholestasis). Because postprandial hyperlipidemia is so common in dogs, serum samples should ideally be collected on patients after an overnight fast (12-15 hours). If hyperlipidemia is documented on a non-fasted sample, triglycerides and cholesterol testing should be repeated on a fasted sample before further specific diagnostics and treatments are recommended.

Dr. Alexaner Saver

TABLE 1

	Triglycerides	Cholesterol
Mild	150 - 399 mg/dL	300 - 499 mg/dL
Moderate	400 - 999 mg/dL	500 - 749 mg/dL
Severe	≥1000 mg/dL	≥750 mg/dL

Diagnostic workup

Once post-prandial hyperlipidemia is ruled out, the diagnostic focus shifts to identifying a secondary cause of hyperlipidemia. A primary cause is presumed if no secondary causes are apparent after diagnostic workup, and the patient's breed has been associated with a familial hyperlipidemia. The poster-child breed for primary hyperlipidemia is the Miniature Schnauzer, which have been found to be affected by extremely high rates of fasting hypertriglyceridemia (33-56%).

The breadth and components of each individual patient's diagnostic workup will be heavily dependent on signalment, history (including medication history), clinical signs and other localizing abnormalities on minimum database laboratory testing. For example, a middle-aged Miniature Schnauzer that has incidental severe hypertriglyceridemia may do well with a limited diagnostic workup, compared to an elderly Shetland Sheepdog with polyuria-polydipsia, proteinuria and a mixed hepatopathy. Common diagnostic tests that should be considered include pancreatitis testing, hyperadrenocorticism testing, hypothyroidism testing, proteinuria quantification & workup, paired bile acids, and abdominal ultrasound.

See Table 2 (Page 3). Canine hyperlipidemia etiologies with commonly observed lipid derangements.

Treatment goals

There are no universally accepted cut-offs for when to start treatment for hypertriglyceridemia or hypercholesterolemia. A pragmatic approach would be to monitor borderline and mild cases and pursue specific treatments in patients with moderate-to-severe hyperlipidemia. This is based on the idea that with increasing hyperlipidemia, the risk of deleterious metabolic effects (eg. pancreatitis, hepatopathy or insulin resistance) presumedly increases. When treatment is instituted, the ultimate treatment goal should be to maximize lipid reduction and minimize the adverse effects, invasiveness, and cost of therapy. In practical terms, this means targeting a reduction in lipids to within or just above (triglycerides < 400 mg/dL or cholesterol < 500 mg/dL) reference interval. Nonetheless, dogs with mild hyperlipidemia should not be ignored. Even when hyperlipidemia is mild, investigation and treatment for underlying secondary diseases may prevent important complications. A classic example of this is the diagnosis of hypothyroidism and early biliary mucocele due to a subtle tip off (mild hypocholesterolemia) on routine screening bloodwork. Early diagnosis

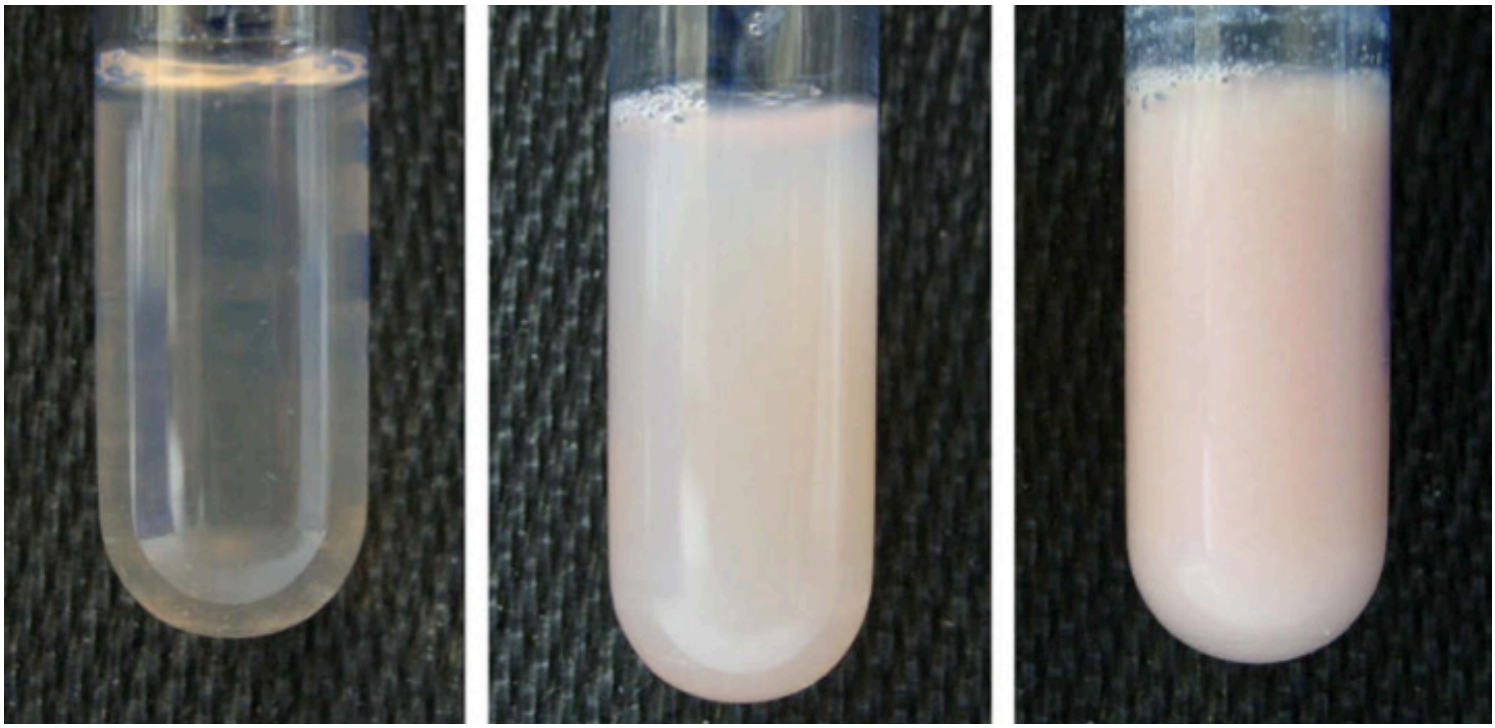

Figure 1: Canine serum samples that show clear serum (left tube), turbid serum (middle tube), lactescent serum (right tube). Source: J Small Anim Pract. 2015;56(10):595–605.

TABLE 2

	Hypertriglyceridemia	Hypercholesterolemia
Primary		
Miniature Schnauzer	X	
Shetland Sheepdog		X
Beagle	X	
Secondary		
Pancreatitis	X	X
Protein-losing nephropathy		X
Hyperadrenocorticism	X	X
Hypothyroidism	X	X
Diabetes mellitus	X	
Obesity	X	X
Hepatic insufficiency	X	X
Cholestasis	X	X
Glucocorticoid administration	X	X
Phenobarbital administration	X	

TABLE 3

	Dose	Potential Adverse Effects	Comment
Fenofibrate (TriCor®)	6-10 mg/kg PO Q24H	Gastrointestinal upset, hepatotoxicity, myotoxicity, cholelithiasis, & rhinitis	Recommended first line fibrate in dogs based on canine-specific safety & efficacy data, and wide availability in the US
Bezafibrate	4-10 mg/kg PO Q24H	Gastrointestinal upset, hepatotoxicity, myotoxicity, cholelithiasis, & rash	No FDA-approved formulation – compounding required
Gemfibrozil (Lopid®)	10 mg/kg PO Q12H	Gastrointestinal upset, hepatotoxicity, myotoxicity, cholelithiasis, rash & bone marrow suppression	Not recommended due to lack of canine safety & efficacy data, and increased rate of adverse effects in humans

and medical management of these conditions in this specific patient may in turn prevent the need for them to undergo invasive gallbladder surgery.

Treatment options

Ultra-low-fat diet

A traditional first-line treatment for hyperlipidemia in dogs has been dietary fat restriction by use of prescription ultra-fat restricted diets. This is a safe, inexpensive method of treatment with the main benefit being that no specific monitoring for adverse effects is required. Improvement in hyperlipidemia is typically expected within a month of diet change. A target fat content of < 2.5g per 100 kcal consumed should be used. Appropriate commercial diets include Hills i/d Low Fat®, Royal Canin Gastrointestinal Low Fat®, & Purina EN Low Fat®). Purina HA Vegetarian® (but not salmon or chicken formulations) has a slightly higher fat content (2.7g per 100kcal), but is a suitable alternative for dogs with dietary intolerance. Owners should also be instructed to feed low-fat treats or fruit and vegetable- based treats (eg. blueberries, apple slices or baby carrots).

Omega-3 fatty acids

Omega-3 fatty acids are another commonly used method of lowering lipids, specifically triglycerides. Benefit in veterinary medicine has only been demonstrated in healthy research dogs, so fatty acid supplementation is usually recommended in conjunction with dietary fat restriction. A daily dose of 200-300mg /kg/day (up to 4000-5000mg/dog/day), inclusive of both eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is recommended. Owners should be prepared for their dogs to develop a malodorous, fishy breath and, less commonly, diarrhea.

Fibrates

Fibrates have been widely prescribed in humans since the 1970s but are an emerging class of therapeutics for hyperlipidemia in dogs. These medications work by altering lipid metabolism (via a class of intracellular receptors known as peroxisome proliferator-activated receptors or PPARs). They have been shown in humans to lower triglyceride levels and very low-density lipoproteins (VLDLs) or “bad” cholesterol, while increasing high-density lipoproteins (HDLs) or “good” cholesterol. The most widely prescribed fibrates in humans include bezafibrate, fenofibrate and gemfibrozil.

In the veterinary sphere, there have been a handful of very promising studies involving the use of bezafibrate or fenofibrate in dogs with hyperlipidemia. These studies have demonstrated that fibrates reliably normalize serum triglycerides in a majority of dogs (86-100%) with a more variable effect on serum cholesterol (54%). These effects have also been shown to hold true in dogs with both primary and secondary hyperlipidemia. In one study, the use of fenofibrate was shown to be even more effective than diet in normalizing serum triglycerides. It is likely that this class of medications will soon be an integral part in managing hyperlipidemia in dogs either as sole therapy or, more likely, as an adjunct to dietary modification and secondary disease treatment.

Fenofibrate (TriCor®) is the recommended first-line fibrate of choice in dogs, given that there are no FDA-approved human formulations of bezafibrate in the United States. Bioavailability is formulation-specific, so a micronized, nanocrystal formulation (eg. TriCor®) should be preferentially selected over a generic formulation. Administration should be with food to further improve bioavailability. Owners should be educated on the potential risks documented in humans (eg. hepatotoxicity &

myotoxicity), however no significant adverse effects have occurred in the relatively sizable canine studies. Interestingly, liver enzyme activity has actually been shown to decrease in both fenofibrate (ALKP) and bezafibrate (ALT), presumedly due to improvement in hepatic lipidosis. Regardless of these reassuring findings, rare or idiosyncratic reactions are possible with all drugs. Patients should therefore undergo a fasted complete blood count & chemistry profile (including triglyceride, cholesterol, ALT, ALKP, GGT, TBili, Crea, BUN and CK levels) prior to starting a fibrate, at 3-4 weeks (for safety), and then again at 6-8 weeks (for efficacy). Dogs that are tolerating their dose but have persistent hyperlipidemia at 6 weeks can be considered for a dose increase. Dogs that develop suspicious clinical signs or new bloodwork abnormalities should have their dose reduced or discontinued.

Dogs with kidney disease should be dosed very conservatively and monitored more closely as fibrates are primarily excreted in the urine. Meanwhile, use of fibrates in dogs with documented hepatic dysfunction and biliary disease disease (especially documented cholelithiasis) should be avoided.

See Table 3 (See Page 4). Fibrate medications options for canine hyperlipidemia. Note: Provided information is based on a combination of anecdotal, human-based medical evidence & veterinary evidence.

Statins

While a staple treatment for hypercholesterolemia in humans, statins are not suitable for hypertriglyceridemia in dogs. Statins used in combination with fibrates have also been shown to increase risk of myotoxicity in humans.

Niacin (Vitamin B3)

Niacin has been used in treatment of hypertriglyceridemia in humans for many years, however limited safety and efficacy data exists for dogs. Niacin can be considered as an alternative to fibrates in dogs that experience adverse effects to a fibrate medication. Dosing is performed at 50-200mg/dog/day with dose escalation every 4 weeks, as needed. Side effects in humans include skin reaction, myotoxicity, hepatotoxicity and hyperglycemia.

Chitosan

Chitosan is a polysaccharide derived from the exoskeletons of small crustaceans. It is used anecdotally to absorb fat from ingesta within the gastrointestinal tract. There are no studies evaluating the safety or efficacy of chitosan in dogs outside of experimental models.

References

1. De Marco V, Noronha KSM, Casado TC, Nakandakare ER, Florio JC, Santos EZ, Gilor C. Therapy of Canine Hyperlipidemia with Bezafibrate. J Vet Intern Med. 2017;31(3):717–22.
2. Miceli DD, Vidal VP, Blatter MFC, Pignataro OP, Castillo VA. Fenofibrate treatment for severe hypertriglyceridemia in dogs. Domest Anim Endocrinol. 2021;74.
3. Munro MJL, Hulsebosch SE, Marks SL, Gilor C. Efficacy of a micronized, nanocrystal fenofibrate formulation in treatment of hyperlipidemia in dogs. J Vet Intern Med. 2021;35(4):1733–42.
4. Xenoulis PG, Steiner JM. Canine hyperlipidaemia. J Small Anim Pract. 2015;56(10):595–605.
5. Xenoulis PG, Cammarata PJ, Walzem RL, Suchodolski JS, Steiner JM. Serum triglyceride and cholesterol concentrations and lipoprotein profiles in dogs with naturally occurring pancreatitis and healthy control dogs. J Vet Intern Med. 2020;34(2):644–52.

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WELCOME MEGAN VAN EEDEN, DVM, DACVIM (SAIM) TO OUR INTERNAL MEDICINE TEAM!

Dr. van Eeden graduated from Cornell University with her BS in Animal Science (Minor in Business), following graduation she obtained her veterinary degree from Western University of Health Sciences in California. She completed a small animal rotating internship at VCA Aurora, followed by a specialty Internal Medicine internship in California. She then went on to complete her Internal Medicine residency at the University of Missouri, which she completed in July 2019. She enjoyed time at a private practice clinic in Charleston, SC prior to joining the MVA team in March of 2022. Dr. van Eeden enjoys the variety of cases that internal medicine brings though she has a special interest in respiratory medicine and immune-mediated diseases.

Outside of the hospital, Dr. van Eeden enjoys spending time outside, running, horseback riding, exploring new areas, and most of all spending time with her family (husband and a baby girl), and animals (three amazing horses, two exceptional dogs and one opinionated cat).

WELCOME BETH OVERLEY-ADAMSON, VMD, DACVIM (ONCOLOGY) TO OUR ONCOLOGY TEAM!

Dr. Beth Overley-Adamson is a board-certified oncologist and Diplomate of the American College of Veterinary Internal Specialists. She graduated from the School of Veterinary Medicine of the University of Pennsylvania in 2000 and completed a one-year general internship, three-year oncology residency, and a two-year oncology lectureship at the University of Pennsylvania as well. She stayed and continued to teach, treat patients, and perform cancer research until the end of 2007. In 2008, she joined the Center for Animal and Emergency Specialists (CARES) in Langhorne, PA. There, she helped create The Cancer Center at CARES. She stayed on until March 2022, when she decided to join the team at the Cancer Center at Metropolitan Veterinary Associates.

Dr. Overley-Adamson is thrilled to be a part of a skilled and compassionate group of professionals that provide our patients with the best possible cancer treatment and care. Outside of MVA, Dr. Overley-Adamson enjoys hiking, playing racquet sports, and spending time with her family, which includes a rescued parrot named Bob and a Border Terrier named Louie.