Portosystemic Vascular Anomalies

Allyson C. Berent, DVM[a,*], Karen M. Tobias, DVM, MS[b]

KEYWORDS

• Shunt • Extrahepatic • Intrahepatic
• Malformation • Embolization

Portosystemic shunts (PSS) are vascular anomalies that redirect blood from the portal vein to the systemic circulation, bypassing the hepatic sinusoids and liver parenchyma.[1–5] Normally, blood draining the stomach, intestine, spleen, and pancreas enters the portal vein and perfuses the liver through the sinusoidal network before entering the hepatic veins, and subsequently the caudal vena cava.[3] Portal blood contains nutrients, trophic hormones (intestinal and pancreatic), bacterial products, and intestinal-derived toxins.[1,2,6] The fetal liver has limited function to process these products, and a large shunting vessel (ie, ductus venosus) normally exists to bypass the hepatic circulation as a protective mechanism. This vessel normally closes shortly after birth, establishing hepatic circulation. If the ductus venosus remains patent, intrahepatic portosystemic shunting persists. Persistence of anomalous connections between the fetal cardinal and vitelline systems results in extrahepatic portosystemic shunting.[3,4]

When blood bypasses the liver, delivery of trophic factors (particularly insulin and glucagon) to the liver is decreased, resulting in poor hepatic development, decreased protein production, reticuloendothelial dysfunction, altered fat and protein metabolism, hepatic atrophy, and eventually hepatic failure. The severity of clinical signs is related to the volume and origin of blood bypassing the liver and may include hepatic encephalopathy (HE), chronic gastrointestinal signs, lower urinary tract signs, coagulopathies, and retarded growth.[2,3,5–7] In animals with portosystemic shunting, concentrations of endogenous and exogenous toxins that are normally metabolized or eliminated by the liver (ammonia, gut-associated encephalopathic toxins, hormone metabolism, benzodiazepine-like substances, aromatic amino acids, and so forth; **Table 1**) increase, whereas normal hepatic metabolic function (gluconeogenesis, urea cycle, uric acid cycle, and so forth)[7–10] decreases. This article discusses anomalous macroscopic venous-venous (portocaval or portoazygous shunts, congenital

[a] Sections of Internal Medicine and Surgery, Veterinary Hospital of the University of Pennsylvania, 3900 Delancey Street, Philadelphia, PA 19104, USA
[b] Department of Small Animal Clinical Sciences, University of Tennessee, 2407 River Drive, Knoxville, TN 37996, USA
* Corresponding author.
E-mail address: aberent@vet.upenn.edu (A.C. Berent).

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Table 1
Toxins implicated in HE

Toxins	Mechanisms Suggested in the Literature
Ammonia	Increased brain tryptophan and glutamine; decreased ATP availability; increased excitability; increased glycolysis; brain edema; decreased microsomal Na,K-ATPase in the brain
Aromatic amino acids	Decreased DOPA neurotransmitter synthesis; altered neuroreceptors; increased production of false neurotransmitters
Bile acids	Membranocytolytic effects alter cell/membrane permeability; blood-brain barrier more permeable to other HE toxins; Impaired cellular metabolism due to cytotoxicity
Decreased a-ketoglutaramate	Diversion from Krebs cycle for ammonia detoxification; decreased ATP availability
Endogenous benzodiazepines	Neural inhibition: hyperpolarize neuronal membrane
False neurotransmitters Tyrosine→ octapamine Phenylalanine → phenyethylamine Methionine → mercaptans	Impairs norepinephrine action Impairs norepinephrine action Synergistic with ammonia and short-chain fatty acids Decreases ammonia detoxification in brain urea cycle; derived from the gastrointestinal tract (fetor hepaticus–breath odor in HE); decreased microsomal Na,K-ATPase
GABA	Neural inhibition: hyperpolarize neuronal membrane; increase blood-brain barrier permeability to GABA
Glutamine	Alters blood-brain barrier amino acid transport
Phenol (from phenylalanine and tyrosine)	Syngergistic with other toxins; decreases cellular enzymes; neurotoxic and hepatotoxic
Short-chain fatty acids	Decreased microsomal Na,K-ATPase in brain; uncouples oxidative phosphorylation, impairs oxygen use, displaces tryptophan from albumin, increasing free tryptophan
Tryptophan	Directly neurotoxic; increases serotonin; neuroinhibition

Data from Refs.[2,6,8,9,19,20]

and acquired), venous-arterial (hepatic arteriovenous malformations [HAVM]), and microscopic venous-parenchymal communications (hepatic portal venous hypoplasia [PVH] or microvascular dysplasia [MVD]), involving communications between the portal vein and systemic circulation.

ANATOMY

The portal vein is formed by the convergence of the cranial and caudal mesenteric portal branches within the mesentery. It provides up to 80% of the blood flow (20% through

the hepatic artery) and 50% of the oxygen content (50% through the hepatic artery) to the liver.[1–7] Additional tributaries from the spleen, stomach, pancreas, and proximal duodenum join the portal vein before its bifurcation. In dogs the portal vein divides into left and right branches and the left branch divides further to supply the central and left lobes. In the cat the portal vein divides directly into left, central, and right branches.[3,5] The portal vein then branches into smaller venules whereby the blood enters the parenchyma at the portal triads, travels through the hepatic sinusoids, and drains to the central veins, which then confluence to larger hepatic venules and hepatic veins that drain into the caudal vena cava. As it travels through the sinusoids, the portal blood is delivered to the hepatocytes and cleansed by the reticuloendothelial system. If this path is interrupted by an anomalous vessel(s), blood is diverted away from the liver and reaches the systemic circulation before hepatic circulation and cleansing.

PSS can either be congenital or acquired. Congenital PSS most commonly occur as single vessels that provide direct vascular communication between the portal venous supply and the systemic venous circulation (caudal vena cava or azygous vein), bypassing the liver. They commonly occur as a single intra- or extrahepatic communication. Rarely some animals have 2 or more congenital communications. Twenty percent of dogs with PSS have multiple acquired shunts secondary to chronic portal hypertension. Increased portal pressures lead to the opening of fetal, vestigial blood vessels, which reduces the hydrostatic pressure load of the portal veins. Acquired shunts are usually multiple, tortuous, and extrahepatic in nature and are most frequently located near the kidneys. The most common causes for acquired extrahepatic shunts (EHPSS) are hepatic cirrhosis, noncirrhotic portal hypertension (NCPH), HAVM, and congenital PVH.

The types of congenital hepatic vascular malformations found in dogs and cats include single intrahepatic portocaval shunts, single extrahepatic portocaval shunts, portal vein atresia with resultant multiple portal-caval anastomoses, HAVM, and PVH (formally called microvascular dysplasia).[2,11] PVH can be seen with or without portal hypertension. For the purpose of this review, PVH without hypertension is referred to as MVD-PVH and PVH with hypertension as NCPH. Approximately 25% to 33% of congenital PSS are intrahepatic (IHPSS) in dogs and cats. Single EHPSS are noted in 66% to 75% of cats and dogs with congenital PSS, with the most common location being portocaval.[1–3,12] Most IHPSS are found in larger-breed dogs, whereas most EHPSS are seen in smaller breeds.[12] Some EHPSS, such as portoazygous or portophrenic shunts, may be associated with less severe clinical signs, possibly because of intermittent compression by the diaphragm or engorged stomach. Dogs with IHPSS generally have the largest volume of portal blood diverted through their shunt, resulting in more severe clinical signs at an earlier age.[1,2,13]

PVH without a macrovascular shunt is a microscopic pathologic malformation of the hepatic microvasculature, previously called MVD.[11] PVH can occur as an isolated disease or in association with macroscopic PSS. PVH can occur with or without concurrent portal hypertension. It has been suggested that MVD-PVH may represent persistent embryonic vitelline veins, resulting in direct shunting of blood from portal venules to central veins, and finally to the systemic circulation, resulting in microvascular shunting.[11,14] Clinical signs in dogs with MVD-PVH can be similar to PSS, although they are often less severe, present later in life, and have a better long-term prognosis with medical management alone. Breeds overrepresented are the Cairn terrier and Yorkshire terrier.[11,15] Animals with PSS or MVD-PVH have the same histologic changes and preoperative clinical signs, therefore the 2 conditions cannot be distinguished.

HAVM is a rare condition comprised of single or multiple high-pressure arterial and low-pressure venous communications. The condition, previously termed hepatic

arteriovenous fistulae (HAVF), is more appropriately named a malformation because most affected animals have numerous communications rather than a single fistula. The condition is usually congenital and has been described in dogs and cats.[16,17] Typically a branch of the hepatic artery communicates directly with the portal vein by multiple (tens to hundreds) aberrant shunting vessels within the liver. This creates a high pressure system, resulting in hepatofugal blood flow and arterialization of the portal vein. Because of excessive portal hypertension, multiple EHPSS open to decompress the portal system.[2,3,16]

PATHOPHYSIOLOGY

Most of the clinical signs associated with PSS result from HE, the pathogenesis of which is complex and largely unknown in our veterinary patients. HE is a neuropsychiatric syndrome involving a gamut of neurologic abnormalities that manifest if more than 70% of hepatic function is lost.[8,10,18–20] The healthy liver serves a filtration function against a multitude of neurotoxic substances that are absorbed across the gastrointestinal barrier. If liver function is altered or shunting occurs, the liver cannot appropriately perform its role in either metabolism or substance clearance. Toxic substances subsequently accumulate in the systemic circulation and alter multiple aspects of central nervous system (CNS) function. More than 20 different compounds can be found in increased concentrations in the circulation if liver function is impaired (**Table 1**).[8–10,18,19] Ammonia may be considered the most important because increased concentrations trigger a sequence of metabolic events that have been implicated in HE in rats, humans, and dogs.[9,10,18,19] Ammonia is the easiest substance measured in veterinary patients and treatments to decrease ammonia concentration reduce the signs of HE. The degree of encephalopathy is not well associated with the blood ammonia levels,[21] however, suggesting that other suspected neurotoxins are also important in the pathophysiology.

DIAGNOSTIC EVALUATION

Signalment

Congenital EHPSS are most commonly seen in the small- and toy-breed dogs. In a study of more than 2,400 dogs in North America, odds ratios for development of PSS were near 20 or greater for breeds such as the Yorkshire terrier, Havanese, Maltese, Dandie Dinmont terrier, pug and miniature Schnauzer.[5,12,22] In cats, EHPSS are more common,[3,23] although IHPSS have been reported.[24,25] PSS seem to be most commonly reported in domestic short hair, Persian, Siamese, Himalayan, and Burmese cats.[4,26–28] Intrahepatic shunts are overrepresented in larger-breed dogs with an increased prevalence in the Irish wolfhound, retriever (Labrador, golden), Australian cattle dog, and Australian shepherd.[3,4,26,29–31] Left divisional IHPSS have been considered heritable in the Irish wolfhound,[32,33] and right divisional IHPSS have been overrepresented in males and Australian cattle dogs in Australia.[31] Inheritance has been documented in the Maltese dog and is also believed to occur in the Yorkshire terrier.[3,4,34] The Cairn terrier has been documented to have hereditary MVD-PVH, which is believed to be an autosomal inherited trait; Yorkshire terriers are also overrepresented with this condition.[11,15]

History

Most dogs and cats evaluated for congenital PSS present with signs of chronic or acute illness at less than 1 to 2 years of age, although some animals have presented at greater than 10 years of age.[12,35] This condition is far more common in dogs than

cats. Median age of animals with multiple acquired EHPSS was 3 years (range 7 months to 7 years), and the median age of dogs diagnosed with MVD-PVH was 3.25 years (range up to 10 years).[2,11] There is no clear gender predisposition in dogs; however, male cats may be overrepresented.[1,2] The history typically suggests the patient has shown failure to thrive since birth, is small in stature (or the runt of the litter), has weight loss (11%) or failure to gain weight, has anesthetic intolerance, is dull or lethargic at times, and displays bizarre behavior (41%–90%; star-gazing, head-pressing, staring into walls or corners, random barking, intermittent blindness, pacing, or aggression).[1,2,5,12,36] Some animals present with a history of hematuria, stranguria, pollakiuria, or urinary obstruction (20%–53%). Polyuria and polydipsia (PUPD) are common complaints in dogs, and the cause has been associated with various theories, including increased secretion of ACTH and associated hypercortisolism, poor medullary concentration gradient because of a low blood urea nitrogen (BUN) level, increased renal blood flow, and psychogenic polydipsia from HE.[3,5,6] Correlation of the onset of signs with meal ingestion has been reported in only 30% to 50% of patients.[5] Gastrointestinal signs of vomiting, pica, anorexia, or diarrhea are also common.[2]

Abdominal effusion is seen in 75% of dogs with HAVM[16] and has been reported in dogs with congenital PSS and severe hypoalbuminemia. Abdominal effusion is most common if the animal has a concurrent protein-losing enteropathy, which can be associated with GI ulceration/bleeding or inflammatory bowel disease with or without lymphangiectasia. The author has found abdominal effusion to be common in dogs with IHPSS.

Clinical Signs

The 3 most common systems affected are the CNS, the gastrointestinal tract, and the urinary tract. Nonspecific signs have been described earlier. Signs of HE can be either obvious or subtle, and are typically associated with bizarre behaviors (as discussed earlier). More obvious CNS signs include ataxia, unresponsiveness, pacing, circling, blindness, seizures, and coma.[3,7,13,36] Gastrointestinal signs, such as vomiting, diarrhea, anorexia, or gastrointestinal bleeding/melena/hematemesis, occur in approximately 30% of dogs but are less frequent in cats.[5,12,13,24] Ptyalism is extremely common in cats (75%) and is believed to be a manifestation of HE or gastrointestinal upset.[5,6,24,36]

Signs of lower urinary tract disease (stranguria, pollakiuria, hematuria, dysuria) are common in dogs with PSS. Because of decreased urea production, increased ammonia excretion, and decreased uric acid metabolism, ammonium urate stones may develop. These were documented in 30% of patients with PSS in 1 study and can result in secondary bacterial urinary tract infections.[12]

Other congenital defects reported in animals with PSS include cryptorchidism (up to 30% of cats and 50% of dogs in some studies) and heart murmurs.[3,5,37,38] Copper-colored irises inappropriate for the breed have also been documented, particularly in cats.[39] Animals with MVD-PVH have a similar signalment and clinical signs to those described earlier, although these animals are typically older and their signs are milder.[5,11]

Intrahepatic PVH with associated portal hypertension has been described in a variety of breeds of dogs.[40,41] This condition has recently been termed idiopathic NCPH. Other names for this similar condition include hepatoportal fibrosis,[42] idiopathic hepatic fibrosis,[43] veno-occlusive disease,[44] and nonfibrosing liver disease.[45] Diagnosis is based on the presence of portal hypertension with a patent portal vein and lack of cirrhosis on liver biopsy. Affected animals are often purebred

dogs; Doberman pinchers (27% of dogs) are overrepresented. Dogs most affected are less than 4 years of age and weigh more than 10 kg.[40] Signs are similar to those of PSS or cirrhosis; concurrent portal hypertension results in ascites (in 60%), PUPD, gastrointestinal upset, HE, weight loss and multiple EHPSS. The underlying cause of this condition is unknown but speculation includes severe, diffuse intrahepatic vascular malformations without concurrent cirrhosis, resulting in portal hypertension.

Clinical signs associated with HAVM result from PSS and portal hypertension. The condition has been reported in dogs of all sizes and in a small number of cats.[5,16] Gastrointestinal signs are common, and many dogs present with stunted growth and lethargy.[16] Ascites was documented in 75% of dogs, and heart murmurs were documented in 20%.[16] Signs of HE are reported less frequently with HAVM. In some animals, the sound of turbulent blood flow (bruit) can be heard over the fistula when the liver is auscultated.

CLINICAL DIAGNOSIS

Clinicopathologic Findings

In animals with PSS, the most common hematological changes include mild to moderate, microcytic, normochromic nonregenerative anemia (60%–72% of dogs, 30% of cats).[3,46,47] The cause of the microcytic anemia is not fully known, although studies suggest a defective iron-transport mechanism, decreased serum iron concentrations, decreased total iron-binding capacity, and increased hepatic iron stores in Kupffer cells. This suggests that iron sequestration may be the cause.[3,46,47] Typically, microcytosis resolves after shunt fixation. Microcytosis is not reported in dogs with MVD-PVH.[5,11] Erythrocyte target cells are commonly seen on morphology evaluation in dogs and poikilocytes in cats.[48] Leukocytosis can occur and is suspected to be secondary to stress or inadequate hepatic endotoxin and bacterial clearance.[1,2,12,29,49]

Serum biochemical abnormalities are extremely common in animals with PSS. In dogs the most common deficiencies include hypoalbuminemia (50%), decreased BUN (70%), hypocholesterolemia, and hypoglycemia, which result from decreased hepatic synthesis. In cats hypoalbuminemia is uncommon, but decreased BUN concentrations are typical.[24,50] Mild to modest increases (2- to 3-fold) in alkaline phosphatase (ALP) and alanine aminotransferase (ALT) are also reported. These abnormalities are typical of any hepatic vascular anomaly and levels of biochemical changes are not a hallmark for any 1 of these particular conditions. The ALP is typically higher than the ALT with PSS and likely secondary to increased bone isoenzyme in growing animals.[5]

Abnormalities on urinalysis include decreased urine specific gravity (>50% are hyposthenuric or isosthenuric) and ammonium biurate crystalluria.[3,5,36,51] Decreased urine specific gravity most likely results from polydipsia and poor medullary concentration gradient.[6,51] Hyperammonuria from a deficient hepatic urea cycle, along with inappropriate uric acid metabolism, results in excessive ammonia and urate excretion in the kidneys and ultimately ammonium biurate crystalluria (26%–57% of dogs and 16%–42% of cats)[38,52,53] or stone formation (30% of dogs in 1 study).[12,39,51] Proteinuria can be seen and this is suspected to be secondary to glomerular sclerosis or another glomerulopathy. In 1 study of 12 dogs, 100% had evidence of a moderate to severe glomerulofibrosis or membranoproliferative glomerulonephritis.[54] This link between severe liver disease and glomerulonephritis has been seen in humans for many years and has been speculated to be secondary to the accumulation of antigens bypassing hepatic clearance.[55]

Liver function testing

Fasting (12 hours) and 2-hour postprandial serum bile acids (SBA) are the most widely used tests for evaluating liver function in animals with PSS. Bile acids, which are synthesized in the liver from cholesterol, conjugated, secreted into the bile canaliculi, and stored in the gallbladder, are then released into the duodenum after a meal, aiding in fat emulsification, metabolism and lipid absorption. Bile acids are reabsorbed from the ileum, transported into the portal venous system, and extracted by hepatocytes for recirculation.[56,57] By measuring these levels this entire circuit is evaluated. Bile acid concentrations are affected by the timing of the gallbladder contraction, the rate of intestinal transport, the degree of bile acid deconjugation in the small intestine, the rate and efficiency of bile acid absorption in the ileum, the portal blood flow, and the function of the hepatocyte uptake and canalicular transport. Although increases in postprandial bile acids have been found to be 100% sensitive for detection of a PSS in dogs and cats in some studies,[56,58] others have found that paired samples are 100% sensitive, but not individual measurements. There is a small subset of animals that have normal postprandial bile acids with elevated fasting samples, and an even larger number that have normal fasting and elevated postprandial bile acids.[12,56] It has also been found that normal Maltese dogs have elevated serum bile acids without evidence of hepatocellular dysfunction. Increases in bile acids are not specific to PSS and have been reported with other hepatobiliary diseases, cholestasis, glucocorticoid or anticonvulsant therapy, tracheal collapse, seizures, and gastrointestinal disease.[48,59]

If a false-negative bile acid test is suspected, measurement of plasma ammonia can be performed. Basal ammonia in fasting animals is close to 100% sensitive[60] so that an ammonia tolerance test is rarely necessary to detect PSS. Bile acid concentrations have been shown to be somewhat less sensitive but also considerably less specific than ammonia to detect portosystemic shunting.[60,61] An ammonia tolerance test (ATT) is always abnormal in dogs with PSS[62,63] but should be avoided in animals in which the basal value is already highly increased.[62,63] The ATT gives semiquantitative values of the degree of portosystemic shunting and can therefore be used to evaluate the postoperative course after surgical attenuation of the shunt. The ATT can be performed by administration of ammonium chloride orally or rectally. The rectal route is much better tolerated and easy to perform, and is therefore the best way for routine use. Samples are evaluated before and 30 minutes after (or 20 and 40 minutes for semiquantitative analysis[62]) ammonium chloride administration (100 mg/kg [not to exceed 3 g]; 2 mL/kg of a 5% solution in water) with a deep rectal catheter. Plasma separation and laboratory analysis need to be done within 20 minutes of sample collection, making this test difficult to perform in many practices. However, nowadays a reliable and affordable desktop analyzer brings this sensitive and specific test for portosystemic shunting within reach for routine use.[61] Prolonged fasting, a low-protein diet, and administration of lactulose may decrease the basal ammonia concentration, but they do not affect the ATT.[12,38,64,65] False-positive tests in Irish wolfhound puppies[66] have been documented due to an inborn error of ammonia metabolism in this breed.[12]

Coagulation profiles

Prolonged coagulation times are found in most dogs with PSS before fixation; however, spontaneous bleeding is rare and does not usually occur until surgical intervention is attempted.[67,68] In 1 study, postoperative mortality increased in those dogs that had a dramatic worsening of their coagulopathy after surgical fixation.[69] Because the liver parenchymal cells synthesize most of the clotting factors (I, II, V, IX, X, XI, and XIII [and VIII by way of the liver vascular endothelium]), animals in liver failure, as seen

in PSS, would be expected to have deficiencies in some of these factors. Approximately 65% to 80% of factor loss must occur before prothrombin time (PT) or activated partial thromboplastin time (PTT) becomes prolonged.[10,67] The liver is also involved in the regulation of coagulation by aiding in the clearance of the activated factors so that regeneration of inactivated factors and fibrinolytic factors can occur.[67–71] Dogs with PSS may have prolonged PTT, without prolonged PT, potentially because of impaired hepatic synthesis, qualitative abnormalities, and clearance of coagulation factors.[67–71] The factors that were evaluated to be deficient involved the common (factors II, V, and X) and the extrinisic pathway (factor VII), which suggests that the PT should be prolonged as well. The exact reason for this has not been clarified.[67] Platelet counts in dogs with PSS were also lower preoperatively than in normal dogs and even more so after surgery (a 27% decrease from baseline).[67] This may be supportive of a postoperative consumptive coagulopathy.

Abdominal effusion

Ascites is rarely seen in dogs with single congenital PSS unless there is severe hypoproteinemia, severe GI bleeding, or portal hypertension (HAVM, NCPH, or acquired multiple EHPSS). Typically, the fluid for any of these conditions would be a clear pure transudate.[48]

Histopathology

Most dogs with congenital PSS have microscopic changes in liver biopsy samples, including ductular proliferation, hypoplasia of intrahepatic portal tributaries, hepatocellular atrophy (lobular), arteriolar proliferation or duplication, lipidosis and cytoplasmic vacuolar changes (lipogranulomas), smooth muscle hypertrophy, increased lymphatics around central veins, and Ito cell and Kupffer cell hypertrophy.[6,51,72–75] Some animals have evidence of mild fibrosis around the central veins, and some have signs of necrosis or inflammation.[5,6,72] One recent article evaluating histopathologic data and prognosis in dogs with congenital macroscopic EHPSS or IHPSS did not find any statistical association between histologic features and survival times.[72] Another recent article investigated the presence of lipogranulomas in liver biopsy samples of dogs with PSS (55.4% of cases).[75] Lipogranulomas were defined as focal lesions consisting of cells (Kupffer cells or macrophages) with cytoplasmic brown pigments (ceroid and hemosiderin) and lipid vacuoles.[75] Although some investigators have suggested an association between lipogranulomas and a poor prognosis, no evidence of this has been documented.[72]

Histologic changes in dogs with PVH-MVD and NCPH are similar to those with macroscopic congenital shunts.[11,40–45] Dogs with NCPH often have more significant fibrosis extending along the portal tracts or bridging to other portal areas and central veins.[40] Biopsies from unaffected liver lobes in dogs with HAVM also show similar findings to those with venovenous PSS. The liver tissue in close proximity to the malformation often has largely dilated portal venules, marked arteriolar hyperplasia and muscular proliferation, and sinusoidal capillarization. Some portal veins have evidence of thrombus formation and recanalization.[5,16]

Diagnostic Imaging

PSS are easily diagnosed with various imaging modalities. Survey abdominal radiographs often show microhepatica (60%–100% of dogs and 50% of cats)[3,5] and bilateral renomegaly. In dogs with PVH the liver and kidneys are often normal in size.[5,11,15] Marginally radiopaque calculi can be seen in the bladder, ureters, or kidneys. To diagnose a macroscopic shunt definitively, imaging such as abdominal ultrasonography

(AUS), angiography (portal or arterial), computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) is needed.

Abdominal ultrasonography

Ultrasound is the most widely used diagnostic tool for PSS in many practices. It is noninvasive, does not require general anesthesia like angiography (although sedation makes finding EHPSS more reliable in many circumstances), and does not require special licensing/handling (like scintigraphy). Decreased numbers of hepatic and portal veins, a subjectively small liver, and an anomalous vessel are readily seen with ultrasound in PSS. Extrahepatic shunts are typically more difficult to diagnosis due to the small patient and vessel size, and the presence of gas in the bowel and lungs obscuring the image. Multiple EHPSS are often harder to find, and are typically located near the kidney. There is considerable variation in the reported accuracy of ultrasonography for detection of shunts (sensitivity 74%–95% and specificity 67%–100%).[76–78] Overall sensitivity is higher for IHPSS (95%–100%).[5,76] The results of ultrasound are dependent of the equipment, operator, and experience. Using a well-evaluated protocol for ultrasonographic examination, it is possible to reach high sensitivity and specificity.[79] Color-flow and pulse-wave Doppler imaging are useful to look for changes in flow direction; classically, HAVM have hepatofugal flow, and venous-venous shunts have hepatopedal flow in the portal vein. Ultrasound is also useful for detecting uroliths in dogs and cats with vascular anomalies.[76,80]

Scintigraphy

Transcolonic scintigraphy is a useful, noninvasive method for detecting PSS. Technetium pertechnetate (^{99m}Tc pertechnetate) is the radioisotope most commonly used.[81] A bolus of the isotope is infused high into the colon, per rectum, and the animal is imaged using a gamma camera. In animals, the isotope is taken up by the colonic veins, which drain to the caudal mesenteric vein and then the portal vein. In a patient with a PSS, the isotope is delivered from the portal vein to the heart, bypassing the liver, and then returning to the liver through the arterial circulation. In a normal patient, it should take approximately 8 to 14 seconds before it reaches the heart, reaching the liver first.[81] If a shunt is present, a shunt fraction can be calculated, giving an estimate of the percentage of portal blood bypassing the liver. A fraction <15% is considered normal, with most dogs with shunt having fractions >60%. Some cats (52% in 1 study) have lower fractions than dogs.[82] There is considerable variation in shunt fraction calculations so comparisons at different time points are difficult and should not be used to assess changes reliably.[83] The half-life of technetium pertechnetate is 6 hours, so animals must be isolated for at least 24 hours after the procedure. Transcolonic scintigraphy does not give morphologic information on the type and location of the shunt, cannot differentiate IHPSS from EHPSS, and cannot differentiate between a single or multiple shunts. The information obtained with transcolonic scintigraphy is therefore comparable with that of the ammonia tolerance test. Scintigraphy is typically normal in dogs with MVD-PVH if there is no macrovascular PSS.[16] Another group evaluated the use of trans-splenic portal scintigraphy for the diagnosis of PSS, using $^{99M}TCO_4^-$.[84] Trans-splenic scintigraphy was useful for differentiating portoazygous from portocaval shunts, MVD-PVH from PSS, and, in some patients, single congenital from multiple acquired shunts. Clearance times are faster with trans-splenic scintigraphy and a smaller amount of radionuclide is used, reducing exposure to personnel.

Computed tomographic angiography (CTA)

Computed tomographic angiography is the gold standard for the evaluation of the portal venous system in human medicine.[85] It is noninvasive, fast, and provides

images of all portal tributaries and branches from a single peripheral venous injection of contrast. CTA can be performed with accuracy in dogs and cats of any size, and images can be reconstructed and manipulated for further evaluation after the study is complete. Dual-phase CTA provides a complete evaluation of portal and hepatic vasculature and is considered superior to single-phase CT.[86] This study is most valuable in animals with suspected IHPSS or HAVM or in animals in which ultrasound is not clear and more invasive imaging is not desired. CTA is helpful in planning surgical or interventional radiologic (IR) approaches to IHPSS or HAVM, which can eliminate excessive liver dissection or manipulation, and minimizing contrast load during IR procedures.

Magnetic resonance angiography

MRA also provides a three-dimensional preoperative image of the shunt(s), aiding in preprocedural planning. Magnetic resonance imaging without the use of gadolinium-enhanced angiography was less promising with sensitivities ranging from 63% to 79%, although the specificity was 97%.[5]

Portovenography

Portography is less commonly performed in many large facilities than previously because of availability of less invasive imaging modalities (ultrasound, scintigraphy, CT angiography). Surgical mesenteric portography is the most commonly performed angiographic diagnostic test for documenting PSS in dogs and cats. This procedure requires a laparotomy, portable fluoroscopy (C-arm; or closing an abdomen after jejunal or splenic vein catheterization to transport the patient to a standing fluoroscopy unit, and then returning to the operating room for shunt repair), and intravenous contrast material. Sensitivity of intraoperative portography has been reported to be between 85% and 100% and is dependent on patient positioning.[3–5] An alternative to surgical portal venography is percutaneous ultrasound-guided splenic venography, performed with simultaneous ultrasound access and fluoroscopic evaluation of contrast material. Caudal EHPSS can be missed with this technique if the portal branch communicates with the caudal vena cava in a more caudal location than the splenic vein and retrograde flow is absent. Injection of contrast material into the mesenteric artery (cranial mesenteric arteriography) with access through the femoral artery has also been performed, but is less in favor than other modalities due to its more invasive nature and the difficult interpretation of portal flow after venous dilution of contrast occurs (**Table 2**).[1–3,5,6,8]

TREATMENT

Medical Management

Medical management of animals with portovascular anomalies is required in patients with MVD-PVH or NCPH, or for macrovascular shunts for which surgery is not possible or declined, and is recommended before surgical or IR treatment. Medical management controls the clinical signs associated with shunting but does not treat the underlying diminished hepatic perfusion from the portal vein.

When a patient presents with signs of HE, abrupt stabilization is required and aggressive efforts to decrease the ammonia levels to near normal should be implemented. Intravenous fluid therapy to replace and maintain hydration is necessary if an animal presents recumbent and unable to drink, or dehydrated from gastrointestinal fluid losses. Potassium supplementation is often needed due to potassium depletion from chronic diarrhea; hypokalemia may also contribute to HE.[8,36] Metabolic acidosis may also contribute to HE and should be corrected slowly with fluid therapy.

Table 2
Medical managements of portal vascular anomalies

Symptom	Therapy
Bacterial translocation/decreasing bacterial byproduct absorption (ammonia)	Cleansing enemas with warm water or 30% lactulose solution at 5–10 mL/kg Oral lactulose: 0.5–1.0 mL/kg by mouth every 6–8 h to effect 2–3 soft stools/d Antibiotics Metronidazole 7.5 mg/kg intravenously or by mouth every 12 h Ampicillin 22 mg/kg intravenously every 6 h Neomycin 10–22 mg/kg PO q8h (avoid if any evidence of intestinal bleeding, ulcerations or renal failure)
Coagulopathy (symptomatic; postoperative)	Fresh frozen plasma 10–15 mL/kg over 2–3 h Vitamin K_1 1.5–2 mg/kg subcutaneously or intramuscularly every 12 h for 3 doses then every 24 h
Gastrointestinal ulceration (common with IHPSS, treat before intervention) (common with HAVM due to portal hypertension)	Antacid Famotidine 0.5–1 mg/kg/d intravenously or by mouth Omeprazole 0.5–1 mg/kg/d by mouth Esomeprazole 0.5 mg/kg intravenously every 12–24 h Misoprostol 2–3 μg/kg by mouth every 12 h Protectant Sucralfate 1 g/25 kg by mouth every 8 h Correct coagulopathy
Seizure control	Benzodiazepines (controversial) Phenobarbital (16 mg/kg intravenously, divided into 4 doses for loading over 12–24 h) Potassium bromide (should be avoided in cats because of bronchospasm) Loading 400–600 mg/kg/d divided over 1–5 d by mouth with food; can be given per rectum if needed Maintenance 20–30 mg/kg/d by mouth Sodium bromide can be used if an intravenous form is necessary Propofol 0.5–1.0 mg/kg intravenous bolus, CRI at 0.05–0.1 mg/kg/min (controversial)
Decrease cerebral edema	Mannitol 0.5–1.0 g/kg bolus over 20–30 min
Nutritional support	Moderate protein restriction 18%–22% for dogs and 30%–35% for cats (on dry matter basis); dairy or vegetable proteins preferred Vitamin B complex supplementation (1 mL/L intravenous fluid therapy) Multivitamin supplementation
Hepatoprotective therapy (for chronic conditions that are unable to be fixed MVD, NCPH, MEHPSS, and so forth)	*S*-Adenosylmethionine (SAMe) 17–22 mg/kg/d by mouth Ursodeoxycholic acid 10–15 mg/kg/d Vitamin E 15 IU/kg/d Milk thistle (silymarin) 8–20 mg/kg divided every 8 h L-Carnitine 250–500 mg/d (cats)

Glucose should be supplemented in the intravenous fluids, particularly in young puppies with PSS in which glycogen stores and gluconeogenesis are minimal. Therapy for HE includes cleansing enemas with warm water or lactulose, oral lactulose therapy, antibiotic therapy (metronidazole, ampicillin, or neomycin), and anticonvulsant therapy if necessary. Using a benzodiazepine antagonist, such as flumazenil, has been shown to be of benefit in humans with HE-induced coma, because GABA and its receptors have been implicated in HE.[8] Mannitol is often considered in patients with severe HE, or after significant seizure activity. In humans there is an association between HE and cerebral edema.[2,8]

Seizure control is often initiated with low-dose midazolam (a benzodiazepine that is preferred to diazepam due to the lack of propylene glycol as a carrying agent, which requires liver metabolism). Once the seizure is controlled, loading with either phenobarbital, potassium bromide, or sodium bromide can be considered (doses are given in **Table 2**).

Lactulose, a disaccharide that is metabolized by colonic bacteria to organic acids, can be administered either by enema or orally. It promotes the acidification of colonic contents, trapping ammonia in the form of ammonium, while decreasing bacterial numbers and eliminating ammonium and bacteria in the feces. The osmotic effect will result in catharsis, reducing fecal transit time and exposure to bacteria for proliferation and ammonia production. Antibiotics will decrease GI bacterial numbers, allowing for a decrease in ammonia production, and will help to decrease the risk of associated bacterial translocation and systemic bacterial infections. In patients that have signs of bleeding, or are significantly anemic or coagulopathic, packed red blood cells, whole blood, or fresh frozen plasma may be of benefit. If there is evidence of HE, fresh whole blood should be used, because stored blood has high ammonia levels.

Nutritional management is important in patients, particularly young animals, that have extremely poor body conditions. The diet should be readily digestible, contain a protein source of high biologic value (enough to meet the animal's needs, but not enough to encourage HE), supply enough essential fatty acids and maintain palatability, and meet the minimum requirements for vitamins and minerals. Low-protein diets should not be used routinely unless HE is noted. Milk and vegetable proteins are lower in aromatic amino acids (tyrosine and phenylanaline) and higher in branched-chain amino acids (BCAA), such as valine, leucine, isoleucine, than animal proteins. These sources are less likely to precipitate HE.[2,8]

Gastric bleeding/ulceration should be treated with acid receptor blockade, such as famotidine or omeprazole, along with sucralfate. Animals with IHPSS and HAVM have a predisposition to the development of gastrointestinal ulcerations.[83,84] Since the authors started life-long antacid therapy in dogs with IHPSS, the morbidity associated with GI bleeding has decreased dramatically (see section on Interventional Radiologic Management). For the same reason, nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided in any dog with IHPSS or HAVM.

Ascites and fibrosis may be seen in patients with HAVM and NCPH, as discussed earlier. It is rarely seen in animals with PSS unless there is severe hypoalbuminemia. If ascites results from decreased oncotic pressure, colloidal therapy should be considered. If the ascites is secondary to portal hypertension, administration of diuretics and a low-sodium diet should be considered. Spironolactone is the initial diuretic of choice because of its potassium-sparing effects. Furosemide may be necessary as well but should be used with caution, because it potentiates further hypokalemia. There are several drugs that theoretically decrease connective tissue formation and may be helpful in patients with hepatic fibrosis. Prednisone (1 mg/kg/d), D-penicillamine (10–15 mg/kg twice a day), and colchicine (0.03 mg/kg/d) have been recommended.

Supportive nutraceutical therapy has been recommended for a variety of liver diseases and is usually unnecessary in portovascular anomalies that can be fixed either surgically or interventionally. Nutraceuticals that may be useful for animals that do not have a correctable condition (MVD, NCPH, multiple EHPSS) include *S*-adenosyol-L-methionine (SAMe), ursodeoxycholic acid, vitamin E, and milk thistle (silymarin).

Progonsis with Medical Management Alone

Prospective studies on the medical management of dogs or cats with portosystemic vascular anomalies have not been reported. In 1 retrospective study of 27 dogs with congenital PSS evaluated after long-term medical management alone, 52% were euthanized with a median survival time (MST) of 9.9 months and 15% were lost to follow-up. One third of the animals survived long term (MST of 56.9 months; range 5 months to >7 years), with many of those still alive at the time of evaluation.[29] Of the 27 dogs, 9 had EHPSS and 17 had IHPSS. Dogs with IHPSS on medical management alone often had persistent neurologic signs with treatment compared with dogs with EHPSS whose clinical signs were either similar or occurred less often once medicated.[29] Of dogs with IHPSS, 65% were euthanized, mostly due to uncontrolled signs of HE. One third of dogs with EHPSS were euthanized because of persistent clinical signs. There were no correlations between levels of bile acid, serum protein, albumin, ALP, ALT, and MCV and survival times.[29]

Presurgical Considerations

Patients that are cachectic, encephalopathic, or unstable should be managed medically until they can tolerate the stress of anesthesia and surgery (as discussed earlier). Patients in poor body condition or young animals should be managed medically with a strong effort to put on weight before shunt fixation. One study of IHPSS found a worse outcome in dogs <10 kg at the time of shunt fixation.[87] Cats with preoperative, uncontrolled, generalized seizures should be given phenobarbital (2–4 mg/kg every 8 to 24 hours) 2 to 4 weeks before surgery, with the final dosage ultimately based on blood levels and response to therapy. In dogs with preoperative generalized seizures, potassium bromide is preferred because of limited hepatic effects. Prophylactic use of anticonvulsants is not recommended in patients that are not seizing before surgery.

Anesthetic agents that are metabolized by the liver, highly protein-bound, or hepatotoxic should be used with caution because of poor hepatic function and hypoalbuminemia. Anesthesia can be induced with opioids, propofol, or mask delivery of isoflurane or sevoflurane in oxygen, and maintained with isoflurane or sevoflurane. Intraoperative treatment with hetastarch or dextrose (2.5%–5%) is recommended in patients with hypoalbuminemia or hypoglycemia, respectively.

Exploratory Laparotomy

A definitive diagnosis of extrahepatic PSS can usually be made during exploratory laparotomy if the veterinarian is familiar with the anatomy of the abdomen.[83] Most extrahepatic portocaval shunts terminate on the caudal venal cava cranial to the renal veins at the level of the epiploic foramen. Occasionally, they may travel along the lesser curvature of the stomach and terminate on the phrenic or left hepatic vein cranial to the liver. Portoazygous shunts usually traverse the diaphragm at the level of the crura or aortic hiatus. Thorough exploration is warranted in all dogs with single congenital PSS because of the possibility, although rare, of a second shunt.[12,88] In addition, the bladder should be palpated for calculi if preoperative ultrasonography was not performed. IHPSS are more difficult to detect during exploratory surgery. If

not readily visible, they may be located intraoperatively by palpation, portography, ultrasound, catheterization by way of the portal vein, or measurement of portal pressure changes during digital vascular occlusion or portal or hepatic vein branches.[3]

Many surgeons obtain liver biopsies to provide a basis for future comparison. Unfortunately, preligation liver biopsies cannot be used to differentiate or prognosticate animals.[72] Because PSS are considered hereditary in many breeds, castration or ovariohysterectomy of affected animals is recommended.[89,90]

Surgical Options for Shunt Occlusion

Congenital PSS can be completely or partially ligated with nonabsorbable sutures or gradually attenuated with an ameroid constrictor, cellophane band, or hydraulic occluder.[69,91–96] Gradual attenuation is preferred to reduce the risk of postoperative complications. Extrahepatic shunts are occluded as close to their terminus as possible to reduce blood flow from shunt tributaries. Blood flow through intrahepatic shunts is usually reduced by attenuating the portal vein branch supplying the shunt or the hepatic vein draining the shunt.[97] Rarely, intrahepatic shunts are approached through a venotomy during inflow occlusion.[98,99]

Suture ligation

Shunt ligation in dogs is often performed with silk because of its superior handling characteristics. Nonabsorbable synthetic monofilament is recommended in cats because of the risk of shunt recanalization.[27] Nonencephalopathic dogs can often tolerate complete shunt ligation; however, up to 80% of animals undergoing acute shunt occlusion require partial attenuation.[69,100] Degree of attenuation is based on visual inspection for evidence of portal hypertension, such as pallor or cyanosis of the intestines, increased intestinal peristalsis, cyanosis or edema of the pancreas, and increased mesenteric vascular pulsations.[101] In addition, the surgeon can measure portal and central venous pressures. Recommendations for postligation pressures include a maximum portal pressure to 17 to 24 cmH_2O, maximal change in portal pressure of 9 to10 cmH_2O, and maximal decrease in central venous pressure of 1 cmH_2O.[3] Objective pressure measurements should not be used as the sole criterion for degree of shunt attenuation, because blood pressures can vary with depth of anesthesia, hydration status, phase of respiration, degree of splanchnic compliance, and other systemic factors.

Pre- and postligation, intraoperative mesenteric portograms have been used to evaluate portohepatic blood supply in animals undergoing suture attenuation of congenital PSS. Absence of arborizing intrahepatic vasculature on preligation portograms has been correlated with greater occurrence of postoperative complications.[74,97]

Long-term outcome, however, is not correlated with portogram findings before or after temporary shunt occlusion.[102] Results of intraoperative mesenteric portography cannot be used to determine the degree of shunt attenuation.[103]

Some investigators recommend second surgery for animals undergoing partial suture ligation of congenital PSS.[96,102,104] Partially attenuated shunts can be completely ligated during a subsequent surgery in 75% of animals.[96] Liver function returns to normal in up to 70% of dogs undergoing a single partial ligation, however, indicating that many shunts continue to narrow after the initial attenuation.[69,95,105]

Ameroid constrictors

Ameroid constrictors (Research Instruments N.W., Inc, Lebanon, OR 97355; researchinstrumentsnw.com) have an inner ring of casein that is surrounded by a stainless steel sheath. Casein is a hygroscopic substance that swells as it slowly absorbs

body fluid, reducing the ring's internal diameter by 32%.[95] It also stimulates a fibrous tissue reaction that results in gradual shunt occlusion over 2 or more weeks. In some animals, thrombus formation could result in more rapid obstruction of partially attenuated shunts. The choice of ameroid constrictor size for PSS occlusion is based on shunt diameter; preferably, the constrictor should have an internal diameter larger than the shunt. Extrahepatic PSS are most commonly attenuated with ring of 5 mm inner diameter; intrahepatic shunt attenuation may require rings of 5 to 9 mm inner diameter.

Before placement of an ameroid constrictor, the perivascular fascia is gently dissected away from the shunt. Dissection should be minimized to prevent postoperative movement of the ring and subsequent acute shunt occlusion. The ameroid constrictor is slipped over the flattened vessel, and the slot in the constrictor ring is obstructed with a stainless steel key. Measurement of portal or central venous pressures is unnecessary with ameroid constrictor placement as long as the shunt is not attenuated at the time of surgery.

Cellophane bands

Cellophane bands can be constructed from clear, nonmedical-grade cellophane like that used to wrap flowers and candy baskets. The cellophane is cut into 1 by 10 cm strips and gas sterilized. During surgery, a strip is folded longitudinally into thirds to make a thick, flexible band. The shunt is dissected with right-angle forceps, which are then used to gently thread the band around the shunt. The band is held in place by securing the ends together with surgical clips; excess cellophane is removed 1 to 2 cm beyond the clips. Like ameroid constrictors, cellophane bands cause fibrous tissue reaction and gradual shunt occlusion.[95] Initially, attenuation of the shunt to less than 3 mm in diameter was performed to encourage complete shunt closure.[26] In more recent studies, complete occlusion was demonstrated in dogs and cats that underwent cellophane banding without intraoperative attenuation.[92,106]

Hydraulic occluders

Hydraulic occluders has been used for gradual attenuation of IHPSS.[91] A hydraulic occluder consists of a silicone and polyester cuff (DOCXS Biomedical Products and Accessories, Ukiah, CA) connected by tubing to a vascular access port (Access Technologies, Skokie, IL).[91,95] The cuff is secured around the shunt with suture and the attached access port is inserted under the skin. After surgery, a small amount of sterile saline is injected through the port every 2 weeks to gradually inflate the cuff. Shunt closure usually occurs in 6 to 8 weeks and is not dependent on fibrous tissue formation.[91] In most animals, the vascular access port is left in place permanently.

Complications of Portosystemic Shunts Attenuation

Acute complications of shunt attenuation include refractory hypoglycemia, prolonged anesthetic recovery, hemorrhage, seizures, intraoperative hemorrhage, and portal hypertension. Hypoglycemia occurs in 44% of dogs after EHPSS attenuation and is refractory to dextrose administration in 29% of affected dogs.[107] Dogs that have refractory hypoglycemia or delayed anesthetic recovery may respond to glucocorticoid administration (eg, dexamethasone, 0.1–0.2 mg/kg intravenously). In dogs that have undergone acute shunt ligation, packed cell volume, platelet count, and coagulation times should be monitored because platelet count and coagulation factor activity significantly decrease after surgery, as discussed earlier.[67]

Clinical signs of portal hypertension include pain, abdominal distension from ileus or ascites, decreased central venous pressure, prolonged capillary refill time, pale mucous membranes, poor peripheral pulses, and gastrointestinal hemorrhage.[3,89]

Acute portal hypertension is most commonly seen in animals undergoing suture ligation. Mild portal hypertension may result in ascites and wound drainage and is usually self-limiting. Ascites may improve with administration of hetastarch. Animals with severe ascites may require diuretics or abdominal drainage if respiration is compromised. Moderate portal hypertension is treated with intravenous crystalloids, hetastarch, gastrointestinal protectants (eg, omeprazole and sucralfate) and systemic antibiotics. Affected animals are evaluated for hypotension and evidence of disseminated coagulopathy (DIC). Ligature removal should be performed immediately in animals with severe clinical signs, such as DIC, or hypotension that does not respond to fluid therapy. Multiple EHPSS have been reported to occur after ameroid placement in dogs and cats for single congenital EHPSS in nearly 10% to 20% of cases.[5]

Postoperative seizures develop in 3% to 7% of dogs and 8% to 22% of cats after shunt attenuation.[12,35,50,69,88,92–94,96,102,105,108] Seizures may occur up to 80 hours after surgery and are not associated with hypoglycemia, hyperammonemia, or attenuation technique. Initial treatment includes intravenous boluses of midazolam or propofol. If seizures persist or reoccur, the animal is anesthetized with an intravenous bolus of propofol (5–8 mg/kg) and maintained under anesthesia on a propofol continuous-rate infusion (CRI; 0.1–0.2 mg/kg/minute). There is a suggestion that propofol may not eliminate cerebral seizure activity when monitored on EEG, and other injectable anticonvulsants should be considered, although in the authors' experience propofol has been effective in seizure management of PSS patients. Mannitol is administered intravenously every 6 hours to reduce intracranial swelling. Electrolyte and glucose abnormalities are corrected, and supportive care is provided. Propofol is discontinued after 12 hours. Some patients may benefit from a low dose of acepromazine before propofol is discontinued, because anxiety during anesthetic recovery may be difficult to differentiate from early seizure activity. If seizures reoccur with anesthetic recovery, the animal is reanesthetized with a propofol bolus and CRI, and treatment with intravenous barbiturates is instituted. Some animals may require 72 hours of anesthesia to resolve seizure activity. Once the animal has recovered from anesthesia, oral anticonvulsant therapy (phenobarbital in cats; potassium bromide or phenobarbital in dogs) is initiated. Prognosis is poor for animals with postoperative seizures; mortality rates are high and those that survive often continue to have neurologic problems.[88,94,96,109,110]

The most common chronic complication of PSS attenuation is persistence or recurrence of clinical signs. Differentials include continued flow through the original shunt, the presence of a second shunt, development of multiple acquired shunts, or the presence of congenital PVH. In animals with cellophane bands or ameroid constrictors, high-dose steroids can interfere with fibrous tissue formation and shunt closure. Animals with clinical signs or biochemical changes that indicate liver dysfunction should be evaluated with ultrasonography, scintigraphy, portography, computed tomography, or magnetic resonance imaging for evidence of shunting. Surgical intervention is recommended for patients with a second shunt or clinical signs related to persistent flow through the original shunt. If shunting is not detected, the most common cause is congenital PVH (MVD-PVH), which can be confirmed by histologic evaluation of liver biopsy samples. Animals that have focal or generalized seizures, have minimal hepatic dysfunction, and do not respond to medical management for encephalopathy should be evaluated for central neurologic disorders.

Prognosis for Congenital Portosystemic Shunts Treated Surgically

In dogs with congenital EHPSS, mortality rates were 2% to 32% after ligation, 7% after ameroid constrictor placement, and 6% to 9% after cellophane

banding.[12,69,92–94,102,105] In dogs with IHPSS, mortality rates were 6% to 23% after ligation, 0% to 9% after ameroid constrictor placement, and 27% after cellophane banding with intraoperative attenuation.[12,26,69,98,111,112] The most common cause of death after PSS attenuation is severe persistent neurologic signs. Other causes include intraoperative hemorrhage, postoperative coagulopathy, portal hypertension, and hemorrhagic gastroenteritis.[69,94] Age is not correlated with mortality or long-term complications; however, degree of shunt closure during ligation is correlated with postoperative mortality.[12,35,69,104,113]

In surviving dogs available for follow-up, good to excellent outcomes were noted in 84% to 94% of animals undergoing ligation, cellophane banding, or ameroid constrictor placement for EHPSS.[26,69,94] Most dogs continued to have mildly increased bile acids.[12,69,102]

Clinical outcome was more variable in surviving dogs after IHPSS attenuation. Good to excellent outcomes were noted in 70% to 89% of dogs with IHPSS that underwent ameroid constrictor placement,[94,111] 76% to 100% of dogs that underwent ligation,[94,98] and 50% of dogs that underwent cellophane banding with intraoperative attenuation[93] In many dogs, clinical signs resolved despite persistent shunting.[94,105,114] Immediate survival was 100% for 10 dogs undergoing hydraulic occluder attenuation of intrahepatic shunts, but long-term survival was only documented in 8/10 dogs, with 2 lost to follow-up.[91] Clinical signs resolved in all dogs, although 1 dog required reinflation of the cuff 9 months after surgery and a second developed sinus tracts that resolved with port removal.[91] In dogs undergoing ameroid constrictor placement, preoperative hypoalbuminemia was associated with persistent postoperative shunting.[94] Preoperative hypoalbuminemia or leukocytosis, occurrence of seizures after surgery, and persistent shunting at 6 to10 weeks after surgery were predictive of poor long-term outcome.

In cats, perioperative mortality rates are 0% to 4% after ligation or ameroid constrictor placement, and 0% to 23% after cellophane banding.[50,96,106,108] Up to 75% of cats have postoperative complications.[108] The most common complication is neurologic dysfunction, including generalized seizures in 8% to 22% and central blindness in up to 44%.[50,96,108] Blindness usually resolves within 2 months after surgery.[108] Of surviving cats available for follow-up, good or excellent long-term outcome was reported in 66% to 75% undergoing ligation, 33% to 75% undergoing ameroid constrictor placement, and 80% undergoing cellophane banding.[50,96,106,108,115] Excellent outcome has been reported in 25% of cats with persistent shunting, and continued or recurrent neurologic abnormalities have been reported in 57% of cats with normal scintigraphy or hepatic function tests.[50,108]

Surgical Treatment of Hepatic Arteriovenous Malformations

Treatments for HAVM include liver lobectomy, ligation of the nutrient artery, or fluoroscopically guided glue embolization of abnormal arterial vessels.[16,116] Most HAVM are located in the right or central liver lobes, and 25% involved 2 lobes. Lobectomy may be challenging because of proximity to the gall bladder and caudal vena cava and extensive vascularity. Temporary occlusion of the portal vein and celiac artery is recommended during partial lobectomy to reduce intraoperative hemorrhage.[116] Complications of surgery include hemorrhage, portal hypertension, systemic hypotension, bradycardia, and portal or mesenteric vein thrombus formation.[16] Perioperative survival of dogs undergoing surgery alone was 75% to 91%.[16] Long-term outcome of dogs treated with surgery alone was fair or good for 38% to 57%. Overall, 75% of dogs continue to require dietary or medical management of clinical signs.[16]

Interventional Radiologic Management

Interventional radiology (IR) uses contemporary imaging modalities, such as fluoroscopy, to gain access to various parts of the body through a small incision (jugular vein for the treatment of IHPSS or femoral artery for the treatment of HAVM). Devices can be introduced percutaneously through these small holes and deployed once inside the vessel in the proper position. With the use of contrast, catheters, wires, and embolization devices (coils, vascular occluders, cyanoacrylate glue, stents, and so forth), shunts can be attenuated either abruptly (cyanoacrylate, coils, vascular occluders) or slowly (coils). Because of the technical difficulty of surgery for these 2 conditions, along with the high perioperative complication rates reported (0%–77%),[87,91,93,98,108,111,117] these minimally invasive alternatives are currently being investigated and performed in a small number of facilities around the world.[2,25,118–125] In the author's practice, IR procedures involving portovascular anomalies are mainly reserved for IHPSS and HAVM; EHPSS are routinely fixed surgically.

Percutaneous Transjugular Coil Embolization

Transvenous coil embolization has been described from various institutions in the past decade,[2,25,118,120–125] for repair of IHPSS and EHPSS[124,125] in dogs and cats.[118] The most common complication of this technique has been coil migration, which has been diminished with the addition of caval stent placement before coil deployment. Portal hypertension, which is 1 of the most common complications reported with surgical fixation, was not commonly seen in the patients treated with PTCE.

Percutaneous venous access to the jugular vein is obtained. Under fluoroscopic guidance, a guidewire is passed down the jugular vein into the cranial vena cava, through the right atrium, and into the caudal vena cava (CdVC) (**Fig. 1**A). The shunting vessel is then selected (hepatic vein to portal vein) (**Fig. 1**A). Next, a catheter is advanced over the guidewire and the guidewire is subsequently removed (**Fig. 1**B). An angiogram is performed, using contrast material under fluoroscopic guidance, and visualized with digital subtraction (DSA), confirming shunt location and anatomy (**Fig. 1**B). Next, in a similar fashion as above, a catheter is placed into the caudal vena cava, caudal to the shunting tributary, and another angiogram is performed marking the communication of the shunt to the caudal vena cava (**Fig. 1**B). With a measuring catheter, the maximal diameter of the vena cava is determined facilitating sizing for stent placement (**Fig. 1**B). Once the location of the shunt entry point into the CdVC is identified and the size of the cava is determined, a wire is advanced back into the CdVC and the catheters are removed. Next, an ensheathed, laser-cut, self-expanding nitinol stent is advanced over the guidewire into the CdVC (**Fig. 1**C), ensuring that the entire mouth of the shunting vessel is covered. Then, the sheath of the stent is removed as the stent is deployed in the chosen location (**Fig. 1**D). Finally, using the guidewire and catheter, the shunt is again selected through the interstices of the stent (**Fig. 1**E) and an angiogram is performed as above, to confirm that the shunt is completely covered by the stent (**Fig. 1**F). Through the catheter, thrombogenic coils are placed into the shunt to monitor portal pressures. Coils are added until the mouth of the shunt is covered or the portal pressures increase to >10 CmH_2O over baseline or to a maximum of 20 cmH_2O (**Fig. 1**G, H). The stent is used as a cage to prevent coil migration cranially. The procedure allows an abrupt (presence of the coils) and a slow attenuation of the shunting vessel; the thrombogenic coils allow a clot to form, organize, and occlude the blood flow. If necessary additional coils can be easily added at a future date if clinical signs persist, liver functional parameters do not improve, or medications cannot be weaned. The addition of coils has been necessary

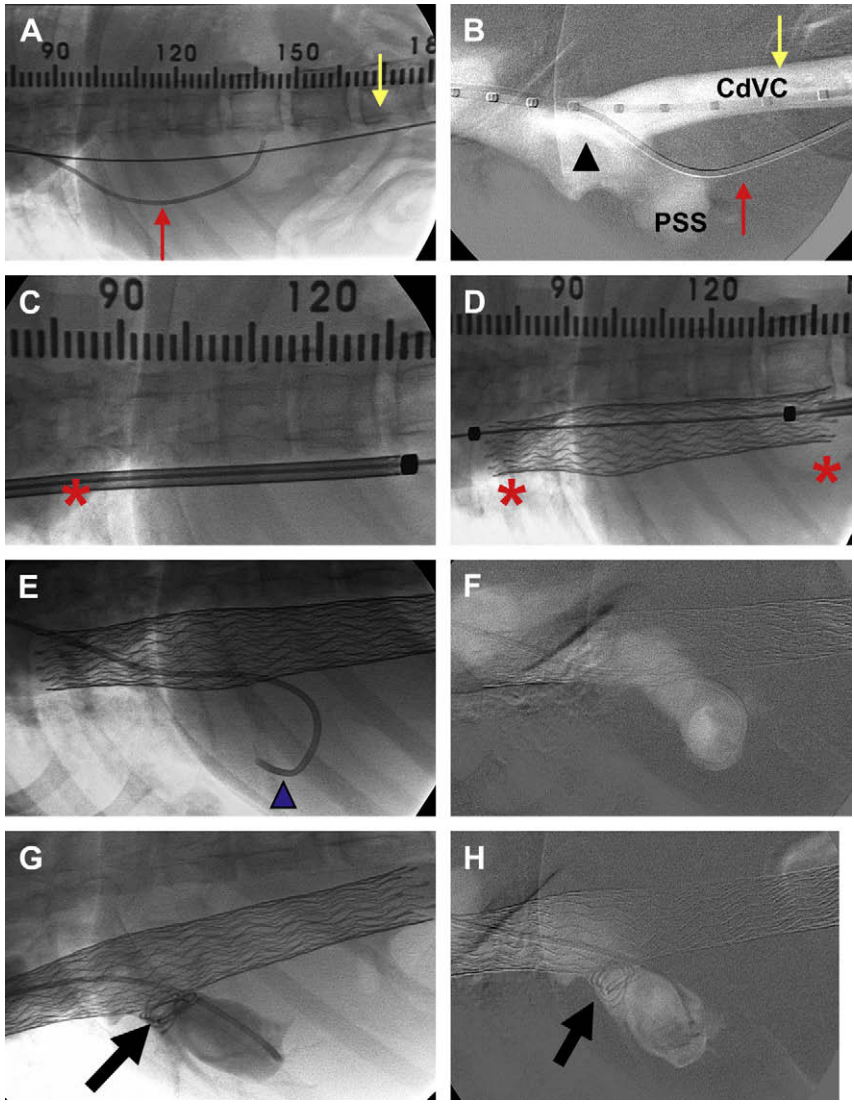

Fig. 1. A study of a dog with a right divisional IHPSS, during a PTCE. The animal is placed in dorsal recumbency with the head to the left and the tail to the right of the image. (*A*) A guidewire (*yellow arrow*) is placed from the jugular vein, through the cranial vena cava and the CdVC and extending down the CdVC. A catheter ends in the portal vein (*red arrow*), extending from the jugular vein, through the cranial and CdVC, transversing the right hepatic vein, the portosystemic shunt (PSS) and extending to the portal vein. (*B*) An angiogram being performed under DSA fluoroscopy. Contrast material is in the CdVC and portosystemic shunting vessel (PSS). The mouth of the shunt is identified (*black triangle*). Using a marker catheter (*yellow arrow*), the magnification is adjusted for, and the vena cava can be accurately measured for appropriate selection of stent size. (*C*) Over a guidewire, the ensheathed stent (*red asterisk*) is advanced to cover the mouth of the shunt that was previously determined in (*B*). (*D*) The stent is then deployed in the selected location with each end confirmed to cover the shunt (*red asterisk*). (*E*) The mouth of the shunt is again selected with a catheter (*blue triangle*) and (*F*) another angiogram is done using contrast, to confirm that the stent is covering the entire mouth of the shunt. This image is under DSA. (*G*) Through the catheter, thrombogenic coils are placed in the shunting vessel (*black arrow*). (*H*) Once completed the catheter is removed and the stent and coils remain in place until a final angiogram is performed under DSA and final portal pressures are obtained.

in <10% of cases. In the rare cases in which portal perfusion is excellent, the shunt can be occluded abruptly. This has been performed in approximately 5% of cases.

Complications

Of 70 patients undergoing this procedure, fewer than 5% had perioperative complications in our experience,[87] (Weisse and Berent, direct communications, Philadelphia, PA, July 2008). Complications included coil migration, excessive bleeding at the site of the jugular catheter postprocedure, and aspiration at the time of induction before the procedure. Of 40 dogs reported in abstract form,[118] the long-term mortality rate was 30% and more than 50% of the deaths were secondary to severe GI ulcerations and bleeding. More than 30% of dogs have (or had) evidence of GI ulcerations either before or after PTCE. Since initiating life-long antacid therapy at the time of diagnosis, the overall long-term mortality rate (6 months to >7 years follow-up) has decreased dramatically, with fewer than 3% of deaths secondary to GI ulcerations.

Because GI bleeding has become so apparent, nearly all dogs with IHPSS undergo upper GI endoscopy with gastrointestinal biopsies before PSS correction. Evidence of petechiation and active or healing ulcerations are commonly seen. More than 85% of dogs with IHPSS have evidence of moderate to severe lymphoplasmacytic with or without eosinophilic mucosal and submucosal inflammation. Hypergastrinemia, which is currently being evaluated in a large group of dogs, does not seem to be associated with or prognostic to the development of GI ulceration in dogs with IHPSS, EHPSS, or normal age-matched dogs. Visual endoscopy scores, gastrointestinal histopathology, and gastrin levels seem to have minimal statistical correlation with overall outcome in the author's preliminary data. Morbidity and mortality have significantly improved since the start of life-long antacid use. The only prognostic factor appreciated as a marker for GI bleeding and postprocedural gastrointestinal symptoms (severe vomiting, diarrhea, and inappetance) is albumin; concentrations $\leq$1.8 g/dL increase the odds of bleeding by more than 5 times and the odds of chronic vomiting and diarrhea by 4.7 times. Treatment of dogs, particularly those with IHPSS, with life-long antacid therapy (particularly, omeprazole) has improved the morbidity and mortality rates.

Hepatic Arteriovenous Malformations Cyanoacrylate Glue Embolization

Hepatic arteriovenous fistula/malformations (HAVM) are rare vascular anomalies involving multiple arterial communications to the portal vein. Because they usually involve multiple, rather than a single communication, the term malformation is more appropriate than fistula. These communications are usually from the hepatic artery, but have been seen to involve other arteries, such as the gastroduodenal artery and left gastric artery. Angiography helps to determine the origin of these numerous vessels. Due to high-pressure arterial blood shunting to the portal vein, there is severe portal hypertension and this most commonly results in multiple EHPSS to help decompress the portal vein. Cyanoacrylate glue embolization has been performed in 11 cases to date at the author's institution (University of Pennsylvania).

Access to the femoral artery is obtained and, under fluoroscopic guidance, a wire is advanced retrograde into the aorta, and the hepatic artery is selected by way of the celiac artery. A catheter is advanced over the wire and an angiogram is done using contrast material and digital subtraction (DSA). The communication can be appreciated (**Fig. 2**A), and centrifugal blood flow is seen as the contrast material enters the portal vein traveling caudally until it reaches the multiple EHPSS, whereby it travels through the caudal vena cava cranially. Then, the small vessels feeding the malformation are selected with a microcatheter, and cyanoacrylate (a glue) is infused. The glue polymerizes and occludes the small communications of the malformation.

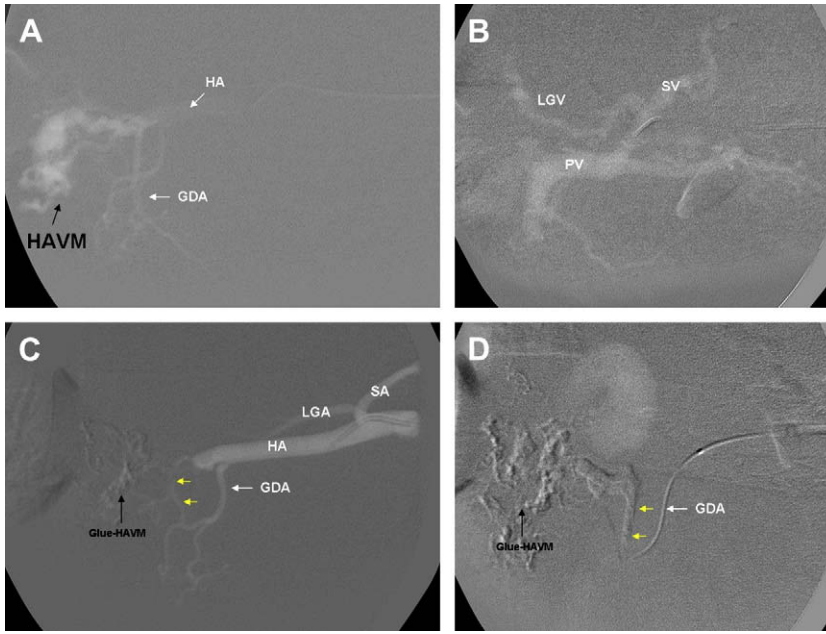

Fig. 2. Fluoroscopic images of a glue embolization in a 4-month-old female intact boxer with an HAVM. Left is cranial and right is caudal. (*A*) Angiogram from the hepatic artery (HA) showing the contrast filling the gastroduodenal artery (GDA) and the malformation (HAVM). (*B*) Hepatofugal portal flow after the malformation is filled is traveling in the wrong direction caudally down the portal vein (PV) resulting in retrograde filling of the left gastric vein (LGV) and splenic vein (SV). (*C*) After glue is injected into the hepatic artery the malformation is filled. The contrast is seen to stop at the hepatic arterial branch but there is still filling of the malformation from a branch of the GDA (*yellow arrows*). (*D*) A microcatheter in the branch off the GDA filling with glue (*yellow arrows*).

Cyanoacrylate infusion is continued until the flow into the portal vein from the artery is eliminated, or dramatically decreased (**Fig. 2**).

Complications with this procedure include nontarget embolization of glue entering the portal system to the extrahepatic shunts, or elsewhere, on catheter removal. These events have not been clinically significant and have not resulted in any long-term complications. After this procedure, most dogs require life-long medical management due to continued shunting from their multiple EHPSS. Recurrence of arteriovenous communications can occur and recurrence of clinical signs has been seen requiring serial embolizations. Long-term survival is considered good with this technique.

POSTOPERATIVE CARE

After surgery or IR treatment, patients are maintained on intravenous fluids until they are eating and drinking. Dextrose is added to the fluids if the blood glucose level is less than 80 mg/dL. Patients are monitored for hypoglycemia, hypothermia, delayed anesthetic recovery, hemorrhage, seizures, and signs of portal hypertension. Animals usually require opioid analgesics such as buprenorphine for 1 to 3 days. Sedation with a low dose (0.01–0.02 mg/kg intravenously) of acepromazine may be necessary if dogs are vocalizing or abdominal pressing, because these activities will increase

portal pressure. Acepromazine does not precipitate seizures in dogs with shunts; however, it should not be used in hypotensive animals.

A protein-restricted diet and lactulose are continued after surgery until liver function improves. Frequently, animals can be weaned off lactulose within 4 to 6 weeks. Bile acids and a biochemical panel are evaluated 2 to 3 months after the surgery. If liver function is normal, medical management is discontinued. Clinical response to diet change can be evaluated in animals with mildly elevated bile acids and normal albumin. If bile acids are moderately increased, medical management is continued and animals are rechecked 5 to 6 months after surgery. Typically, patients are weaned off the medical therapy 1 month after IR treatment, and this weaning process takes approximately 2 months starting with the metronidazole, then the lactulose, then transitioning to an adult maintenance dog food. If this is all well tolerated, blood count and serum biochemical parameters improve (albumin, BUN, cholesterol, MCV, and glucose), and no return of clinical signs occurs, then the outcome is considered good, regardless of the results of bile acids tests. Many articles on congenital PSS fixation[12,69,87,104] have shown that return of bile acids to normal is not necessarily correlated with long-term outcome.

Acquired Extrahepatic Shunts

Multiple acquired EHPSS are seen in animals with chronic portal hypertension secondary to HAVM, NCPH, or chronic hepatitis/cirrhosis. Dogs with acquired shunts often present with signs of HE and ascites.[3,40,41] Ligation of the individual shunts is not considered appropriate or effective because they are typically relieving the portal hypertension. Constriction of the caudal vena cava surgically, termed caval banding, has been attempted to redirect blood flow from the EHPSSs to the portal vein.[3,126,127] Complications that can occur include ascites, hindlimb edema, development of other portoazygous shunts, and persistent poor portal perfusion. The survival times in animals undergoing caval banding is similar to those treated medically.[126]

Multiple EHPSS have been reported to occur after ameroid placement in dogs and cats for single congenital EHPSS in nearly 10% to 20% of cases.[5] Treatment should be aimed at controlling the clinical signs of HE and slowing the progression of the liver disease.

SUMMARY

Portovascular anomalies are most commonly seen as congenital communications in dogs and cats. Fixation, whether surgical or interventional, should be considered in all cases in which it is possible to improve perfusion to the liver, and ultimately liver function. Medical management before fixation is always recommended. If surgery is not recommended or not possible, long-term medical management can be successful in approximately 30% of cases. New modalities such as PTCE or glue embolization facilitate treatment of more complicated conditions such as central divisional IHPSS and HAVM.

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