

Help!
My Dog was
Diagnosed
with a
Liver Problem!

*Understanding Common Liver
Disorders in Yorkshire Terriers
and Other Breeds.*

DR. KAREN TOBIAS

Brief Overview of Portosystemic Shunts

What is a liver shunt?

A liver shunt is a blood vessel that carries blood around the liver instead of through it. In some animals a liver shunt is a birth defect (“congenital portosystemic shunt”). In others, multiple small shunts (“acquired portosystemic shunts”) form because of severe liver disease such as cirrhosis.

“Congenital PSS and MVD are related genetic disorders causing malformation of the liver circulation.”

—Center

Why do animals with shunts have problems?

In the normal animal, food and other ingested materials are broken down or digested in the intestines and absorbed into the portal blood stream, where they are carried to the liver. The liver stores some of the food for energy, processes some of it into safe chemicals, and uses some of it to make proteins and other substances. Because the blood bypasses the liver in dogs with shunts, toxins may build up in the bloodstream or kidneys. Additionally, the animal lacks the necessary materials to give it a ready source of energy and to help it grow.



What are the most common types of portosystemic shunts (PSS)?

There are a number of types of portosystemic shunts. Those present at birth are classified as “congenital.”

1. Single extrahepatic shunt: a single shunting vessel that is located outside the liver. This is the most common type of congenital shunt.
2. Single intrahepatic shunt: a single shunting vessel within the liver. These are congenital and most commonly seen in large-breed dogs.
3. Extrahepatic multiple acquired shunts: When blood pressure in the portal system becomes too high (portal hypertension), multiple small blood vessels will open up to shunt blood around the liver. Multiple acquired shunts occur as a result of end stage liver disease (cirrhosis) and portal hypertension. These are not congenital and they are not surgically correctable.



Microvascular Dysplasia & Congenital Portal Vein Hypoplasia

What is microvascular dysplasia?

Microvascular dysplasia (MVD) is a pathologic change in which the microscopic portal vessels of the liver are underdeveloped (“hypoplastic”); if severe, the associated liver tissue also appears shrunken or “atrophied”. These pathologic changes occur in animals that have congenital shunts. They are also seen in dogs with multiple acquired shunts that have cirrhosis or other causes of portal hypertension, which is known as non-cirrhotic portal hypertension. More often, however, MVD occurs in dogs that have no shunts, no portal hypertension, and often no clinical signs of illness.

“PVH-MVD... when severe, can cause clinical signs and blood work changes similar to PSS, though usually to a lesser extent.”

—Tobias

In those animals, the underlying condition is called congenital portal vein hypoplasia (PVH). Because this is the most common cause of MVD, many clinicians use the terms interchangeably. Unfortunately, PVH-MVD occurs in the same breeds that are commonly affected with congenital extrahepatic PSS (Maltese, Yorkies, Cairn terriers, etc.) and, when severe, can cause clinical signs and blood work changes similar to congenital PSS. PVH-MVD is congenital and is not surgically treatable.

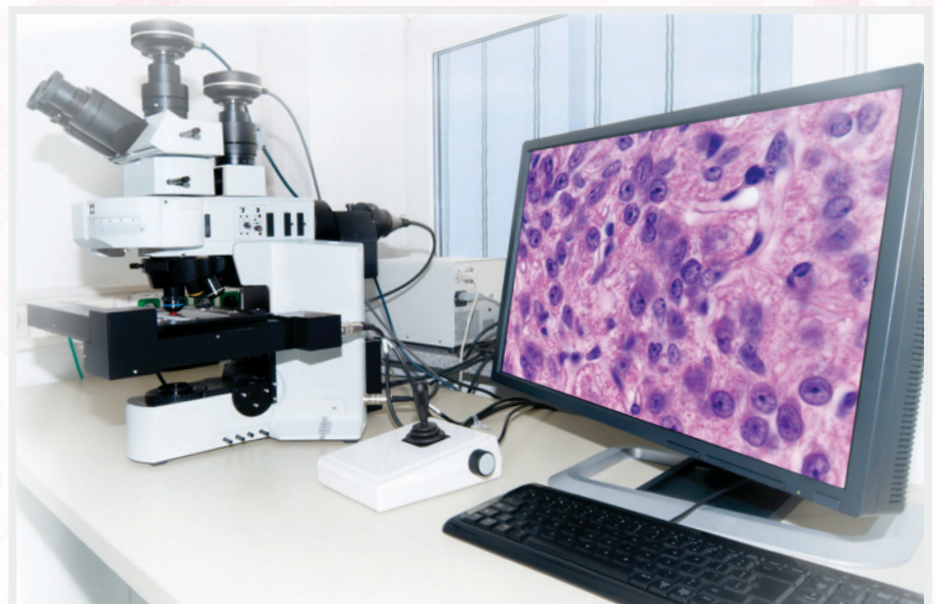
Clearing up the confusion

Reading about congenital portal vein hypoplasia in scientific literature and on the internet can become confusing because this condition is known by several names, including “microvascular dysplasia” (MVD) and “hepatportal microvascular dysplasia” (HMD). Because pathologists use the terms MVD or HMD to describe the same changes seen on liver biopsy for

several conditions (including congenital portosystemic shunts), the World Small Animal Veterinary Association standardized the name to “primary congenital portal vein hypoplasia.” (Cullen 2009). Here we’ll use the term PVH-MVD to make sure everyone understands which condition is being discussed.

Understanding liver function

To understand the clinical problems associated with shunts and PVH-MVD, we first need to understand how the liver works. The liver performs an incredible number of functions to maintain health of animals, including filtering out toxins, manufacturing or storing sugar for energy, processing drugs and other chemicals, and making proteins. Most of the blood that is carried to the liver for these processes arrives via the portal vein, which drains the intestines, stomach, pancreas, and spleen. Within the liver, the portal vein branches into smaller and smaller vessels so that the blood can percolate throughout the tissues to the individual liver cells where all the work is performed. When portal blood is diverted around the liver or the microscopic vessels within the liver are underdeveloped or absent, the liver can no longer perform its normal functions efficiently. Clinical signs therefore result because the animal cannot clear out toxins or process drugs, lacks the building blocks for growth and repair, and develops side effects from excretion of excess ammonia into the urine.



Clinical Signs & Diagnosis

Clinical signs of dogs with congenital portosystemic shunts (PSS)

Animals with congenital PSS often present at a young age, unless blood flow through the shunt is small or intermittent. Dogs with congenital PSS are often small in size and have poor muscle mass and hair coats; breeders may note they are the “runts” of the litter. Most commonly these dogs have behavior changes such as weakness, a quiet demeanor, or dull attitude. Occasionally neurologic signs can be more severe, particularly if blood sugar is low or if excessive amounts of protein are consumed. In those instances, the dogs may pace, circle, act blind, press their heads against the wall, or even have seizures. Because the liver is no longer efficiently processing ammonia from proteins, large amounts of the toxin are excreted into the kidneys and bladder where the ammonia can concentrate into spikey crystals (ammonium biurate crystals) or condense into stones (urate stones) that are not visible on plain x-rays. Both crystals and stones will result in urinary tract inflammation and infection. Dogs with congenital PSS may also urinate more frequently, and therefore drink more, because they lose the ability to concentrate their urine. Occasionally dogs will be nauseous, causing poor appetite, vomiting, or excessive salivation. Some dogs may even develop stomach ulcers. Neurologic and gastrointestinal signs can vary from day to day. (Figure 1)

| | |
|--------------------------------|---|
| General Signs: | Smaller body stature, pediatric hypoglycemia (especially toy breeds; can cause neurologic signs), failure to grow, poor muscle development, poor hair coat |
| Gastrointestinal Signs: | Finicky eater, intermittent vomiting, diarrhea, episodic inappetence, anorexia, weight loss, gastrointestinal ulceration |
| Urinary Signs: | Urinary tract infections (e.g., cystitis), urinary obstruction, excessive thirst (polydipsia), excessive urination (polyuria) |
| Neurologic Signs: | Behavior changes, lethargy, sudden aggressiveness, dull mentation, may seem less intelligent, dementia, stupor, pacing, circling, muscle tremors, head pressing, apparent blindness, seizures, coma |
| Other: | Jaundice (acquired PSS), ascites (acquired PSS), bleeding problems (acquired PSS) |

Figure 1. Table of clinical signs in dogs with shunts.

Clinical signs of dogs with multiple acquired portosystemic shunts

Dogs with multiple acquired PSS are often middle-aged or older, although puppies can develop the condition. Sometimes the owners may have noted a previous episode of illness or toxin ingestion associated with severe liver disease. If the biliary system was affected by the initial problem, the dog may have a yellow tint to its skin, gums, and the whites of its eyes and its urine may be very dark. If the portal pressure is very high or the dog is not making enough protein, fluid will collect in the belly cavity (“ascites”). In dogs with severe liver disease, blood will not be able to clot effectively, and the owner may notice tiny or even large patches of bruising.

Clinical signs of dogs with PVH-MVD

Many dogs with PVH-MVD are “asymptomatic”; in fact, most Yorkies and Maltese that have this condition have no signs at all. However, some dogs do present with clinical signs that develop early or later in life. These dogs may either have a very underdeveloped liver or they may have another condition (e.g., epilepsy, toy breed hypoglycemia, hydrocephalus, inflammatory bowel disease, or behavioral issues) that is the actual cause of the signs. Unlike dogs with shunts, dogs with PVH-MVD rarely have neurologic signs from hepatic encephalopathy.

How we can tell if clinical signs are caused by PVH-MVD

We can't be sure that clinical signs in dogs with increased bile acids and liver biopsy results consistent with PVH-MVD are actually caused by the liver abnormality. If the biopsy changes are very severe, for instance, or the liver is inflamed or full of scar tissue, it is likely that clinical signs are related to those changes. However, if the biopsy changes are mild, the dog may actually have some other condition. We are especially suspicious that another condition is present if clinical signs do not go away with appropriate medical management.

What is hepatic encephalopathy?

Hepatic encephalopathy (HE) is a group of neurologic signs or behavior changes caused by severe liver disease. It has been recognized in animals with congenital or acquired PSS, end-stage liver disease, and congenital urea cycle enzyme deficiencies. Clinical signs include lethargy, dementia, stupor, and coma. Muscle tremors, motor abnormalities, and focal and generalized seizures have also been reported. The etiology of hepatic encephalopathy is probably dependent on several factors, including circulating toxins, alterations in amino acid concentrations, and increased cerebral sensitivity to drugs and toxins. A variety of toxins are implicated in the condition, with the most notable being ammonia. It is important to realize that some of these signs are seen with other conditions; if a dog has seizures but its liver function is normal or it does not respond to medical management of liver dysfunction, it is quite likely that the seizures are not caused by a shunt or PVH-MVD.

Conditions that trigger HE

Hepatic encephalopathy can be precipitated by high protein meals, intestinal hemorrhage (such as from parasites), transfusion with stored blood, infection, dehydration, constipation, and drugs such as anesthetics, analgesics, and tranquilizers.

What are common laboratory changes found with congenital PSS?

A basic work-up for a dog suspected to have congenital PSS includes a complete blood count (CBC), chemistry analysis (biochemistry), urine analysis, and measurement of bile acids. Some veterinarians may also check protein C and ammonia concentrations; however, these tests require special processing to make sure they are accurate. Common laboratory changes include the following:



- Small red cells (“microcytosis”) on CBC, and sometimes increases in white blood cells.
- Decrease in total protein, albumin, BUN (blood urea nitrogen) on chemistries. Animals may also have increased liver enzymes or low cholesterol.
- Decreased urine specific gravity on urinalysis. Animals may also have ammonium biurate crystals or evidence of urinary tract infection (white blood cells, red blood cells, protein, and bacteria) in their urine sediment.
- Increases in fasting and fed serum bile acids. Bile acids are usually $>70\mu\text{mol/liter}$ in dogs with PSS.
- Increased blood ammonia, especially 6 hours after a meal.
- Decreased protein C activity.

On plain abdominal x-rays, the liver is usually smaller than normal. Unfortunately, urate bladder stones may not show up on an x-ray, but they can be seen with ultrasound. Ultrasound can also be used to try and find the shunt and to rule out cirrhosis of the liver.

What are common laboratory changes found with congenital PVH-MVD?

Except for increases in bile acids, laboratory results for dogs with PVH-MVD may be completely normal. In fact, dogs with PVH-MVD usually have normal fasting bile acids, red cell size, BUN, protein, albumin, cholesterol, and Protein C activity. Their fed bile acids are often <70µmol/liter, and it is rare for them to have ammonium biurate crystals, bladder stones, or dilute urine. However, some dogs with PVH-MVD can be more severely affected, while some dogs with congenital portosystemic shunts that flow only intermittently can be mildly affected. Additionally, liver biopsy results are usually the same, so laboratory results alone cannot be used to diagnose either condition.

What are bile acids?

Bile acids are produced in the liver and stored in the gallbladder between meals. When a dog eats a meal, particularly one with fat in it, the gall bladder contracts, and the bile acids are released into the intestines, where they help break down and absorb fats. Along with other nutrients and chemicals, bile acids are reabsorbed from the intestines and carried by the portal system back to the liver, where they are removed from the blood by liver cells and stored again in the gallbladder until they are needed. Dogs with liver disease such as inflammation, portosystemic shunts, or PVH-MVD have increased blood bile acid concentrations because the chemicals are not brought back to the liver by the blood (for instance, with a liver shunt), or the liver cells are unhealthy and therefore unable to remove the chemicals from the blood.

How is the bile acid test performed?

Bile acids are measured after an overnight fast (“preprandial” or fasting bile acids) and then 2 hours after eating (“postprandial” or fed bile acids). Although fat is the most potent stimulator of gallbladder contraction and subsequent bile acid release, any type of food can be used. Therefore, the owners cannot blame high bile acids on the type of meal used.

“Owners cannot blame high bile acids on the type of meal used.” —Tobias

Why are the fasting bile acids sometimes higher than the fed sample?

Usually bile acids are lowest after an overnight fast; these bile acids are called “preprandial” because they are measured before a meal. Two hours after a meal, bile acid concentrations are usually at their highest; these bile acids are “postprandial” because they are measured after eating. About 20% of dogs will have a gallbladder contraction in the middle of the night that will increase the first bile acid sample, making it essentially “postprandial”. This is why we measure 2 samples. (Figure

2) If either sample is abnormal (above 15-20 micromoles/L, depending on the lab), the animal is considered to have some sort of liver disease.

If either sample is abnormal...the animal is considered to have some sort of liver disease

—Tobias

Bile Acid (VBA)

Table with 5 columns: Test Name, Value, Unit, Reference Range, and Note Number. Row 1: Bile Acid Fasting, 174.2, umol/L, (0.0 - 12.0), 1

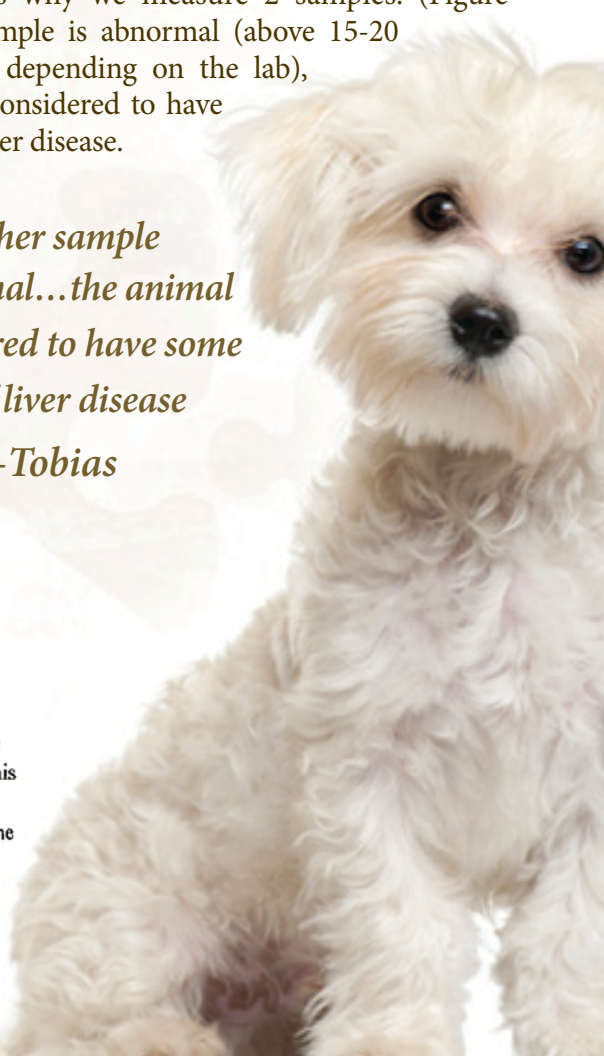
Bile Acid, 2 HR Post (VPBA)

Table with 5 columns: Test Name, Value, Unit, Reference Range, and Note Number. Row 1: Bile Acid 2HR Post, 162.9, umol/L, (5.0 - 25.0), 3

Notes:

- 1 No significant hemolysis or lipemia present. KJK 02/11/11 04:56
2 The preprandial bile acid value is sometimes increased relative to the postprandial bile acid value due to contraction of the gall bladder in the absence of gastric emptying. This may occur with habituation of the animal to eating at a certain time of day or may be stimulated by smell of food. If this happens, the serum bile acid values for both baseline and postprandial samples should be compared to the reference range listed for the postprandial bile acid.
3 No significant hemolysis or lipemia present. KJK 02/11/11 04:56

Figure 2



What techniques or handling requirements are used for the bile acid test?

Unlike ammonia and protein C measurements, no special techniques are required for handling and storage of serum for bile acid samples. The most important step is to separate the serum from the red cells. After that, the serum sample can be sent by regular mail or courier to a lab; it does not need to be refrigerated or frozen.

Can bile acids be used to diagnose PSS or PVH-MVD?

Most dogs with congenital PSS have high fasting and fed bile acids, while dogs with PVH-MVD usually have normal fasting and increased fed bile acids. Bile acids can increase with any liver disease, so high bile acids are not specific to congenital portosystemic shunts or PVH-MVD. To be certain a dog has a PSS or PVH-MVD, advanced imaging and liver biopsy are required. That being said, if a Yorkie puppy presents with signs of hepatic encephalopathy, has ammonium biurate crystals, has chemistry and CBC changes consistent with a shunt, and its bile acids are over 100 micromoles/L, the most likely diagnosis is a congenital extrahepatic PSS. If a Yorkie has no clinical signs, normal urine and biochemistry results, and mildly increased postprandial bile acids, the most common cause is PVH-MVD.

Can abnormalities other than liver disease cause high bile acids?

About 95% of bile acids are reabsorbed through the intestines and sent to the portal system. That means that anything that decreases absorption of fat and nutrients from the intestines (e.g., diarrhea or thickened intestines) will decrease bile acid resorption and, therefore, concentrations of bile acids in the blood. Anything that increases intestinal absorption (e.g., inflammation or constipation) can have the opposite effect and therefore potentially increase blood bile acid concentrations. However, because a normal liver is so effective at removing bile acids from the bloodstream, we do NOT expect normal dogs to have high bile acids. Owners may want to blame diet changes, stress, or other conditions for their dog's high bile acids, but high bile acids only occur if there is liver disease.

How young can you test a patient for liver dysfunction by measuring bile acids?

No one really knows how early we can detect increased bile acids in dogs with congenital PSS or PVH-MVD. Liver function is considered to be normal by 8 weeks of age, and PSS have been diagnosed in dogs as young as 4 weeks old. If bile acids are abnormal at 8 weeks of age, liver disease should be suspected, and the puppy's blood should be retested at 12 weeks of age for abnormalities in bile acids and chemistries. Because congenital PSS and PVH-MVD are so common in certain breeds (e.g., Yorkies, Maltese, Cairn terriers, Havanese, Irish Wolfhounds), susceptible breeds should have their bile acids and chemistries evaluated at 4 to 6 months of age for evidence of liver dysfunction. This will help the veterinarian develop an individualized health care plan for each pet and will alert the owners of the potential for future illnesses.

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Do all dogs with PVH-MVD have increased bile acids?

Most affected dogs will have at least a small increase in one of their bile acids samples; however, in rare cases we have seen Yorkies with normal bile acids that have mild liver biopsy changes consistent with PVH-MVD.

Do all dogs with congenital PSS have increased bile acids?

Almost all dogs with PSS will have increased bile acids; however, congenital PSS have been reported in dogs with bile acids as low as 17 μ moles/L (normal, <20 μ moles/L). It is likely these dogs have a shunt that gets compressed intermittently: for instance, one that runs along or through the diaphragm.

Can bile acids be used to monitor the dog's status?

Bile acid concentrations have not been correlated with the severity of liver disease (or shunting) and vary from day to day within the normal or the abnormal range. Obviously, bile acids of 300 micromoles/L are much worse than bile acids of 25 micromoles/L. However, many dogs may have bile acids of 40 one day and 80 the next. Because of differences in how much bile is being held within the gallbladder at one time, how much the gallbladder contracts, how fast the bile is moving through the intestines, and how much of it is being reabsorbed, we cannot say that the dog is worse when the bile acids are 80. We can only say that the bile acids are increased on both days and the liver is still not working properly.

Why is this important?

It means we need to use other methods to monitor how a dog with PVH-MVD or one that has undergone repair for a congenital shunt is doing long-term. If your dog has PVH-MVD, we do not expect the bile acids to ever be normal (unless they were high for another reason). So, instead of measuring bile acids, we will look at the dog's

“Bile acid concentrations have not been correlated with the severity of liver disease (or shunting) and vary from day to day...”

—Tobias

chemistries to make sure the dog can still make protein, albumin, BUN, and glucose and that its liver enzymes remain normal. That will give us much more information than changes in bile acids.

Can protein C be used to differentiate shunts from PVH-MVD?

Protein C is a measure of an animal's ability to stop clots from forming or to break them down. If you had a low protein C, you would be much more likely to develop clots in your legs during long plane flights. Like many clotting factors, protein C is made in the liver and is decreased with severe liver disease and PSS. Most dogs with PVH-MVD do not have severe liver disease, so they will have normal protein C activity. Unfortunately, however, a few dogs do not follow these rules. Currently there is no blood test that is 100% accurate for differentiating shunts from PVH-MVD or other conditions.

How do we differentiate congenital portal vein hypoplasia and congenital PSS?

Many liver diseases can cause the same laboratory changes seen in dogs with congenital PSS or severe PVH-MVD. Therefore, to confirm the diagnosis, advanced imaging and liver biopsy are required. Shunts can be detected with trans-splenic scintigraphy, MRI, or a CT (“Cat” scan) or by an experienced ultrasonographer. If no shunting is found on these tests, a liver biopsy is obtained to confirm the diagnosis of PVH-MVD and rule out other liver diseases caused by inflammation, infection, or toxins. If no shunting is seen on CT or scintigraphy and the liver biopsy is positive for MVD, then the dog has PVH-MVD. Alternatively, an experienced surgeon may elect to explore the abdomen to look for a shunt and to obtain liver biopsies. If no shunt is found, a portogram (contrast x-ray study of the blood vessels) can be performed during surgery. The final x-ray, or “portogram”, highlights all the vessels to the liver and any shunting vessels carrying blood around it.

How do we differentiate multiple acquired PSS from congenital PVH-MVD and congenital PSS?

Unlike most dogs with congenital PVH-MVD, dogs with PSS, whether congenital or acquired, will have scintigraphies that are positive for shunting. It is important to realize, however, that a very small percentage of dogs with PVH-MVD are so severely affected that they develop multiple acquired shunts. A liver biopsy is therefore necessary to determine the specific cause of multiple shunts. With a scintigraphy or ultrasound, an experienced radiologist or other specialist may be able to tell that the blood flow patterns seen on the images are more consistent with either multiple acquired shunts or a single congenital shunt. However, to be absolutely certain a dog has multiple acquired PSS versus a congenital PSS, a vascular study (a CT, MRI, or portogram) or exploratory surgery may be necessary.

Differential Diagnoses

The term “differential diagnosis” refers to conditions that cause similar signs or blood work changes. For instance, any liver disease could cause the blood work changes seen in dogs with congenital PSS, including increases in ammonia and bile acids and decrease in Protein C. Besides liver disease, formation of ammonium biurate crystals and urate stones can occur with certain metabolic conditions; these are particularly common in Dalmatians. Hepatic encephalopathy must be differentiated from distemper, hydrocephalus, hypoglycemia, toxicities, and epilepsy and even behavior changes.

Comparison of results from dogs with congenital portal vein hypoplasia (PVH-MVD) and congenital extrahepatic portosystemic shunts.

| Characteristics | Portal Vein Hypoplasia | EH CPSS |
|--|--|--|
| Signalment | Small/toy breed dogs | Small/toy breed dogs |
| History | Usually asymptomatic | Usually symptomatic |
| Response to treatment | No effect if only sign is increased bile acids | Often good |
| Albumin, glucose, BUN, MCV (red cell size), urine specific gravity | Usually normal | Usually abnormal |
| Liver enzymes | Normal to increased | Normal to increased |
| NH ₄ biurate crystals | Usually absent | Often present |
| Fasting bile acids | Usually normal | Usually abnormal |
| Fed bile acids | Usually <70 μmol/L | Usually >70 μmol/L |
| Protein C activity | Usually >70% | Usually <60% |
| Liver biopsy | MVD | MVD |
| Ultrasound | Normal or small liver | May see small liver, big kidneys, shunt, evidence of crystals in urinary tract |
| Scintigraphy | Normal | Shunting |
| CT, MRA, Portogram | Normal | Shunting |

Terminology:

Asymptomatic: No clinical signs.

BUN: Blood urea nitrogen—a compound made in the liver from ammonia.

CT: Computed tomography—usually combined with a contrast study to outline blood vessels.

MCV: Mean corpuscular volume—a measure of red cell size.

MRA: Magnetic resonance angiography—a noninvasive method for examining blood vessels.

NH₄: Ammonium—a byproduct of bacterial metabolism of proteins.

Protein C: An anticlotting factor produced in the liver.

Signalment: Characteristics of an animal, such as age, gender, or breed.



...no special techniques are required for handling and storage of serum for bile acid samples.

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If bile acids are abnormal at 8 weeks of age, liver disease should be suspected, and the puppy's blood should be retested at 12 weeks of age for abnormalities in bile acids and chemistries. Because congenital PSS and PVH-MVD are so common in Yorkies...bile acids and chemistries should be evaluated at 4 to 6 months of age for evidence of liver dysfunction. This will help the veterinarian develop an individualized health care plan for each pet and will alert the owners to the potential for future illnesses.

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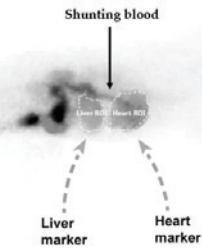


“If no shunting is seen on CT or scintigraphy and the liver biopsy is positive for MVD, then the dog has PVH-MVD.”

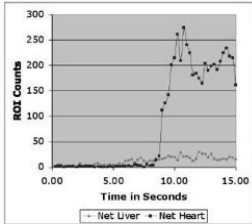
—Tobias

What is Scintigraphy?

Note how Bella's heart is visible on the scan. Normally, the radioactive material stops at the liver.

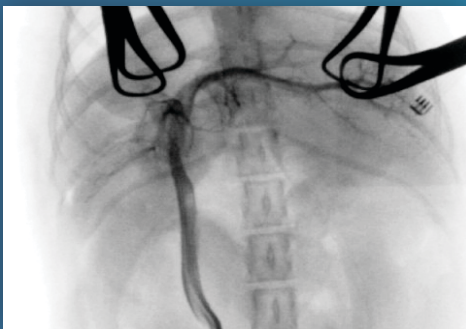


Σ Liver Activity 535
Σ Heart Activity 4,845
Shunt Fraction 90.1%

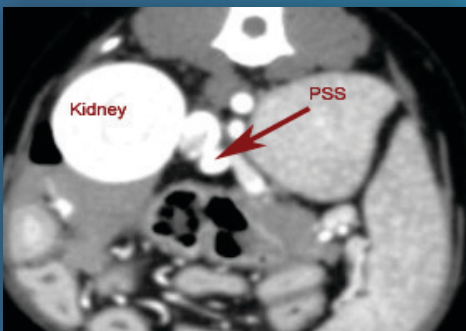


Most of Bella's blood is going to the heart instead of the liver. Her shunt fraction is 90% and should be less than 5%.

What is a Portogram?



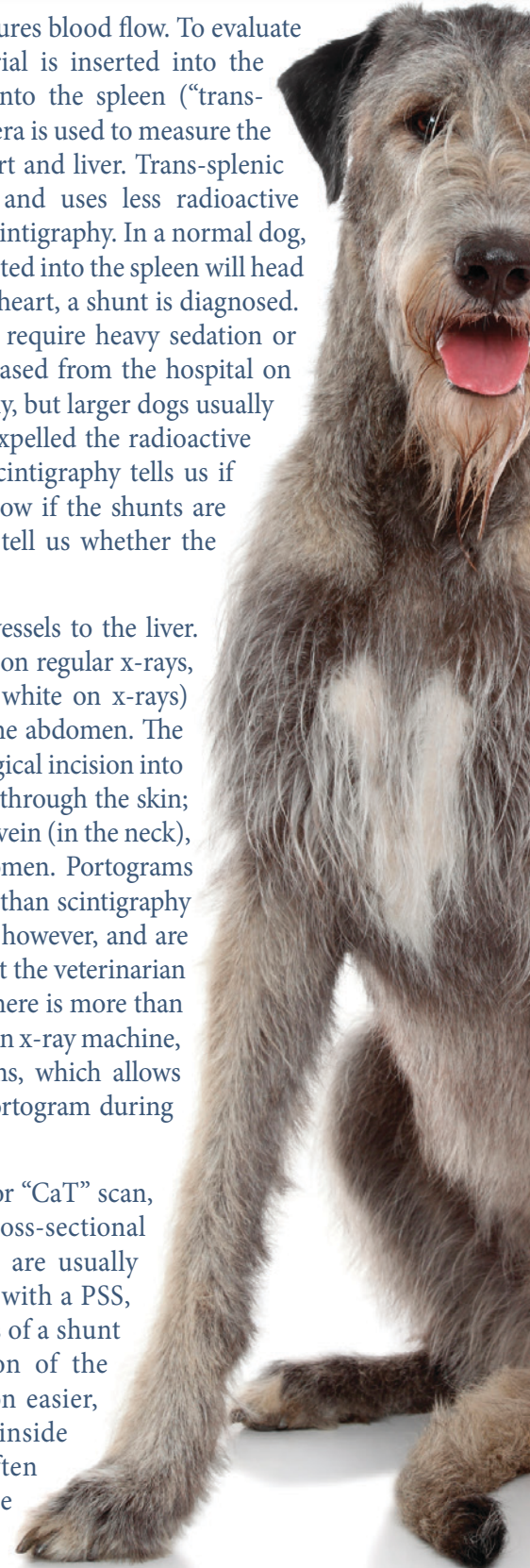
What is a CT Scan?



Scintigraphy is a nuclear scan that measures blood flow. To evaluate a dog for a shunt, a radioactive material is inserted into the colon (by a high enema) or injected into the spleen (“trans-splenic” scintigraphy), and a special camera is used to measure the amount of radioactivity in the dog’s heart and liver. Trans-splenic scintigraphy produces a better image and uses less radioactive material, so it is preferred over colonic scintigraphy. In a normal dog, over 95% of the radioactive material injected into the spleen will head to the liver; if more than 5% goes to the heart, a shunt is diagnosed. Scintigraphy is safe and quick but does require heavy sedation or anesthesia. Small dogs can often be released from the hospital on the same day of trans-splenic scintigraphy, but larger dogs usually need to stay overnight until they have expelled the radioactive material by defecation and urination. Scintigraphy tells us if shunting is present and often lets us know if the shunts are congenital or acquired, but it does not tell us whether the shunt is inside or outside of the liver.

A **portogram** is an x-ray of the blood vessels to the liver. Because blood vessels are not easily seen on regular x-rays, a contrast material (a liquid that looks white on x-rays) must be injected into a blood vessel in the abdomen. The injection can be performed through a surgical incision into the belly; by injecting the spleen directly through the skin; or by passing a catheter down the jugular vein (in the neck), through the heart, and toward the abdomen. Portograms require anesthesia and are more invasive than scintigraphy or CT scans. They are usually quite safe, however, and are able to provide a picture of the PSS so that the veterinarian can see where it is located and whether there is more than one. Many board certified surgeons have an x-ray machine, called a C-arm, in their operating rooms, which allows them to quickly and safely perform a portogram during surgery.

Computed tomography, known as CT or “CaT” scan, is a technique that provides multiple cross-sectional x-rays of bones and organs. CT scans are usually performed under anesthesia. In a dog with a PSS, a CT can be used to make the diagnosis of a shunt and to determine the specific location of the shunt. This makes surgical intervention easier, particularly when the shunt is hidden inside the liver. Preoperative CT scans are often performed on large breed dogs because they usually have intrahepatic shunts.



“To be certain a dog has PVH-MVD, advanced imaging and liver biopsy are required.”

—Tobias

Liver biopsy

Liver biopsy can be obtained by open surgical technique (“laparotomy”) (Figure 3) or by laparoscopy (use of a scope). Ultrasound-guided needle biopsies are not recommended because small liver size in dogs with congenital PSS and PVH-MVD increases the risk of complications, and because the small sample size obtained by needle makes diagnosis of MVD difficult. Some clinicians recommend taking samples from multiple liver lobes, since the amount of disease could differ from lobe to lobe. The liver samples (Figure 4) are placed in formalin and sent to a pathology laboratory, where they will be processed and examined under a microscope. (Figure 5)

“If a Yorkie has no clinical signs, normal urine and biochemistry results, and mildly increased postprandial bile acids, the most common cause is PVH-MVD.”

—Tobias

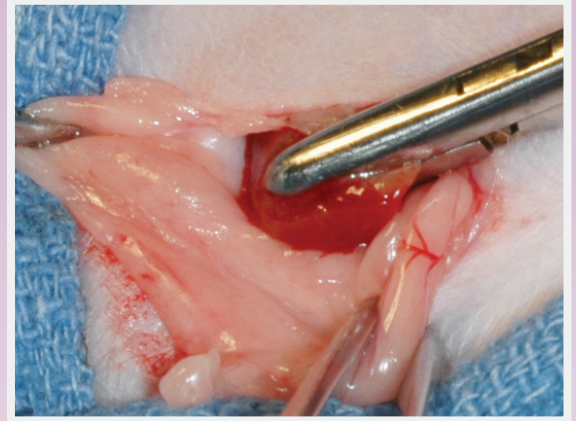


Figure 3. A liver biopsy can be taken through a small abdominal incision with a special instrument.

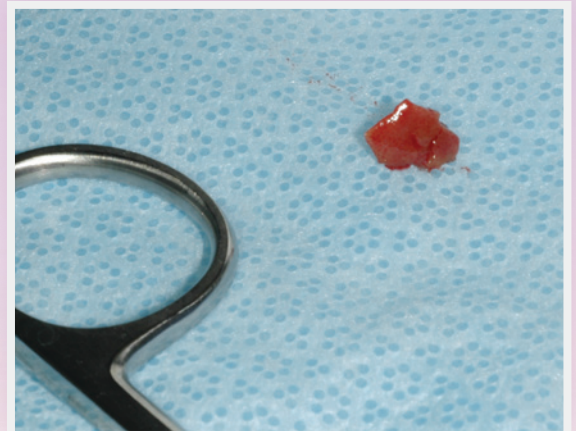


Figure 4. This liver sample measures about a fourth of an inch wide.

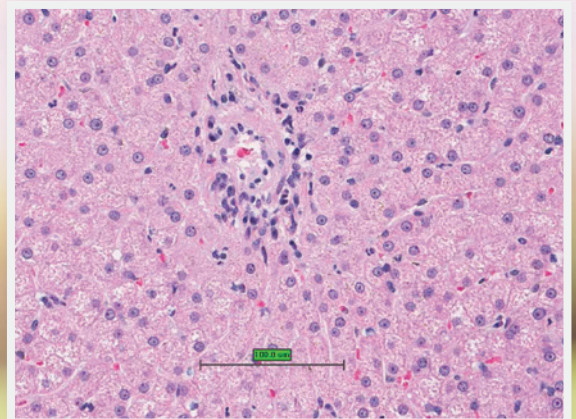


Figure 5. Micrograph taken of a slide from a liver biopsy specimen revealing the classic pathology of MVD.

Medical & Nutritional Management

What medical management is recommended for dogs with liver shunts?

Diet

The most important treatment of dogs with shunts and other serious liver diseases is an appropriate diet. The liver is responsible for removing the toxic products of protein metabolism. When the liver is not functioning correctly, ammonia and other waste products accumulate; in addition, proteins broken down by bacteria in the colon can release toxins into the bloodstream. Therefore, liver diets tend to be moderately restricted in protein. Protein sources should be high quality and readily digestible, and they may contain higher concentrations of branched chain amino acids (e.g., vegetable and dairy sources of protein). Dogs with liver disease also need higher levels of zinc, vitamin E, vitamin K, and omega-3 fatty acids and reduced levels of manganese and copper compared with normal dogs.

What brands of dog food are recommended for dogs with shunts and other serious liver disease?

Veterinary therapeutic liver diets such as Hill's Prescription Diet l/d Canine Hepatic Health and Royal Canin Veterinary Diet Hepatic Formula provide quality proteins that are readily digestible in the small intestine, reducing ammonia and toxin production. Protein concentrations in these diets are higher than those in many of the kidney diets. This is important because animals with liver disease that receive too little protein will break down their own muscle tissue to make up for any deficiencies. These diets also have the appropriate balance of other nutrients critical for patients with liver

disease, and they have been thoroughly tested to verify their quality. In fact, Hill's l/d was developed under the supervision of one of our veterinarians at University of Tennessee.

How much protein and fat does my dog need?

There is no one nutrient percentage that is good for all dogs with liver disease. Some dogs have severe liver dysfunction and can't tolerate any extra protein; others need the extra protein. Some are fat, some are athletic,

“In fact, Hill's l/d was developed under the supervision of one of our veterinarians at University of Tennessee.”

—Tobias

some are young, and some are underweight. Based on research, however, we know that dogs with liver disease need at least 2.1 grams of crude protein per kg body weight each day. A good rule of thumb is to feed a diet that has a total of 40 to 50 grams of protein (including any yogurt or snacks!) for each 1000 Kcals. Veterinary therapeutic diets are about 18% protein on a dry matter basis. Dogs with liver disease do not need fat restricted, so they can receive normal or higher levels of fat in the diet.

How much protein is in veterinary therapeutic liver diets?

The following chart provides information about Science Diet l/d Hepatic Health and Royal Canin Hepatic veterinary therapeutic diets.

| Diet | Calories | Protein % (Dry matter basis) | Grams of protein per 1000 Kcal |
|----------------------------|---|------------------------------|--------------------------------|
| Science Diet l/d Canned | 1392/kg of food, or 515 kcal/370 g (13 oz.) can | 17.6% | 39 |
| Science Diet l/d Dry | 4050 kcal/kg of food, or 388 kcal/ 8 oz. cup | 17.8 % | 41 |
| Royal Canin Hepatic Canned | 1347/kg of food, or 621 kcal/420 g (14.4 oz.) can | 17.2 % | 41.4 |
| Royal Canin Hepatic Dry | 3785/kg of food, or 356 kcal/8 oz. cup | 16.9% | 40.5 |

What about over-the-counter diets?

Most over-the-counter (e.g., store-bought) diets do not contain the proper balance and type of proteins, carbohydrates, fats, vitamins, and minerals for dogs with liver disease. Another concern is digestibility: while the pet food label can give us a rough idea of the contents, it provides no information about quality and digestibility of ingredients. Veterinary therapeutic diets have undergone rigorous testing and are therefore usually preferred for patients with liver disease. If owners are adverse to feeding the veterinary therapeutic diets, they can attempt to match the ingredients list and nutrient content of the over-the-counter product to those of the veterinary diets; however, currently there are no over-the-counter diets appropriate for dogs with liver shunts. The best option for owners is to consult with a veterinary nutritionist for advice on homemade diets or diet blends.

“...currently there are no over-the-counter diets appropriate for dogs with liver shunts.”

—Tobias

Why is it so hard to read pet food labels?

An excellent question! There seems to be no consistency among dog food companies in terms of the way they label their food. On the label you will find the ingredients listed, in descending order, by weight. You may also see a guaranteed analysis, which shows the minimum (or maximum) of specific nutrients such as proteins, fats, carbohydrates, and minerals. These are not exact numbers because components change from batch to batch. For example, the label on Hill's I/d Hepatic Health kibble lists a minimum of 14.5% crude protein, but it actually has more protein than that. Specifics about nutrients are usually not listed on pet food labels.

So how do I compare nutrients in diets?

Comparing nutrients themselves can be very confusing because there are several ways pet food companies report a diet's nutritional contents: on an as fed basis, a dry matter basis, as percentage metabolizable energy, or as grams per 1000 Kcals. When veterinary nutritionists

compare diets, they actually collect information from the company so they can determine the total amount of each nutrient per kg or 1000 Kcal of food. A pet owner would almost need a nutrition degree to do an accurate comparison; that's why we leave it up to the experts!

Information on preparing homemade diets

Homemade diets formulated by veterinary nutritionists can be used for dogs that have congenital PSS or PVH-MVD. There is some risk to the use of a homemade diet because changes in the diet content can make it unbalanced. This most often occurs when an owner decides to change the ingredients, but it can also occur if the quality of the dietary components change. For instance, diets that include chicken breast will have a different fat and calorie content than those made with the darker, thigh meat. Over several months, this could lead to nutritional imbalances. If you are interested in feeding a homemade diet, you will need to work closely with your veterinarian or a veterinary nutritionist to make a diet that is complete, balanced, and healthy for your pet. Pet owners can contact a board-certified veterinary nutritionist at www.acvn.org or consult with our nutritionists at University of Tennessee <https://vetmed.tennessee.edu/vmc/SmallAnimalHospital/Nutrition/Pages>.

Probiotics

Unfortunately, we don't know whether dogs with shunts will respond to the addition of probiotics, or “good bacteria”, to their diet, but it doesn't hurt to try them. Probiotics have been shown to decrease inflammation and improve health for several conditions, including inflammatory bowel disease. The best source of probiotics is a packaged form such as VSL3 (1/10th of a sachet per 10 pound body weight per day) or Culturelle (1/2 an adult capsule or one child's granule packet per 10 pounds body weight per day). Another option is to supplement the diet with yogurt containing live, active cultures. Although yogurt doesn't provide very many bacteria compared with prepackaged probiotics, it has been shown to reduce signs of hepatic encephalopathy in people, and it also provides soluble fiber and a high quality protein that is “liver friendly”.



Yogurt brand and amount

Look for a brand that has not been heat treated after the addition of healthy bacteria; some brands will even have a “Live & Active Cultures” seal from the National Yogurt Association. Amounts are calculated based on the protein content of the yogurt and the total calories in the dog’s diet. For instance, 2.2 ounces of Activa vanilla yogurt can be added to each 1000 kcals of food, or 1 tsp of Chobani nonfat plain Greek yogurt for each 100 kcals. A rough dosage is 1-2 tsp of yogurt once or twice a day for a small Yorkie.

Is it okay to add fish oils?

Veterinary therapeutic liver diets already have high levels of EPA/DHA - the good fats in fish oil. However, if the dog is not on a liver diet, our nutritionist recommends supplementing with fish oils at about 250-300mg of EPA/DHA per 10 pounds of body weight.

What about treats?

Treats are okay if they are safe for pets and do not add additional protein. However, treats should not make up more than about 10% of a dog’s diet. For example, if you have a dog that eats 200 calories per day, it shouldn’t have more than 20 calories per day from sources other than a liver diet. One treat that should never be given to dogs with liver disease is rawhide bones, which are chock full of non-digestible or poor quality proteins.

Other Supplements

Some veterinarians will prescribe supplements that reduce inflammation of the liver, such as denosyl (“SAM-E”) and silymarin (milk thistle). While these



supplements can be purchased over-the-counter, their content and manufacturing are not regulated by the FDA. Therefore, use of veterinary products is recommended, since these have been appropriately tested for active ingredients. Denamarin (Nutramax Laboratories) is a common brand; the chewable form is preferred because it has greater absorption and causes less stomach upset. Use of these nutraceuticals in dogs with congenital PSS or PVH-MVD has not been studied, so no one knows whether they make any difference in these dogs. Owners should never give any supplements that could have negative effects on their pet’s liver, nor should they use any chemical products around their house that have risks of toxicity.

“...lactulose must be dosed carefully: too much could result in diarrhea.”

—Tobias

Lactulose

Lactulose syrup is a double sugar that is broken down by bacteria in the colon into two simple sugars. This reaction is beneficial in several ways. First, the reaction produces an acidic environment that reduces ammonia absorption and that may be unattractive to troublesome bacteria. Second, the resulting sugars cause an increase in fluid content in the feces, which makes them move out faster so there is less time for toxins to be produced or absorbed. Because of this second effect, lactulose must be dosed carefully: too much could result in diarrhea. In general, owners should give a dose that results in 2 to 3 soft-but-formed stools per day. For most Yorkshire terriers, that means 0.5 to 2 mls by mouth 2 to 3 times each day. The dose should be decreased if diarrhea or cow pie stools develop and increased for dogs with hard, dry feces. Dogs that vomit when given lactulose may do better with a powdered form.

Antibiotics

Antibiotics are prescribed for animals with active infections (for instance, urinary tract infections) or those with neurologic signs. Certain antibiotics will kill off the bacteria in the colon that are causing ammonia production. Antibiotics are not used routinely, however, because of potential side effects.

“We know that dogs with PVH-MVD that are presented because of illness can and do respond to medical management.”

—Tobias

How is PVH-MVD treated in a dog that has clinical signs of liver disease?

Dogs with PVH-MVD that have clinical signs, ammonium biurate crystals, or abnormal blood chemistries (for instance, high liver enzymes, low protein, low albumin) can be medically managed just like dogs with congenital PSS. Most critical is the use of a protein-restricted diet.

“Dogs with PVH-MVD that have clinical signs...can be medically managed just like dogs with congenital PSS. Most critical is the use of a protein-restricted diet.”

—Tobias

What about dogs with PVH-MVD that are “asymptomatic” and have normal chemistries?

There are no studies on medical management of dogs with PVH-MVD that only have increased bile acids. Therefore, we have no idea whether affected dogs have a shortened lifespan and whether medical management makes any difference.

Don't bother to ask whether lactulose, diet, yogurt, SAM-e, milk thistle, antibiotics, or anything else will be helpful to your 'asymptomatic' dog; the fact is, nobody knows! All we can tell you is that many of our “normal” Yorkie patients have mildly increased bile acids and live long lives without any special treatment, as long as they don't get sick from something else.

—Tobias

What does the term “response to therapy” mean?

One option for owners of dogs with PVH-MVD is to base the need for medical management on “response to therapy”. In simple terms, “response to therapy” is what happens to the animals when a treatment is started or stopped. In other words, if dietary change or administration of medications makes the animal feel worse, the treatment should be discontinued; if it makes the animal feel better, it should be continued. One problem with a positive response is a “placebo effect”, which commonly happens when owners give their animals treatments. The owners believe it will work and therefore see positive changes in their dogs, even if those changes are not really caused by the treatment. A more scientific method for monitoring response to therapy in dogs that have abnormalities in their blood chemistries or ammonia is to monitor these blood chemicals for changes when treatment is started or stopped. For dogs with high blood ammonia, the ammonia concentration should drop to normal levels when appropriate treatment is given.



Routine Veterinary Care & Prognosis

What type of rechecks are recommended for dogs with PVH-MVD?

Blood chemistries and ammonia, if available, can be rechecked every 6 to 12 months to make sure that the dog is producing a sufficient amount of proteins and no signs of inflammation or organ failure are present. Bile acids do not need to be rechecked—they do not correlate well with the amount of liver damage and will only cause unnecessary worry for owners.

“...because systemic illness may hit them harder than dogs with normal livers, it’s important to continue any recommended preventatives.”

—Tobias

Can dogs with congenital PVH-MVD receive vaccinations and flea and tick preventatives?

Because dogs with PVH-MVD are susceptible to all the usual parasites and viruses, and because systemic illness may hit them harder than dogs with normal livers, it’s important to continue any recommended preventatives. Heartworm, flea, and tick preventatives and vaccines should be given as usual. If owners are concerned about the stress vaccinations may place on their pet, they can ask their veterinarian to develop a schedule so that administration of individual vaccines is separated by at least a few weeks. Preventative care is also safe and highly recommended for dogs with congenital PSS, whether or not the shunts have been repaired.

Can vaccinations cause PVH-MVD?

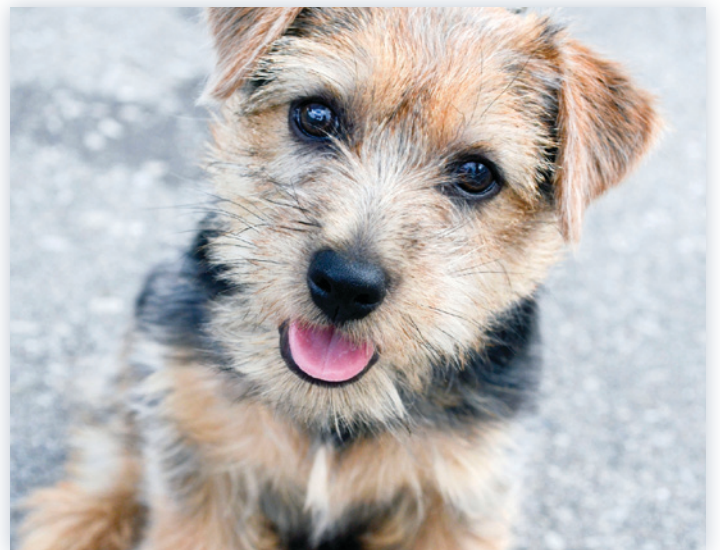
PVH-MVD is not caused by vaccines because it is a congenital disease. It is important to continue routine vaccinations and preventatives in these dogs so they do not get other conditions that can make them ill.

What is the prognosis for dogs diagnosed with congenital PVH-MVD?

Despite the fact that there is no research, we can comfortably say that dogs with mild increases in bile acids and no other evidence of liver disease or clinical signs may live normal lifespans, even if they receive no medical or dietary treatment. In fact, most Yorkie owners never know their dogs have PVH-MVD because they never test for it. Based on a routine survey of bile acids from 139 healthy Yorkies, we suspect that over half of all Yorkies have this condition. Perhaps we have even bred for it by selecting for smaller and smaller dogs.

So what about the dogs that have clinical signs?

We know that dogs with PVH-MVD that are presented because of illness can and do respond to medical management. We also know that many of these dogs will live for years when kept on an appropriate diet. In most cases, dogs with PVH-MVD succumb from other conditions, including old age. Rarely, the condition will progress to liver failure. That is why yearly or twice yearly check-ups are recommended.



“A liver biopsy helps veterinarians determine the underlying cause and the prognosis and differentiate congenital and acquired causes.”

—Tobias

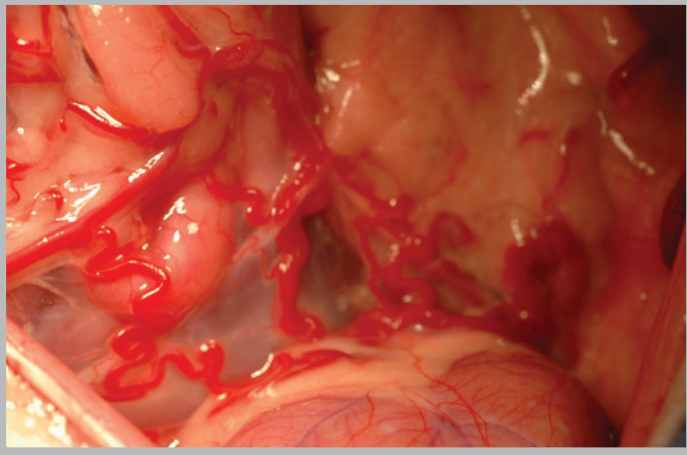


Figure 6. Multiple acquired shunts are often small, tortuous vessels near the kidneys.

What is the prognosis for dogs diagnosed with multiple acquired PSS?

Dogs develop multiple acquired shunts (Figure 6) for a variety of reasons, including severe liver inflammation or infection, liver cancer, biliary disease, heart disease, and other conditions that increase blood pressure within the liver. On rare occasions, dogs with PVH-MVD will also develop multiple acquired shunts, if they are born with very few, or no, small portal venules within their livers. Prognosis for multiple acquired shunts depends on whether the underlying cause can be corrected (for instance, infection or heart disease treated) and the type and severity of the liver's reaction to that cause. If the liver has hardened from scar tissue (“cirrhosis”) or there are few portal vessels within the liver (severe PVH-MVD), the liver may never recover. A liver biopsy helps veterinarians determine the underlying cause and the prognosis and differentiate congenital and acquired causes.

Medical management of dogs with multiple acquired shunts includes the same supportive and nutritional care described for congenital PSS and hepatic encephalopathy, in addition to the use of medications that reduce the risk of gastrointestinal ulcers (e.g., omeprazole) or decrease fluid accumulation in the abdomen (diuretics such as furosemide and spironolactone).

What is the prognosis for dogs diagnosed with congenital PSS that are only treated medically?

About 50% of dogs with congenital PSS will live long lives if they are medically managed appropriately and they don't get other illnesses. The dogs that do well on medical management alone are usually the ones that are less severely affected based on their clinical signs and blood work. The outcome is much better, however, for dogs with congenital PSS that undergo surgical closure with an ameroid constrictor (Figure 7) or cellophane band or, in the case of an intrahepatic shunt, with embolization

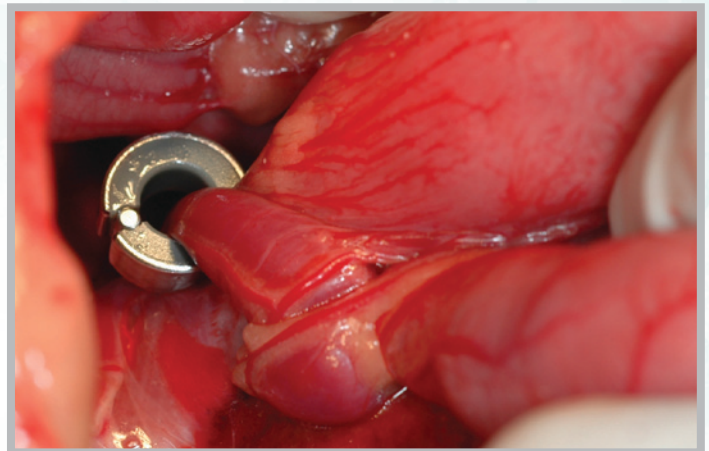


Figure 7. Ameroid constrictor around a large, single extrahepatic shunt running along the stomach.

coils. In fact, 85% to 90% of these dogs do well long term. Surgery does have risks, however, and about 5% of the dogs may die after the procedure because of seizures, pneumonia, or other complications. Yorkies that undergo surgery will almost always have mildly increased bile acids the rest of their lives. This is because they usually also have PVH-MVD, which is not cured by surgery.



Can dogs with liver disease be safely anesthetized?

Absolutely! Dogs with congenital and acquired shunts and other severe liver diseases are commonly anesthetized for diagnostic and therapeutic procedures. The choice of drugs depends on the individual animal: the severity of their liver disease, whether they have other health issues, what their blood work looks like, their life stage, how they've reacted to anesthetics previously, how long the procedure will last, and a variety of other issues. Therefore, each patient should get an anesthetic regimen tailored to its particular needs. In general, dogs undergoing longer procedures that might cause discomfort usually get an injectable opiate (e.g., buprenorphine or butorphanol) and a low dose of sedative before an IV catheter is placed. They are often induced with an intravenous injection of a rapid-acting anesthetic, such as propofol, and are intubated so that anesthesia can be maintained with a gas anesthetic (e.g., isoflurane) in oxygen. This protocol works well for nearly all of our dogs with PSS and PVH-MVD. In addition, local nerve blocks may be performed while the dog is under anesthesia; this is especially helpful if any teeth are being removed. During anesthesia, dogs are often placed on intravenous fluids to help their circulation. During recovery, they are warmed up with forced-air warming blankets or other safe devices and given pain relievers and sedatives as needed.

Should blood work be performed before considering anesthesia in dogs with liver disease?

In most instances, yes—especially blood chemistries. If you have a breed of dog that is prone to liver disease, even mild forms like PVH-MVD, it's important to provide your veterinarian with as much information as possible about your pet's health so that an

“If you have a breed of dog that is prone to liver disease, even mild forms like PVH-MVD, it's important to provide your veterinarian with as much information as possible about your pet's health...”

—Tobias

appropriate anesthetic regimen can be designed. If bile acids have been previously checked, these will not need to be repeated. Instead, your veterinarian will use results of a recent chemistry panel to determine the need for special fluids (e.g., ones that provide sugars, like dextrose, or that support blood pressure if blood proteins are low). Your veterinarian may also want to check a white and red blood cell count and perform a urine analysis to look for anemia, infection, or urinary tract problems.



Genetics, Risk & Breeding

What is the genetic research regarding congenital PVH-MVD?

Dr. Sharon Center, a professor of small animal internal medicine at Cornell's College of Veterinary Medicine, is the principal investigator of a research study funded through Morris Animal Foundation called "Genetics of Portosystemic Vascular Anomalies & Microvascular Dysplasia in Small Breed Dogs." Here is a quote from her last progress update:

"Since the last report, researchers have expanded their genetic analysis to include a larger population of Cairn and Yorkshire Terriers afflicted with PSVA [congenital PSS] or MVD [PVH-MVD]. Cairn Terriers are representative of breeds like Tibetan Spaniels and Miniature Schnauzers with lower genetic trait prevalence (approximately 30 to 35%); Yorkshire Terriers are representative of breeds like Norfolk Terriers, Maltese, Havanese and Papillon with higher genetic trait prevalence (approximately 65 to 90%). Once genetic mutations responsible for PSVA and MVD are identified, the investigators plan to develop genetic tests that can identify carrier animals. These tests could be used to make breeding decisions which could reduce and eventually eliminate the occurrence of these disorders." (Center)

Based on Dr. Center's work, it may not be possible to have a genetic test that differentiates congenital PSS from PVH-MVD. In fact, they may simply represent variations of the same genetic conditions. We can also see that the risk of having the genes for either condition is very high in Yorkies and other toy breeds.

"Until a genetic test is available or the trigger for the condition is determined, it would be prudent to breed only dogs with the healthiest livers...Dogs with congenital PSS should not be bred."

—Tobias

What happens if you breed a dog with congenital PVH-MVD?

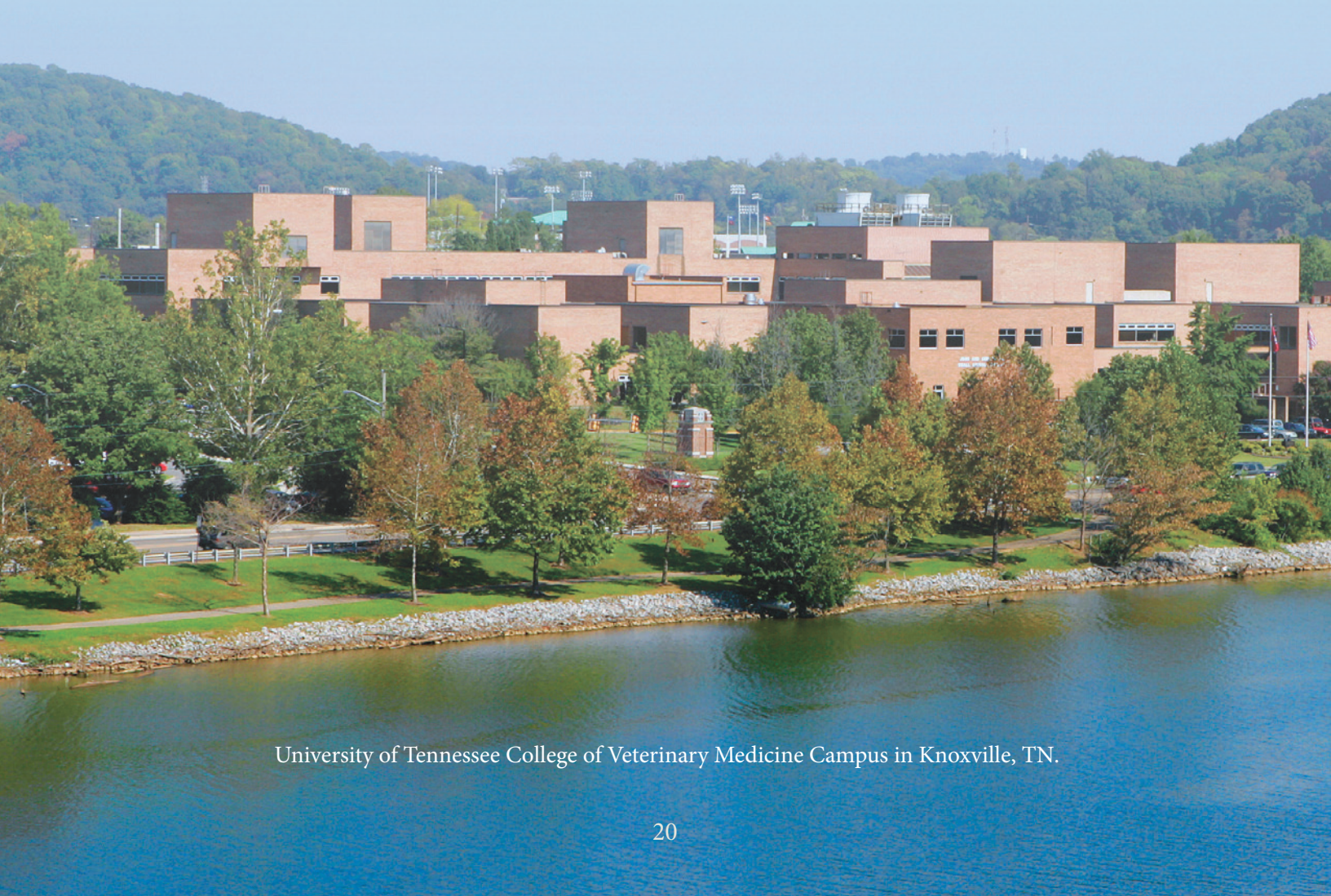
A very difficult question to answer is whether dogs with PVH-MVD should be bred. Based on results of breed analysis, PVH-MVD is an inherited condition. Congenital shunts are also considered hereditary in many breeds. It makes sense, therefore, that we should avoid breeding any dogs that have increased bile acids or other signs of liver disease. However, we can see from Dr. Center's work that many apparently healthy Yorkies carry these genes. Until a genetic test is available or the trigger for the condition is determined, it would be prudent to breed only dogs with the healthiest livers and to reduce inbreeding of affected dogs. Dogs with congenital PSS should not be bred. A reproductive specialist should be consulted for more information.



About the Author



Dr. Karen Tobias is a Professor of Small Animal Soft Tissue Surgery and an ACVS board-certified surgeon at the University of Tennessee College of Veterinary Medicine. She has published over 100 scientific articles and book chapters and is known nationally and internationally for her work on portosystemic shunts in dogs. Dr. Tobias has authored and edited several texts, including *Manual of Small Animal Soft Tissue Surgery* (Tobias; Wiley-Blackwell, 2010); *Veterinary Surgery: Small Animal* (Tobias & Johnston, eds; Elsevier-Saunders, 2011); and *Atlas of Ear Diseases of the Dog and Cat* (Paterson and Tobias; Wiley-Blackwell, 2012).



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