Portosystemic shunts in dogs and cats: laboratory diagnosis of congenital portosystemic shunts

Portosystemische shunts bij honden en katten: laboratoriumdiagnose van congenitale portosystemische shunts

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ABSTRACT

The most frequent laboratory abnormalities in patients with congenital portosystemic shunts (CPSS) are microcytosis, hypoglycemia, hypoalbuminemia, hypoproteinemia, increased liver enzyme activities, decreased blood urea nitrogen (BUN) and urate crystalluria. The microcytosis is probably due to impaired iron transport. Hypoglycemia, hypoalbuminemia, hypoproteinemia and decreased BUN are partly due to decreased hepatic synthesis. Prolonged coagulation times are also common. A presumptive diagnosis of CPSS is based on the combination of the history, clinical signs, clinicopathological abnormalities and abnormal liver function tests such as serum bile acid and venous ammonia concentrations. Nowadays, determination of pre- and postprandial serum bile acids is the most commonly performed liver function test because of the high sensitivity and greater convenience compared to plasma ammonia concentration. Confirmation of the diagnosis is only possible by visualizing the shunting vessel by medical imaging techniques or during surgery.

SAMENVATTING

De meest frequente laboafwijkingen bij patiënten met een congenitale portosystemische shunt (CPSS) zijn microcytose, hypoglykemie, hypoalbuminemie, hypoproteïnemie, verhoogde leverenzymactiviteit, gedaalde ureumwaarde en uraat kristallurie. De microcytose is vermoedelijk het gevolg van een abnormaal ijzertransport. De hypoglykemie, hypoalbuminemie, hypoproteïnemie en gedaalde ureum zijn deels te wijten aan een gedaalde synthesecapaciteit door de lever. Verlengde stollingstijden treden ook frequent op. Een waarschijnlijkheidsdiagnose van een CPSS kan gemaakt worden op basis van het signalement, de anamnese, de klinische symptomen, de bloedafwijkingen en abnormale leverfunctietesten, zoals de concentratie van galzuren en ammoniak. Tegenwoordig is de bepaling van pre- en postprandiale galzuurconcentraties de meest uitgevoerde leverfunctietest omwille van de goede sensitiviteit en het groter gemak vergeleken met de bepaling van ammoniakconcentraties. De bevestiging van de diagnose van een CPSS is alleen mogelijk door de visualisatie van de aanwezige shunt via medische beeldvorming of tijdens chirurgie.

INTRODUCTION

In this article, the most commonly observed abnormalities on complete blood count that can be detected in dogs and cats with congenital portosystemic shunts (CPSS) – serum biochemistry profile, coagulation profile and urinalysis – are reviewed. A presumptive diagnosis of CPSS can only be made based on abnormal liver function. Therefore, much emphasis is placed on the characteristics of the two currently used liver function tests – serum bile acid and plasma ammonia concentration.

CLINICOPATHOLOGICAL ABNORMALITIES

Multiple hematological, biochemical and urinalysis abnormalities can be expected in dogs with CPSS (Table 1). However, there is no pathognomonic finding (Griffiths *et al.,* 1981; Johnson *et al.,* 1987; Tyler, 1990a; Martin, 1993; Lamb *et al.,* 1996; Mathews and Bunch, 2005). Nevertheless, a presumptive diagnosis of CPSS can be made based on signalment, history, physical examination findings and several clinicopathological abnormalities (Birchard and Sherding, 1992; Lamb *et al.,* 1996). The only way to confirm the diagnosis is by visualizing the shunting of the blood by medical imaging modalities or during surgical procedures (Griffiths *et al.,* 1981; Johnson *et al.,* 1987; Tyler, 1990a; Martin, 1993; Lamb *et al.,* 1996; Mathews and Bunch, 2005).

Hematology

Approximately two-thirds to three-fourths of dogs with CPSS have microcytosis (decreased mean corpuscular volume or MCV) with or without concurrent anemia (Griffiths *et al.,* 1981; Johnson *et al.,* 1987; Meyer and Harvey, 1994; Bunch *et al.,* 1995). Other red blood cell conformational changes seen in dogs are target cells and poikilocytes (Center, 1996b). The most common hematological abnormalities in cats are poikilocytosis, microcytosis, mild anemia or spherocytosis (Scavelli *et al.,* 1986; Center, 1996b; Havig and Tobias, 2002; Kyles *et al.,* 2002). In most affected dogs and cats, the microcytosis resolves after successful correction of the CPSS (Bunch *et al.,* 1995). Meyer and Harvey (1994) stated that the observed microcytosis, hypoferremia and increased hepatic iron content suggest a relationship between altered hepatic blood flow and abnormal iron metabolism in dogs with CPSS. Absolute iron deficiency is excluded as the cause of microcytosis in dogs with CPSS because serum iron concentration, serum total iron binding capacity (TIBC) and transferrin saturation are not compatible with an absolute iron deficiency and because of the presence of increased iron content in the liver (Laflamme *et al.,* 1994; Bunch *et al.,* 1995). Due to the high hepatic iron content, especially in the Kuppfer cells, some similarities with anemia of chronic inflammatory disease are present. However, most dogs with CPSS have no evidence of inflammation (Laflamme *et al.,* 1994). It is possible that microcytosis in dogs with CPSS is associated with impaired iron transport due to a decreased ability of the liver to synthesize transferrin. This is confirmed by a low serum TIBC, which is an indirect measure of serum transferrin concentration (Laflamme *et al.,* 1994; Bunch *et al.,* 1995). Consequently, it is believed that altered iron transport, possibly associated with relative but not absolute iron deficiency, is related to microcytosis in young dogs with CPSS (Bunch *et al.,* 1995).

Besides the abnormalities in the red blood cell parameters, increased white blood cell (WBC) counts can also be present in dogs and cats with CPSS (Blaxter *et al.,* 1988; Havig and Tobias, 2002; Kyles *et al.,* 2002; Mehl *et al.,* 2005). Leukocytosis may be associated with translocation of intestinal bacteria into the portal blood and subsequent entering of bacteria into the systemic circulation by bypassing the liver. Otherwise, impaired reticuloendothelial function due to reduction of the effective liver blood flow can also contribute to the risk for leukocytosis (Koblik and Hornof, 1995; Mehl *et al.,* 2005). A high preoperative WBC count may be a predictor of an unsuccessful long-term outcome (Mehl *et al.,* 2005).

Table 1. Overview of the most commonly observed clinicopathological abnormalities in dogs and cats with CPSS (for references, see text).

	Dog	**Cat**
Hematology		
RBC	microcytosis ± anemia target cells poikilocytosis	microcytosis mild anemia poikilocytosis
WBC	(leukocytosis)	(leukocytosis)
Biochemistry		
hypoglycemia	15-30%	Rare
liver enzyme activities	75%	< 50%
hypoalbuminemia	50%	15%
hypoproteinemia	50%	15%
BUN and creatinine	40-60%	10-20%
Urinalysis		
ammonium urate crystalluria	40-75%	13-42%

Serum biochemistry

Routine biochemical alterations are usually mild and non-specific, reflecting mild liver disease (Martin, 1993). The most observed abnormalities in dogs and cats with CPSS are hypoglycemia, mild increases in liver enzyme activities, especially of alanine aminotransferase (ALT) and alkaline phosphatase (ALP), hypoalbuminemia, hypoproteinemia and a decrease in blood urea nitrogen (BUN) and serum creatinine (Table 1; Griffiths *et al.,* 1981; Johnson *et al.,* 1987; Bostwick and Twedt, 1995; Allen *et al.,* 1999; Havig and Tobias, 2002; Kyles *et al.,* 2002; Mehl *et al.,* 2005). The biochemical changes are less consistent in cats than in dogs (Center, 1996b; Tillson and Winkler, 2002). Hyperbilirubinemia is not a feature of CPSS (Scavelli *et al.,* 1986; Birchard and Sherding, 1992; Center, 1996b).

Hypoglycemia is reported in 15 to 30% of dogs and is rare in cats. It mostly affects small breed dogs, especially Yorkshire Terriers and Miniature Schnauzers (Johnson *et al.,* 1987; Bostwick and Twedt, 1995; Center, 1996a; Center, 1996b). Proposed reasons for the hypoglycemia are insufficient gluconeogenesis and hepatic glycogen storage, as well as abnormalities in the response to and metabolism of insulin, glucagon and other counter regulatory hormones (Center, 1996b). Preoperative hypoglycemia is detected less in dogs with intrahepatic shunts (0 to 5%) than in those with extrahepatic shunts (22%), and the degree of hypoglycemia is worse in extrahepatic shunts (Komtebedde *et al.,* 1991; Bostwick and Twedt, 1995). A possible explanation is the greater ability of large and giant breed dogs to maintain adequate glycogen storage in contrast to small dogs. A second explanation may be the increased delivery of hepatotrophic growth factors to the liver in intrahepatic shunts compared to extrahepatic shunts because in the presence of an intrahepatic shunt, a part of the liver still is perfused (Komtebedde *et al.,* 1991; Tisdall *et al.,* 1994; Bostwick and Twedt, 1995).

The mild increase in liver enzyme activities is probably due to hypoxic cellular damage and enzyme leakage as a consequence of the reduced hepatic perfusion (Center, 1996b). This increase is observed in at least 75% of dogs with CPSS and in less than half of the affected cats (Rothuizen *et al.,* 1982; Scavelli *et al.,* 1986; Johnson *et al.,* 1987; Blaxter *et al.,* 1988; Bostwick and Twedt, 1995). Because the majority of patients suffering from a CPSS are young at initial presentation, the increase in serum ALP activity might also be associated with release of the bone ALP isoenzyme (Bostwick and Twedt, 1995; Center, 1996b). One report found a significantly greater increase in serum ALP in intrahepatic shunts than in extrahepatic shunts, although no explanation could be defined (Bostwick and Twedt, 1995).

Hypoalbuminemia and hypoproteinemia are observed in almost half of the dogs and in approximately 15% of the cats with CPSS (Rothuizen *et al.,* 1982; Johnson *et al.,* 1987; Center, 1996b; Havig and Tobias, 2002; Mehl *et al.,* 2005). The main reason is the reduced hepatic synthesis of albumin because of insufficient hepatic mass (Griffiths *et al.,* 1981; Center, 1996b; Mehl *et al.,* 2005). Other factors such as anorexia, intestinal protein loss or blood volume expansion may also contribute to hypoalbuminemia and hypoproteinemia (Center, 1996b; Mehl *et al.,* 2005).

A decrease in BUN and serum creatinine can be detected in 40 to 60% of dogs and 10 to 20% of cats with CPSS (Johnson *et al.,* 1987; Center, 1996b; Walker *et al.,* 2001). The decreased BUN may be caused by the impaired hepatic ability to convert ammonia into BUN in the urea cycle, by fluid diuresis or by the protein-restricted diet (Center, 1996b). The decrease in serum creatinine is probably due to low muscle mass or fluid diuresis (Center, 1996b; Kyles *et al.,* 2002).

In a retrospective study by Bostwick and Twedt (1995), preoperative clinicopathological data suggestive of poor hepatocellular function (such as hypoalbuminemia, hypoglycemia or low BUN) did not indicate a poor prognosis for postoperative survival or complications. This was confirmed in a retrospective study by Mehl et al. (2005), which found, however, that hypoalbuminemia could be a predictor for continued shunting or unsuccessful long-term outcome.

Other, less frequent, biochemical abnormalities that can be observed in patients with CPSS are hypokalemia due to gastrointestinal loss by vomiting or diarrhea; the use of diuretics or occult urinary loss; hypocholesterolemia; respiratory or metabolic alkalosis and hyponatremia (Griffiths *et al.,* 1981; Tyler, 1990a; Center, 1996a; Center, 1996b).

Coagulation profile

Because histopathological examination of a liver biopsy is advised in most patients with CPSS, evaluation of the coagulation profile is recommended pre-operatively (Webster, 2005). In recent studies, a prolonged activated partial thromboplastin time (APTT) and a normal prothrombine time (PT) are commonly observed in dogs with CPSS (Niles *et al.,* 2001; Kummeling *et al.,* 2006). This is due to lower concentrations of clotting factors in dogs with CPSS (Kummeling *et al.,* 2006). In contrast, older studies stated that abnormal coagulation tests are rather unusual in patients with CPSS (Rothuizen *et al.,* 1982; Center, 1996b). However, coagulation times are insensitive in terms of detecting diminished hepatic production of the clotting factors (Mathews and Bunch, 2005). Both APTT and PT are prolonged only when one of the coagulation factors is decreased to less than 30% of its normal plasma activity (Feldman *et al.,* 2000). Fortunately, prolongation of the APTT is usually not associated with bleeding tendencies in dogs with CPSS (Niles *et al.,* 2001).

Urinalysis

Isosthenuric or hyposthenuric urine can be detected in patients with CPSS, especially if polydipsia and polyuria are present (Tyler, 1990a; Center, 1996b; Mathews and Bunch, 2005). From 40 to 75% of dogs and 13 to 42% of cats show ammonium (bi)urate crystalluria (Figure 1; Griffiths *et al.,* 1981; Blaxter

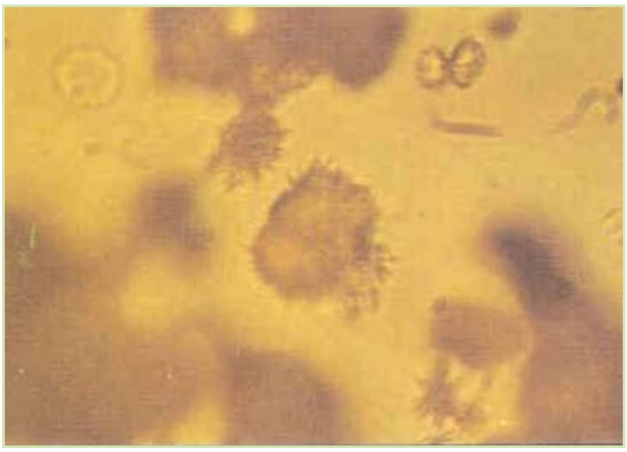

Figure 1. Ammoniumurate crystals in the urine of a dog with a CPSS.

et al., 1988; Tyler, 1990a; Center, 1996b). Hematuria, pyuria and proteinuria may also be present in patients with CPSS, usually in association with urinary tract infection secondary to ammonium (bi)urate crystals or uroliths (Tyler, 1990a; Center, 1996b).

Liver function tests

Changes in routine biochemistry tests are often not specific for liver disease, and serum liver enzyme activities may be normal in patients with CPSS or advanced cirrhosis. Therefore it is necessary to perform at least one liver function test to evaluate patients suspected for CPSS. Measurement of pre- and postprandial serum bile acid and ammonia concentrations largely replaced the use of the classical liver function tests such as the plasma clearance of BSP (sulfobromophthalein) and ICG (indocyanine green) because of their higher sensitivity and specificity and their greater convenience (Center, 1996a). Pre- and postprandial serum bile acid determination is currently the most commonly used liver function test because of the equal sensitivity in detecting hepatic insufficiency, the increased convenience and the stability of bile acids compared to plasma ammonia concentrations (Center, 1996a; Walker *et al.,* 2001).

Methods of commonly performed liver function tests

Serum bile acid concentrations

Bile acids are synthesized from cholesterol in the liver, which maintains a large reserve capacity for this function. Even severe hepatic failure does not result in insufficient bile acid production. After synthesis, bile acids are conjugated to an amino acid in the liver and transported through the biliary system to be stored and concentrated in the gallbladder. The gallbladder is emptied after a meal due to the release of cholecystokinin by the duodenum. In the intestine, bile acids play a role in the solubilization and absorption of lipids. Afterwards, most of them are absorbed actively in the distal ileum, although some are passively absorbed throughout the intestines. Through the portal circulation, the bile acids return to the liver. A normal liver rapidly clears bile acids from the portal blood, mainly in the periportal areas. During each postprandial period, the bile acid pool recycles between 3 and 5 times, but the first-pass hepatic extraction is the most important. This bile acid enterohepatic circulation is highly efficient and only 2 to 5% of the bile acid pool is lost in the feces each day. Furthermore, the normal liver has a high extraction capacity, so that only minor transient increases in postprandial bile acid values are observed (Center *et al.,* 1985; Sutherland, 1989; Center *et al.,* 1991; Center, 1993; Center, 1996a).

Table 2. Summary of the method to determine pre- and postprandial bile acid concentrations.

1. 12- hour fast of the patient
2. Serum collection
3. Feed the patient
   - at least 2 teaspoons for < 5 kg; 2 tablespoons > 5 kg
   - protein- and fat-rich diet
4. Serum collection 2 hours after feeding
5. Determine serum bile acids on both serum samples

Adapted from Center *et al.* (1985) and Center (1993).

To determine bile acid concentrations as a liver function test, serum is collected after a 12-hour fast and 2 hours after feeding (Table 2; Center, *et al.,* 1985; Meyer, 1986; Center *et al.,* 1991; Center *et al.,* 1995; Kyles *et al.,* 2002). The feeding results in an endogenous challenge test in the postprandial period (Center *et al.,* 1985). A sufficient amount of food and a diet with sufficient protein and fat content are necessary to stimulate gastric emptying and to initiate the enterohepatic bile acid cycle by emptying the gallbladder (Center, 1993).

Nowadays, serum bile acids usually are determined by use of an enzymatic assay that measures all 3 α-hydroxylated bile acids, regardless of whether they are conjugated or not (Center *et al.,* 1991; Center, 1993; Williams, 2003). Bile acids are very stable in blood, and the blood samples can be collected and handled routinely. Therefore, serum bile acid concentrations are a popular test for hepatobiliary function and hepatoportal perfusion (Sutherland, 1989; Center *et al.,* 1991; Center *et al.,* 1995). In hemolytic or lipemic samples, the results should be interpreted carefully because of possible interference by hemolysis and lipemia with the 3α-hydroxysteroid dehydrogenase-linked assay (Center *et al.,* 1995).

Venous ammonia concentration

Colonic bacteria degrade urea from dietary protein to ammonia, which is absorbed by the portal circulation. Normally, the liver metabolizes ammonia by converting it into urea and, to a smaller extent, by forming glutamine via glutamine synthetase. In patients with CPSS, the liver cannot perform this function, and this results in hyperammonemia and decreased BUN con-

centrations (Johnson *et al.,* 1987; Walker *et al.,* 2001; Gerritzen-Bruning *et al.,* 2006). Ammonia is the only neurotoxin that can be routinely measured in dogs or cats with hepatic encephalopathy (Center, 1996a; Walker *et al.,* 2001). For accurate ammonia determination, blood should be collected and transported on crushed ice, immediately centrifuged in a refrigerated centrifuge, and assayed as soon as possible because ammonia is very unstable (Rothuizen and van den Ingh, 1982a; Rothuizen and van den Ingh, 1982b; Center, 1996a; Walker *et al.,* 2001; Gerritzen-Bruning *et al.,* 2006). Falsely increased plasma ammonia concentrations can occur for several reasons. Examples of this include delayed plasma separation and ammonia assay, which leads to the liberation of amino residues, hemolysis where ammonia of the erythrocytes enters the plasma, and the contamination of the sample with cigarette smoke, sweat or saliva (Walker *et al.,* 2001; Gerritzen-Bruning *et al.,* 2006). The disadvantage of inconvenient sample collection is largely resolved by simple, reliable and relatively inexpensive in-house methods to determine blood ammonia concentrations (Blood Ammonia Checker II, Menarini Diagnostics) (Gerritzen-Bruning *et al.,* 2006). It has been demonstrated that the results of these in-house measurements correlate well with results from the routinely used enzymatic assay (Sterczer *et al.,* 1999).

Ammonia tolerance tests

For the classical ammonia tolerance test, ammonium chloride (NH4Cl) is administered either using a stomach tube or per rectum. A fasting ammonia sample is collected before the test, and another sample is taken 30 minutes after administration of the NH4Cl (Table 3; Rothuizen and van den Ingh, 1982b; Tyler, 1990a; Center, 1996a). More than a twofold increase in plasma ammonia indicates hepatic insufficiency and/or portosystemic shunting (Center, 1996a; Tillson and Winkler, 2002). The limitations of this test are patient stress, the risk of vomiting and the risk of defecating, any of which requires abortion of the test and finally involves ammonia toxicity (hypersalivation, lethargy) (Walker *et al.,* 2001).

An alternative to the classical ammonia tolerance test is the postprandial ammonia tolerance test, in which the patient is given a diet with a moderate protein count (Table 3). The optimal time for determination of the postprandial venous ammonia is 6 hours after feeding. The important advantages of this challenge test are the convenience and the lower risk for side effects compared to the classical ammonia tolerance test (Walker *et al.,* 2001).

Diagnostic value of liver function tests

Serum bile acid concentrations

Serum bile acid concentrations depend on a number of physiological variables, including hepatoportal circulation, functional hepatic mass, patency of the biliary tree and intestinal absorption (Center *et al.,* 1991; Center *et al.,* 1995). Animals with impaired hepatoportal perfusion, reduced hepatic mass or cholestasis will develop high systemic bile acid concentrations (Center, 1996a). Serum bile acid concentrations are used to allow discrimination between dogs or cats with and without hepatobiliary disease. For diagnosis of hepatobiliary disease, the specificity of serum bile acid concentrations is 100% above the cut-off value of 25 µmol/l in dogs or 20 µmol/l in cats (Center *et al.,* 1991 in Center *et al.,* 1995). The sensitivity of serum bile acid concentrations for detecting hepatobiliary insufficiency is higher than the sensitivity of serum liver enzymes and the classical sulfobromophthalein retention test, and it is equal to the ammonia tolerance test (Center *et al.,* 1985).

A series of papers describe the diagnostic efficacy of pre- and postprandial serum bile acid concentrations for the diagnosis of hepatobiliary diseases and portosystemic shunts. Reported values of the sensitivity for diagnosing portosystemic shunts are between 58 and 100% for preprandial serum bile acid concentrations, depending on the cut-off value used

Table 3. Summary of the ammonia tolerance test procedures.

Classical ammonia tolerance test

1. 12-hour fast
2. Collection of a venous blood sample to determine ammonia concentration
3. Administration of NH_4Cl
   - 100mg/kg with a maximum of 3 grams diluted in 30-50 ml water
   - using a feeding tube or per rectum
4. Collection of a second venous blood sample to determine ammonia concentration 30 minutes later

Postprandial ammonia tolerance test

1. 12-hour fast
2. Collection of a venous blood sample to determine ammonia concentration
3. Feed the patient (diet with moderate protein concentration count: 25% of MER = Maintenance Energy Requirement)
4. Collection of a second venous blood sample to determine ammonia concentration 6 hours later

Adapted from Rothuizen and van den Ingh (1982b) and Walker *et al.* (2001).

in the study, and 100% for the postprandial ones (Center *et al.,* 1985; Center *et al.,* 1991; Center *et al.,* 1995; Meyer, 1986; Kyles *et al.,* 2002; Gerritzen-Bruning *et al.,* 2006). Most reports agree that using the combination of pre- and postprandrial bile acid values provides the most reliable information because this reduces errors made due to gastrointestinal and gallbladder motility variables (Center *et al.,* 1985; Meyer, 1986; Sutherland, 1989; Center *et al.,* 1991; Center, 1993; Center *et al.,* 1995; Center, 1996a). In dogs with CPSS, the fasting serum bile acid concentration can be within normal limits, whereas the postprandial value is almost always abnormal (Center *et al.,* 1985; Winkler *et al.,* 2003). Therefore, a normal pre- or postprandial value does not exclude a CPSS, though it is very unlikely that animals with both normal pre- and normal postprandial values suffer from portosystemic shunting (Winkler *et al.,* 2003).

Serum bile acids cannot be used to differentiate liver diseases because there is a wide overlap between abnormal serum bile acid concentrations of patients with various hepatobiliary disorders. Therefore they are unsuitable as a solitary test to diagnose liver disorders, though they can reveal useful diagnostic patterns if they are combined with other liver tests. For example, abnormal serum bile acid concentrations in the absence of hyperbilirubinemia or increased liver enzyme activities, indicate metabolically quiet liver disease associated with hepatoportal perfusion abnormalities (PSS) or severely reduced hepatic mass (cirrhosis) (Center *et al.,* 1991; Center *et al.,* 1995; Center, 1996a). A strong indication of a perfusion abnormality is the so-called "shunting pattern of the bile acids", which is characterized by normal or moderately increased fasting and profoundly increased postprandial serum bile acid concentrations (Center, 1996a; Center, 1996b). The greatest median pre- and postprandial serum bile acid concentrations are observed in dogs with CPSS (Center *et al.,* 1991). However, there is no relationship observed between the magnitude of the increase in bile acid values and shunt type or the degree of hyperammonemia (Center *et al.,* 1985). Therefore, bile acids cannot be used to estimate the extent of circulatory or tissue compromise (Center, 1996a). Furthermore, preoperative bile acids cannot predict clinical outcome postoperatively or determine if a shunting vessel should be completely or partially ligated (Lawrence *et al.,* 1992; Hottinger *et al.,* 1995; Winkler *et al.,* 2003). Rarely, dogs or cats have preprandial serum bile acid concentrations exceeding the postprandial values. Possible causes, besides sample misidentification, are spontaneous gallbladder contraction during prolonged lack of food or differences in gastric emptying rates, release and response to cholecystokinin, intestinal transit time and gastrointestinal tract flora (Center *et al.,* 1991; Williams, 2003). The optimal time for collection of the postprandial sample may be influenced by reduced intestinal absorption, incomplete gallbladder contraction or altered intestinal transit time. If the sample is not collected at the peak absorption time, the postprandial serum bile acid concentration can be underestimated. It seems that this can be a problem both in clinically normal and in ill dogs, but that it does not play a significant role for dogs with CPSS (Center *et al.,* 1991; Center, 1993; Center, 1996a).

An important advantage of the serum bile acids compared with plasma ammonia determination and the ammonia tolerance test is that they cause less inconvenience for the patient and the clinician (Center *et al.,* 1985). Winkler *et al.,* (2003) stated that paired bile acid tests were significantly more sensitive (100%) than blood ammonia levels (86%). This is in contradiction with the recent findings of Gerritzen-Bruning *et al.,* (2006), who state that fasting plasma bile acid concentrations are less sensitive and considerably less specific than fasting plasma ammonia concentrations for detecting portosystemic shunting (congenital or acquired) either in a general population or in dogs with liver disease. Especially in dogs with liver disease, the fasting ammonia concentration remains highly specific (89.1%), whereas the fasting bile acid concentration loses most of its specificity (17.9%) compared to the general population (specificity 89.3%; sensitivity 67.9%). Therefore, determination of fasting serum bile acid concentrations is an adequate screening test in an otherwise healthy population. However, determination of fasting ammonia concentration is superior in a clinical population because of its higher specificity. An important reason for the lower specificity is the influence of cholestasis on fasting bile acid concentrations, whereas cholestasis has no influence on fasting ammonia concentration (Gerritzen-Bruning *et al.,* 2006). Unfortunately, no sensitivity or specificity scale for postprandial bile acid concentrations was defined in this study. A study by Tisdall *et al.,* (1995) revealed that the determination of serum bile acid concentrations is not a good screening test in Maltese dogs. Almost 80% of Maltese dogs without a portosystemic shunt had postprandial serum bile acid concentrations above the reference range. A possible explanation given by the authors is the presence of an additional substance in the serum of Maltese dogs which reacts with the enzymatic test. In this breed, the plasma ammonia concentration or the ammonia tolerance test should be performed instead of determination of bile acids to screen portosystemic shunt-suspected dogs (Tisdall *et al.,* 1995).

Venous ammonia concentration and ammonia tolerance test

Reported sensitivities of venous ammonia concentrations for diagnosing CPSS vary between 81 and 100% (Griffiths *et al.,* 1981; Rothuizen *et al.,* 1982; Center *et al.,* 1985; Meyer, 1986; Johnson *et al.,* 1987; Blaxter *et al.,* 1988; Tisdall *et al.,* 1994; Walker *et al.,* 2001; Winkler *et al.,* 2003; Gerritzen-Bruning *et al.,* 2006). On the other hand, the sensitivity for diagnosing hepatic diseases other than CPSS is low (28%) because the liver has a high reserve capacity for metabolizing ammonia. Only severe and generalized hepatocellular disorders result in hyperammonemia (Rothuizen and van den Ingh, 1982a; Rothuizen and van den Ingh, 1982b; Center, 1996a; Walker *et al.,* 2001; Gerritzen-Bruning *et al.,* 2006). The specificity for diagnosing CPSS is very high and varies between 89% and 100% (Walker *et al.,* 2001;

Gerritzen-Bruning *et al.,* 2006). Because of this high specificity, the fasting ammonia concentration is a good screening test for CPSS (Gerritzen-Bruning *et al.,* 2006). Only in young Irish Wolfhounds should the results be interpreted carefully because a moderate and transient metabolic hyperammonemia is observed in most pups of this breed (Meyer *et al.,* 1995; Meyer *et al.,* 1996; Kerr and van Doorn, 1999). A variation in the degree and speed of closure of the ductus venosus after birth is hypothesized as being the cause of this transient hyperammonemia in this breed (Meyer *et al.,* 1995). One study stated that the arterial ammonia concentration should be preferred over the venous ammonia concentration because the skeletal muscles are able to remove ammonia from the blood in patients with liver disease (Rothuizen and van den Ingh, 1982a), although arterial ammonia concentration is seldom performed because of technical reasons (Center, 1996a).

There is no relationship observed between the degree of hyperammonemia and the type of shunt and severity of neurological dysfunction (Griffiths *et al.,* 1981; Center *et al.,* 1985; Blaxter *et al.,* 1988). Although fasting ammonia concentrations are increased in most CPSS patients, a CPSS should not be ruled out on the basis of a normal blood ammonia level (Rothuizen and van den Ingh, 1982b; Meyer, 1986; Scavelli *et al.,* 1986; Johnson *et al.,* 1987; Center, 1996a; Winkler *et al.,* 2003). The sensitivity of the ammonia concentrations can be improved by performing an ammonia tolerance test (Center, 1996a; Walker *et al.,* 2001). Almost all dogs and cats with CPSS and normal fasting ammonia values show abnormal ammonia tolerance test results (Rothuizen and van den Ingh, 1982b; Meyer, 1986; Scavelli *et al.,* 1986; Johnson *et al.,* 1987; Tisdall *et al.,* 1994; Meyer *et al.,* 1999). Compared to single venous ammonia concentrations, using the postprandial ammonia tolerance test increases the sensitivity for diagnosing CPSS to 91%, whereas the sensitivity for diagnosing hepatocellular disease remains insufficient (36%) (Walker *et al.,* 2001).

CONCLUSION

A congenital portosystemic shunt is an infrequent disorder in dogs or cats with vague or intermittent clinical signs. A complete blood count, serum biochemistry, a coagulation profile, a liver function test, and urinalysis should always be performed to make a presumptive diagnosis of CPSS.

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