Dogs and cats with congenital portosystemic shunts (PSS) may present with a variety of clinical signs. Signs may be related to the gastrointestinal tract, such as anorexia or poor appetite, vomiting, diarrhea, poor weight gain (“unthriftiness”) and small stature. Signs, usually intermittent, may be related to hepatic encephalopathy (HE) and include lethargy, ataxia, blindness, behavioral changes, weakness, hypersalivation/ptyalism (cats), stupor, seizure and coma. Some owners will report that neurological signs occur post-prandially. Signs can also be related to the urinary tract, primarily hematuria due to urinary calculi. This discussion will focus on management of neurological and gastrointestinal signs. Symptomatic urinary calculi require removal.

Nutritional and medical management of dogs and cats with PSS can be undertaken pre-operatively before shunt occlusion is scheduled, as emergency therapy in a case with severe signs of HE, or as long-term therapy if the signs are adequately controlled. Some dogs (less frequently cats) with congenital PSS can be satisfactorily managed medically for life. One abstract suggested that long-term survival in dogs managed medically was similar to dogs undergoing surgery (Center 2012). A recently published study, however, indicated that survival rate was significantly improved in dogs that underwent surgical treatment. (Greenhalgh 2014). Ninety-seven dogs underwent surgical treatment; 27 were managed medically. Median follow-up time for all dogs was 1,936 days. Forty-five dogs (24 medically managed and 21 surgically managed) died or were euthanized during the follow-up period. Neither age at diagnosis nor shunt type affected survival rate. Frequency of clinical signs was lower in surgically versus medically managed dogs for all follow-up intervals, with a significant difference between groups at 4 to 7 years after study entry. It is noteworthy, however, that the median survival time for medically treated dogs was 836 days from study entry, including one still alive at last contact at 2,948 days. Medical therapy remains a viable long-term option for owners who decline surgical intervention and whose dogs respond adequately to medical therapy.

Medical and nutritional management of PSS cases is usually multimodal and involves a “hepatic” (protein-restricted) diet, lactulose and antimicrobials. Note that protein should not routinely be restricted in the diet of a dog or cat with other types of liver disease unless there is evidence of HE as amino acids are needed for hepatic repair and regeneration.

Nutritional management
Dietary therapy involves adjusting the diet so that optimal quantities and types of nutrients are provided to the animal. In addition, food should be provided to hepatic patients three to four times per day. By dividing the total daily nutrient intake into several smaller meals, these patients will better maintain their appetite and intake. Protein restriction and modification are widely considered to be of major importance in the dietary management of PSS cases. The goal is to minimize the alterations in nitrogen metabolism induced by hepatic bypass. Appropriate adjustments in the type and quantity of protein ingested by the patient will lead to a reduction in blood ammonia and (theoretically) return of circulating branched-chain to aromatic amino acid ratios towards normal. The type and quantity of protein, as well as the frequency of feeding, are all important in reducing clinical signs. A number of dogs medically managed for PSS develop a clinically relevant hypoproteinemia when fed solely a commercial protein-restricted liver diet. These dogs, and potentially all medically managed PSS dogs, can have their hepatic diet supplemented with extra high-quality protein (usually in the form of dairy protein). Recent studies in animals and humans suggest that the main source of ammonia in the portal blood is not ammonia production in the colon as a result of undigested protein entering the lower intestinal tract, but is due to glutaminase activity by small intestinal enterocytes which use glutamine as their main energy source. This activity increases post-prandially when enterocyte metabolic activity increases to allow digestion and absorption of food. This glutaminase activity is sufficient to explain the postprandial HE in dogs with congenital PSS. Hepatic diets may stimulate less small intestinal metabolic activity or less hepatic ammoniogenesis. It is unknown whether it is the protein type or protein concentration that is most important factor (or even some other aspect of the diet) that is responsible for clinical improvement of PSS dogs fed a commercial “hepatic” diet.

For the reasons noted above, protein restriction for dogs with PSS is not without controversy. The focus on protein restriction and reduced colonic ammoniogenesis as the main beneficial effects of a ‘hepatic’ diet may be outdated. There is no good experimental evidence that it is protein restriction that is important in dogs in the dietary management of congenital PSS (Watson 2010). This discussion was recently sparked by the results of a study that compared the outcome of congenital PSS dogs fed protein-restricted diets that were either soy- or chicken-based (Proot 2009). The authors reported a significant reduction in HE score in both the soy protein and chicken-based diets, and a significant reduction in fasting ammonia when the soy-based diet was fed but not when the chicken-based control diet was fed. These arguments follow a similar re-evaluation of protein restriction and the use of lactulose in human medicine. ‘We have entered an exciting phase in research into hepatic encephalopathy, with novel therapies evolving from the discovery of new targets. Lactulose and low-protein diets should no longer be part of standard care, but this does not necessarily mean that these therapies do not work in selected patients. Further trials of lactulose, protein restriction, and newer agents should be
placebo-controlled . . . Current guidelines will need to be revised with strict attention being paid to treating the precipitating factors, with correction of dehydration, electrolyte and acid-base imbalance, constipation, and infection” (Shawcross, 2005).

Cottage cheese is a high quality protein source for animals with PSS (or in hepatic failure). Dogs usually find this food more palatable than cats. Cottage cheese contains no additives, is easily and completely digested and has a good ratio of branched-chain to aromatic amino acids. Studies in dogs with surgically-induced PSS have shown that cottage cheese is superior to intravenous casein hydrolysates in terms of both nitrogen retention and stabilization of plasma amino acid ratios. The efficient digestion of cottage cheese within the small bowel also results in little residue being available for colonic bacteria to metabolize.

Dogs with congenital PSS (or hepatic failure with demonstrated inability to handle higher levels of protein, such as demonstrating that HE is present) should receive a minimum of 2.1 gm of crude protein/kg/day. The protein should be of high biologic value. Cats have a significantly higher protein need and should receive sufficient good quality protein to provide 30 per cent of their calorics needs as protein. In estimating the protein requirements of patients it is important to monitor the serum albumin concentration. If clinical signs improve on reduced protein diets but serum albumin concentrations do not, the protein content of the diet should be supplemented. Pending further study, either dairy or soy-based protein, or possibly cooked egg white is suggested for this supplementation. The author recommends increasing the protein available by 0.5 gm/kg/day at weekly intervals until either protein anabolism is evident from the serum albumin concentration or signs of encephalopathy develop. It is not necessary to increase the protein beyond 5 gm/kg/day. Commercially available reduced protein “hepatic” diets work well in most PSS cases. If animals will eat enough to meet their caloric needs, these diets will usually provide sufficient protein for their metabolic demands.

An easily digested carbohydrate source should form the basis for the bulk of the required daily calories for dogs with PSS. The carbohydrate source chosen should be easily digested so that minimal residues remain in the colon where intestinal flora may convert them to volatile fatty acids. If a homemade diet is being formulated, an inexpensive and useful carbohydrate source that meets these needs is boiled white rice. A high carbohydrate diet provides an easily assimilated source of non-protein calories, which spares body tissues from catabolizing muscle protein for energy, reduces the catabolism of dietary nitrogen for energy, and reduced the risk of hypoglycemia.

Medical management

Lactulose (1-4-beta-galactosidofructose (Cephulac) is highly effective in lowering blood ammonia concentrations. Lactulose is a semisynthetic disaccharide which is not metabolized by mammalian intestinal disaccharidases. When this undigested sugar reaches the colon, intestinal bacteria hydrolyze it to lactic, acetic and formic acids, which dramatically lower colon pH. In addition to the pH effect, when large quantities of unabsorbed solutes are produced in the colon and osmotic diarrhea results. Blood ammonia concentrations are lowered because of several unique attributes of lactulose. By-products of lactulose fermentation produce what is termed ionic trapping of ammonia within the colon. In an acid environment, ammonia (NH3) accepts a proton to form ammonium (NH4+). Ammonium is much less diffusible than ammonia. Thus, ammonium ions remain within the colon and are excreted rather than being absorbed. This effect occurs at a colon pH of 6.2 or less and is most noticeable if the colon pH is 5.0 or lower. In addition to ionic trapping, lactulose apparently inhibits ammonia generation by colonic bacteria through a process known as catabolite repression. By providing a carbohydrate source to intestinal bacteria, less proteolysis, peptide degradation and deamination of bacterial proteins occurs. This results in significantly less ammonia being generated by colonic bacteria than they would produce under other circumstances, and this effect is independent of the pH effect. Lactulose therapy is started at 0.5 mL/kg PO q 8-12 h. The dose is adjusted depending on improvement in neurological signs, weight gain, control of gastrointestinal signs, and serum ammonia concentration. Excess amounts of lactulose will cause soft stools or overt diarrhea, so fecal consistency must also be monitored and used in dosage adjustments. Usually cats require 2.5 to 5 ml three times daily and dogs require 2.5 to 25 ml three times daily. If watery diarrhea develops, the dosage should be reduced.

Non-absorbable intestinal antibiotics are used to suppress potent urea splitting intestinal flora, which contribute significantly to blood ammonia concentrations. The antibiotic used most commonly for this purpose is neomycin sulfate. The recommended dose for use in dogs and cats is 22 mg/kg three times daily initially (twice daily is often satisfactory for long-term use). Other potential beneficial effects of the use of oral antibiotics are to decrease bacterial deamination of amino acids, and reduce the production of aromatic amino acids, circulating false neurotransmitters, and short chain fatty acids by gut bacteria. Occasional rare complications to the chronic use of neomycin are oto- and nephrotoxicity, severe diarrhea, and intestinal malabsorption. Some systemically absorbed antibiotics may be used in animals with HE as alternatives to an aminoglycoside like neomycin. The most commonly selected one is metronidazole (Flagyl). Metronidazole is active against many of the urease-positive, gram negative anaerobes which are potent generators of ammonia in the intestinal tract. Most clinical studies have indicated that metronidazole is equal in effectiveness to neomycin in controlling blood ammonia concentrations. The recommended dose is 10 -15 mg/kg every 8 hours. Toxicity to metronidazole manifests as a variety of CNS signs. The dose selected is lower than may be used in other conditions because of the potential for neurotoxicity and decreased elimination in liver failure. Many animals will improve clinically while receiving almost any
antibiotic but develop signs of illness when antibiotics are stopped. This likely corresponds to the effects the drug has on GI flora, an effect that stops soon after it is discontinued.

Oral lactulose may be used as an alternative to, or in conjunction with, intestinal antibiotics. Human studies indicate that lactulose alone or neomycin alone provides clinical improvement in 80 per cent of humans with chronic encephalopathy. An additional group of patients will benefit from the combination of neomycin and lactulose since these are sometimes synergistic. It is interesting, that neomycin does not impair the effectiveness of lactulose in most patients. Since lactulose requires metabolism by intestinal bacteria and neomycin kills bacteria, one would think that oral antibiotics would be contraindicated for maximal effectiveness of lactulose. Human studies show that neomycin inhibits bacterial degradation of lactulose in less than one-third of patients. Lactulose is degraded by lactulosophilic bacteria of which *Bacteroides* spp predominate. *Bacteroides* spp appear fairly resistant to the effects of neomycin.

The mainstays of therapy for long-term management of PSS dogs are a reduced-protein “hepatic” diet and suppression of urease-containing intestinal bacteria with lactulose and/or neomycin. In addition, steps must be taken to recognize and eliminate any precipitating factors that may induce encephalopathy, such as hypokalemia or constipation. Hepatic encephalopathy may be precipitated by gastrointestinal hemorrhage. Because gastrointestinal bleeding and ulcerations are commonly encountered complication in patients with PSS, administration of a proton pump inhibitor (such as omeprazole, 1.0 mg/kg, PO, q 24 h) to reduce gastric acid production may also be initiated. Levetiracetam (Keppra™) can be used to control seizure activity if dietary and other medical therapies are incompletely effective.

For animals exhibiting severe signs of encephalopathy all oral intake of food should cease until CNS signs abate. This is particularly important for protein. Cessation of food intake eliminates dietary sources of ammonia, toxic amines, aromatic amino acids, and short chain fatty acids that induce encephalopathy. In some cases, catharsis of the colon must be undertaken. Emptying the colon rapidly decreases numbers of colonic bacteria and removes potentially toxic by-products of bacterial metabolism. Enemas should be repeated until no fecal material is evident in the evacuated fluid. Lactulose-containing enemas are much more effective than warm water enemas in reducing blood ammonia concentrations and improving clinical signs. Lactulose is diluted with warm water (30 per cent lactulose, 70 per cent water) and given as a retention enema. Approximately 22 to 33 mg/kg is infused and retained in the colon for 20 to 30 minutes before evacuation.

Lipotropic agents containing methionine should not be used in dogs and cats with PSS or in hepatic failure. Metabolites of oral methionine can induce signs of hepatic encephalopathy quite easily in experimental PSS dogs. It also acts synergistically with short chain fatty acids and ammonia to induce coma. It has been shown that methionine can also induce a severe Heinz body hemolytic anemia in cats at dosages of 0.5 to 1 gm/kg/day.

**Selected readings**


