# Idiopathic noncirrhotic portal hypertension in dogs: 33 cases (1982–1998)

Susan E. Bunch, DVM, PhD, DACVIM; Susan E. Johnson, DVM, MS, DACVIM;
John M. Cullen, VMD, PhD, DACVP

**Objective**—To describe clinical signs, diagnostic findings, and outcome in dogs with idiopathic intrahepatic portal hypertension.

**Design**—Retrospective study.

**Animals**—33 dogs.

**Procedure**—Medical records of dogs with portal hypertension of intra-abdominal origin were reviewed. Dogs with intra-abdominal portal hypertension of vascular causes or with hepatic histopathologic changes consistent with severe diffuse hepatobiliary disease were excluded. History and results of physical examination, clinicopathologic tests, diagnostic imaging studies, histologic examination, and treatment were summarized. Outcome was determined in 26 dogs.

**Results**—Dogs were referred most often because of ascites, intermittent vomiting or diarrhea, and polydipsia of several months' duration. Microcytosis, high serum alkaline phosphatase and alanine transaminase activities, hepatic dysfunction, urine specific gravity ≤ 1.021, and abdominal transudate were the predominant clinicopathologic features. Microhepatia, abdominal effusion, and multiple anomalous venous anastomoses were the major findings of diagnostic imaging. Hepatic histopathologic changes were consistent with idiopathic noncirrhotic portal hypertension and were indistinguishable from those of dogs with surgically created portocaval anastomosis. Outcome was determined for 19 dogs released from hospital; 13 dogs remained healthy with mostly palliative treatment for periods of 5 months to 9 years.

**Conclusions and Clinical Relevance**—The clinical signs, clinicopathologic test results, portal pressure, and gross appearance of the liver of dogs with idiopathic noncirrhotic portal hypertension may be identical to those of dogs with cirrhosis; therefore liver biopsy is crucial. Because the prognosis for idiopathic noncirrhotic portal hypertension is generally favorable, owners of affected dogs should be discouraged from choosing euthanasia. (*J Am Vet Med Assoc* 2000; 218:392–399)

Portal hypertension is the result of sustained impairment of forward (hepatopetal) venous blood flow anywhere along the path from the portal vein to the right side of the heart. Mechanisms include absolute resistance to flow caused by luminal (eg, thrombosis) or extraluminal (eg, hepatic fibrosis and nodular regeneration) conditions, relative restriction to flow associated with massive portal volume overflow (eg, arterioportal fistula), or a combination of these factors.[1] By use of history and physical examination findings, the site of resistance to portal flow can often be localized to prehepatic, hepatic, or posthepatic origin. This information is clinically useful in presumptively determining the underlying cause.[2] Signs attributed to protracted portal hypertension of any cause include ascites and, less consistently, splenomegaly. Hepatomegaly is typical of disorders that cause posthepatic portal hypertension, whereas normal or small liver size is consistent with prehepatic or hepatic causes of portal hypertension. Signs of hepatic encephalopathy associated with portosystemic shunting and gastrointestinal bleeding may also be observed in dogs with portal hypertension caused by prehepatic or hepatic lesions but are not associated with portal hypertension caused by posthepatic lesions.[2-4]

The most common published causes of portal hypertension in dogs are disorders causing right-sided heart failure[5-7] and severe diffuse hepatobiliary disease that results in cirrhosis.[2,4] For dogs with hepatic disease, liver biopsy is needed for accurate diagnosis, treatment planning, and prognosis. Prognosis for dogs with right-sided heart failure can vary widely,[5-7] but prognosis for most dogs with cirrhosis is poor.[4,8]

The purpose of the study reported here was to describe clinical signs, diagnostic findings, and outcome in dogs with idiopathic intrahepatic portal hypertension, which has been recognized infrequently in the United States.

## Criteria for Selection of Cases

Medical records of dogs with a diagnosis of portal hypertension not associated with cardiac or vena caval disease and that had liver biopsy performed between October 1982 and January 1999 were reviewed. Portal hypertension was identified by viewing multiple portosystemic shunt vessels, direct measurement of portal pressure, or both. Dogs for which a vascular cause of portal hypertension had been determined (eg, arterioportal fistula, portal vein thrombosis, hepatic venoocclusive disease) were excluded. Dogs were also excluded if there were histologic liver lesions consistent with severe diffuse chronic hepatobiliary disease (eg, neoplastic cell infiltrates or a combination of necrosis, cholestasis, bridging fibrosis, and nodular regeneration).

## Procedures

Information gathered from each record included signalment, history, physical examination findings,

From the Departments of Clinical Sciences (Bunch) and Microbiology, Parasitology and Pathology (Cullen), College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27606; and the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus OH 43210 (Johnson).

Presented in part at the 15th Annual Forum, American College of Veterinary Internal Medicine, Lake Buena Vista, Florida, 1997.

results of clinicopathologic tests, diagnostic imaging findings, abdominal surgical procedures and observations, histologic liver lesions, treatments, and outcome. Changes in laboratory reference ranges during the years of the study were taken into account when reporting clinicopathologic test results; liver enzyme activities (**alkaline phosphatase [AP]** and **alanine transaminase [ALT]**) were expressed as a multiple of the upper limit of the reference range values (eg, 2 × upper reference limit). Liver biopsy specimens were stained routinely with H&E; sections of each specimen were also stained with Masson's trichrome stain. For comparison, liver biopsy specimens obtained from 10 dogs before and 3 and 4 months after surgical creation of a portacaval shunt[a] were stained similarly and examined. One pathologist (JMC) reviewed all liver specimens. Follow-up information for dogs with naturally occurring disease was obtained after discharge by return visits to the veterinary teaching hospital or referring veterinarian or by telephone or written communication with owners.

## Results

**Signalment**—Thirty-three dogs met inclusion criteria for the study. Age ranged from 3 months to 8 years (mean, 2.8 years; median, 2.0 years). Twenty-six (78.8%) dogs were ≤ 4 years old at time of referral. There were 19 (57.6%) females and 14 (42.4%) males. Thirty-two of 33 dogs were purebred dogs, representing 17 breeds. There were 6 Doberman Pinschers, 5 Cocker Spaniels, and 3 Rottweilers; 14 other breeds were each represented once or twice. Two Standard Schnauzers were littermates. Twenty-three of 32 (72%) dogs were breeds from the sporting, working, herding, or hound groups, according the American Kennel Club classification system. Healthy adult dogs of all but 1 of these breeds are expected to weigh > 10 kg (22 lb). The remaining 9 (28%) dogs were of breeds from the nonsporting, toy, and terrier groups of which adult dogs are expected to weigh < 10 kg.

**History and physical examination findings**—All dogs were referred because of clinical signs of 3 weeks to 1 year in duration; most dogs were referred after signs persisted for 2 to 3 months. The most common historical complaints were abdominal enlargement associated with ascites (20 dogs), gastrointestinal signs (14; signs included intermittent vomiting, diarrhea, or both in 13 dogs, and melena in 1 dog), and polydipsia (11). Ten dogs had diffuse CNS signs believed to be attributable to hepatic encephalopathy. Abnormal physical examination findings included ascites (19 dogs), thin body condition (19), small stature for the breed (5 of 13 dogs ≤ 1 year of age), and melena (1). Six dogs were considered clinically normal by use of physical examination.

**Clinicopathologic findings**—Results of a CBC and serum biochemical profile were available for all dogs. Hematologic results were unremarkable, except for the finding of microcytosis (low **mean cell volume [MCV]**) in 19 (57.5%) dogs (MCV, 57 fl; range, 49 to 62 fl; lower reference limit, 63 fl), mild anemia in 4 (12%) dogs (RBC range, 3.98 to 4.61 × $10^6$ RBC/µl; lower reference limit, 5.0 × $10^6$ RBC/µl), and mild thrombocytopenia in 4 of 30 (13%) dogs for which thrombocyte counts were available (range, 99,000 to 147,000 cells/µl; lower reference limit, 150,000 cells/µl). Serum AP activity was high in 21 (63.6%) dogs (mean, 3.2 times upper reference limit; range, 1.1 to 14.3 times upper reference limit), and serum ALT activity was high in 25 (63.6%) dogs (mean, 5.5 times upper reference limit; range, 1.2 to 26 times reference limit; **Fig 1**). Other serum biochemical abnormalities included hypoalbuminemia in 25 (75.7%) dogs (mean, 2.2 g/dl; range, 1.1 to 2.7 g/dl; lower reference limit, 2.8 g/dl) and low serum urea concentration in 13 (39.4%) dogs (mean, 5.3 mg/dl; range, 3 to 7 mg/dl; lower reference limit, 8 mg/dl). Liver function was assessed in 30 dogs by use of 1 or more of the following tests: preprandial (after withholding food) and 2-hour postprandial or random serum bile acid concentrations (20 dogs); plasma ammonia concentration after withholding of food or after administration of ammonium chloride (16; 0.1 g/kg as a 10% solution,

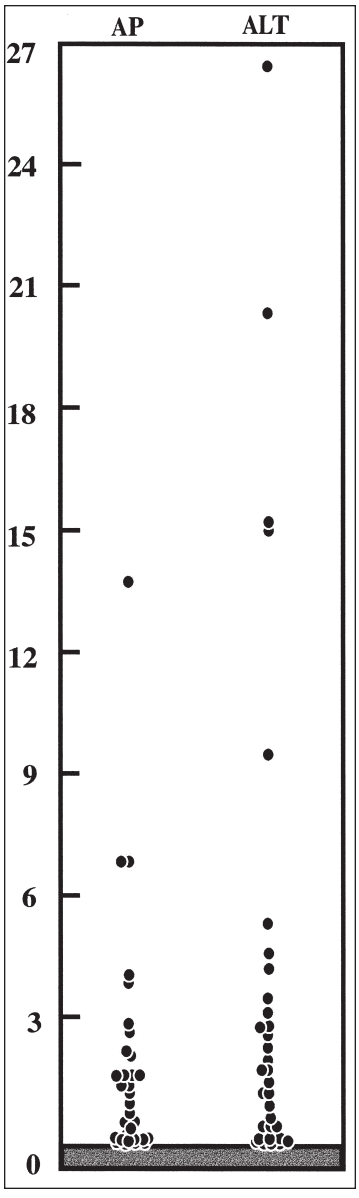


Figure 1—Serum alkaline phosphatase (AP; n = 21) and alanine transaminase (ALT; 25) activities in dogs with idiopathic noncirrhotic portal hypertension. Shaded area at bottom of figure represents reference range; numerals on left side of figure indicate multiplication factor for upper reference limit value (eg, 3 × upper reference limit).

PO); and percentage retention of sulfobromophthalein 30 minutes after injection (9; **Fig 2**). Results of these tests were consistent with liver dysfunction in 28 of 30 dogs. Plasma ammonia concentration after withholding of food was the only test chosen to assess liver function in 2 dogs that had received long-term treatment for hepatic encephalopathy before referral; results were within reference range. Urinalysis was performed in 26 dogs; specific gravity was ≤ 1.010 in 14 (53.8%) dogs and ≤ 1.021 in 18 (69.2%) dogs. Abdominal fluid was analyzed (total and differential nucleated cell counts, specific gravity, and refractive index) in 18 dogs; results were consistent with a pure transudate in all 18 dogs.

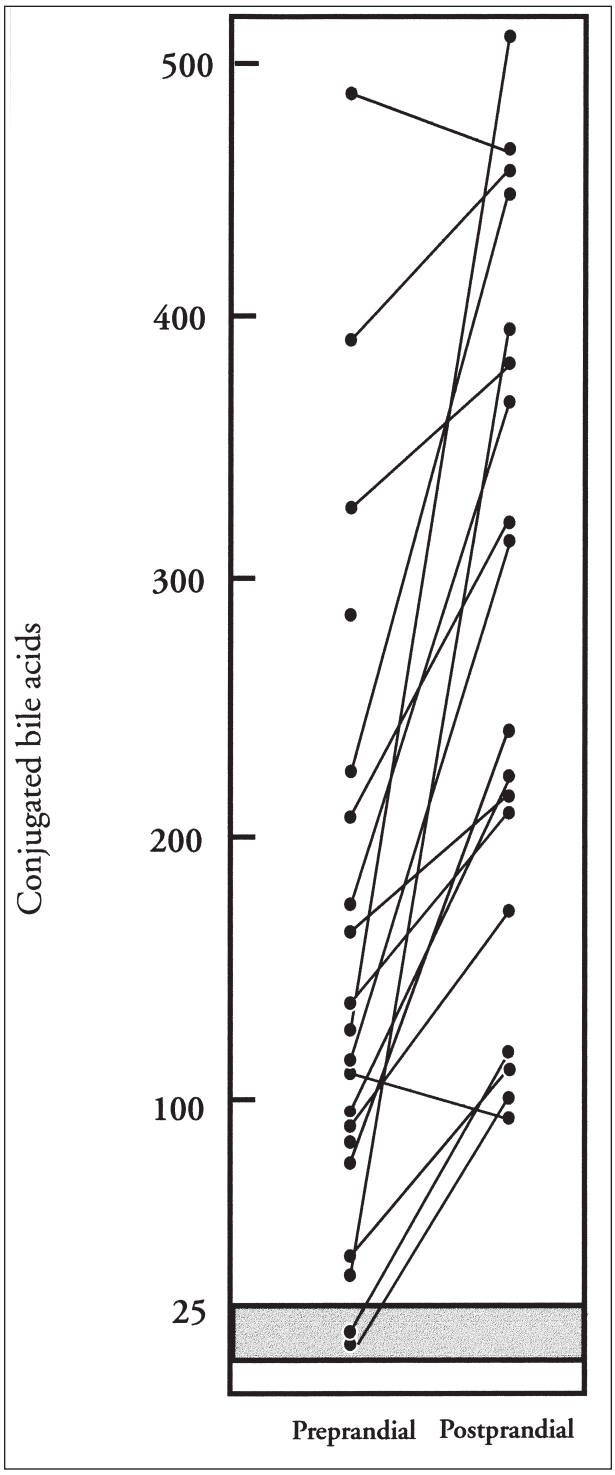


Figure 2—Conjugated bile acid concentrations (µmol/L) determined after withholding of food (preprandial) and 2 hours after a meal (postprandial) in 20 dogs with idiopathic noncirrhotic portal hypertension. Shaded area represents reference range.

**Diagnostic imaging results—**Survey abdominal radiographs were made in 15 dogs; poor contrast (n = 10) and microhepatia (8) were consistent findings. Nephrolithiasis was found in 2 dogs that were 6 and 8 years of age.

Abdominal ultrasonography was performed in 23 dogs. Microhepatia and abdominal effusion were recorded in 16 dogs, and multiple abnormal extrahepatic veins were detected in 16 dogs. Liver texture was described as hyper-, hypo-, or heterogeneously echogenic in 7 dogs and was considered unremarkable in 5 dogs. Other findings that were each recorded in 2 dogs included bilateral renomegaly and enlarged portal vein, and in 1 dog each, splenomegaly, enlarged caudal vena cava, and portal vein thrombus also were recorded. Observations regarding intrahepatic portal vasculature were recorded inconsistently.

**Abdominal surgical procedures and observations—**Liver specimens for histologic examination were obtained by use of exploratory celiotomy in 28 dogs, by percutaneous needle biopsy in 2 dogs, and at necropsy in 3 dogs. Results of contrast mesenteric portography performed in 15 dogs indicated that the extrahepatic portion of the portal vein was patent and that there were multiple extrahepatic shunt vessels in 14 dogs (**Fig 3**). The extrahepatic portion of the portal vein was assessed as a third of the normal size in 1 dog. Intrahepatic portal perfusion appeared normal in 6 dogs, vessels were attenuated and tortuous in 4 dogs, and in 1 dog, the left liver lobe appeared to be perfused poorly, whereas portal perfusion to the rest of the liver was considered acceptable. One dog with a 89.5% shunt fraction, as determined by use of transrectal

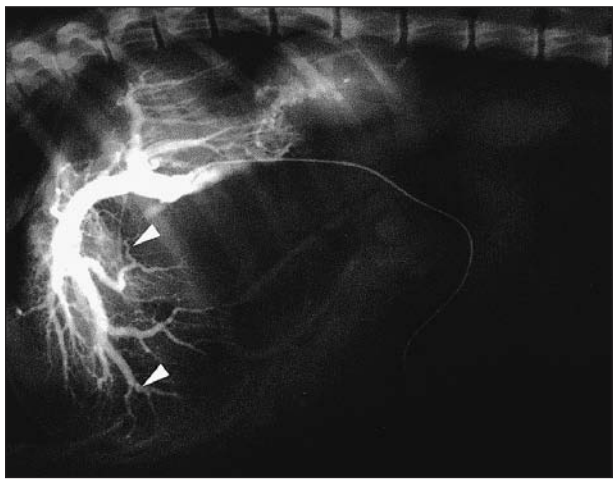

Figure 3—Contrast lateral radiographic view of the extrahepatic portion of the portal vein in a dog with idiopathic noncirrhotic portal hypertension. Notice distended tortuous medium-sized portal venules (arrowheads). Hepatofugal portal flow through portocaval anastomoses clustered around the left kidney is also evident.

scintigraphy, had normal results of a portogram. A contrast aortogram and caudal venacavogram were also performed in 2 dogs; results were unremarkable. In dogs that underwent abdominal surgery, the liver was described as small with a granular or finely nodular appearance. Portal pressure was measured by use of water manometry at the time of abdominal surgery in 13 dogs; values ranged from 8 to 24 cm $H_2O$ (mean, 17.2 cm $H_2O$; median, 18 cm $H_2O$; reference range, 5 to 13 cm $H_2O$).

**Histologic lesions in dogs with naturally occurring disease—**There was a range of histologic lesions in livers of affected dogs. Regardless of biopsy method and specimen size, a characteristic pattern was evident. The sublobar portal tracts were often unaffected, but the smaller divisions of the portal system (the lobular portal tracts) were almost always abnormal. Affected portal tracts were characterized by multiple arterioles. Portal veins were smaller than normal or absent in most portal tracts, although in some portal tracts the portal veins were enlarged (**Fig 4**). The amount of collagen in the portal tracts varied considerably. In dogs that had fibrosis, fine septae of connective tissue often extended into the parenchyma, particularly along the distributing branches of the portal tracts. Uncommonly, fibrosis bridged to other portal areas or to central veins. The connective tissue of the portal tracts was, in some circumstances, abnormally reduced, and the vascular structures were not clearly separated from the liver parenchyma by a distinct limiting plate. In some dogs, the distributing branches of the portal vasculature had more prominent and numerous arterioles, compared with normal livers. In a few dogs, lymphatics in portal tracts were distended. Bile ducts in the portal tracts were usually normal, but in a few instances proliferation of small-caliber bile ducts in the distributing branches of the portal vasculature was observed. Inflammation was consistently absent or limited to small numbers of lymphocytes and plasma cells.

The parenchyma had abnormal lobular architecture associated with considerable variation in the size of hepatic lobules (**Fig 5**). Multifocal areas of hepatocellular atrophy were evident in larger sections of liver but were not always apparent in smaller biopsy specimens. Numerous small arterioles were distributed within the lobules in a haphazard fashion. Lobules were often partially outlined by prominent distributing branches of the portal tracts, but evidence of nodular proliferation of hepatocytes was not detected in the initial biopsy specimens from any of the dogs. In some dogs, hepatocytes appeared vacuolated, but this was not a consistent change. Pigment accumulation, interpreted as lipofuscin and hemosiderin, was commonly observed in small amounts; large accumulations were evident in a few dogs.

Terminal hepatic (central) veins were often smaller than normal, although the perivenular connective tissue was often expanded. Distended lymphatics and small arterioles were commonly apparent within this connective tissue (**Fig 6**). In approximately half of the dogs, there were fine wisps of collagen, detected by use of Masson's trichrome staining, that extended along the margins of the centrilobular sinusoids. Subcapsular sinusoids were enlarged in the dogs that had prominent distention of lymphatics adjacent to the central veins.

**Histologic findings in dogs with surgically created portocaval shunts—**Histologic changes in the livers of 10 dogs that had surgically created portocaval shunts were similar to those found in dogs with natu-

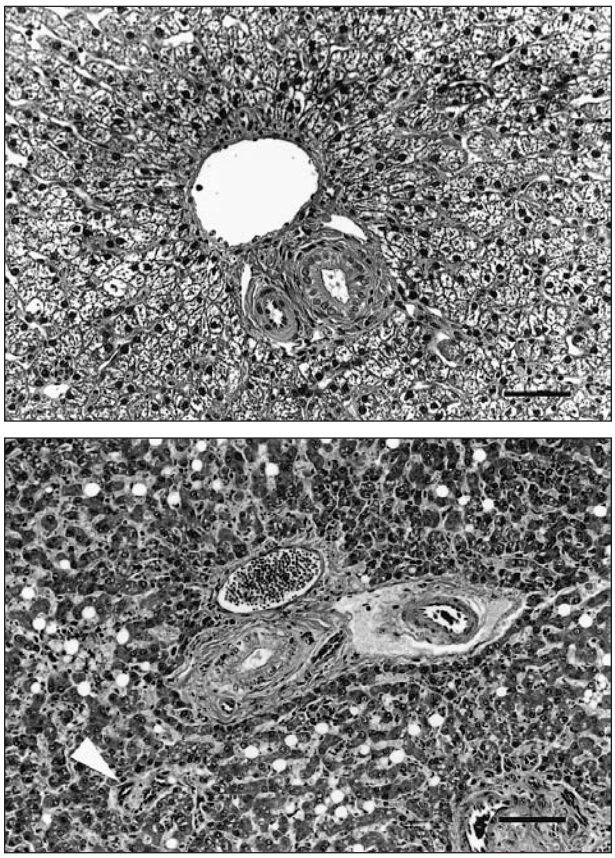

Figure 4—Photomicrographs of portal tracts from a healthy dog (top) and a dog with idiopathic noncirrhotic portal hypertension (bottom). In the dog with idiopathic noncirrhotic portal hypertension, the portal vein is smaller than typical, and multiple arterioles are evident in the adjacent parenchyma (arrowhead). H&E stain; bars = 100 μm.

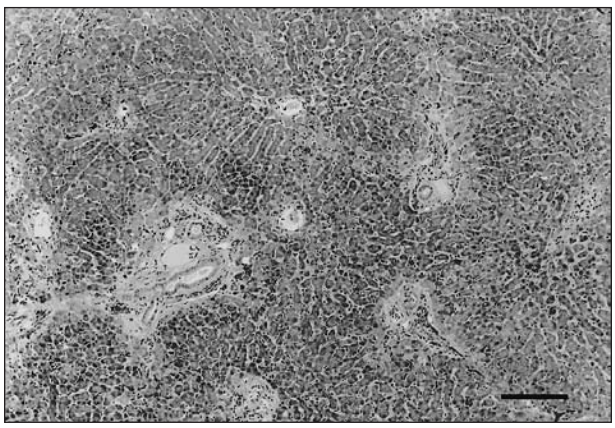

Figure 5—Photomicrograph of a section of liver from a dog with idiopathic noncirrhotic portal hypertension and abnormal lobular architecture. Lobules are smaller than typical. A large portal tract is evident, along with numerous smaller portal tracts that have modest proliferation of arterioles and small portal veins. H&E stain; bar = 180 μm.

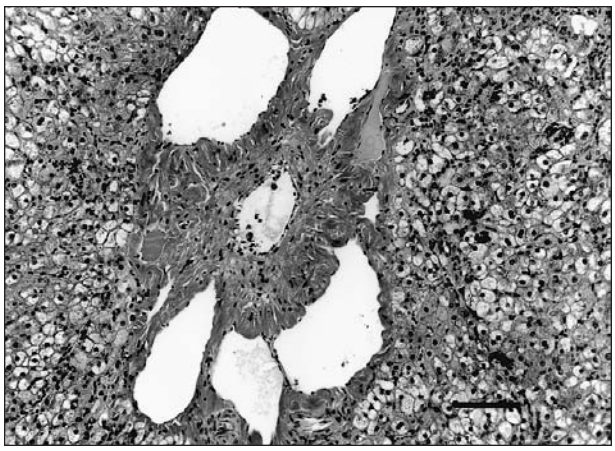

Figure 6—Photomicrograph of a section of liver from a dog with idiopathic noncirrhotic portal hypertension. Notice distention of the lymphatics around the central vein. H&E stain; bar = 100 µm.

rally occurring disease. In the first biopsy specimen of each dog, obtained 3 months after surgery, the liver had a prominent increase in the numbers of arterioles in the portal tracts and within the hepatic parenchyma. In some lobules, arterioles were found in the connective tissue surrounding the terminal hepatic veins. Portal veins were usually collapsed and inapparent, but in some instances they were distended. Some of the distended portal veins appeared to have thickened muscular walls, typical of the change termed arteriolization. There was a moderate increase in the collagenous connective tissue of the portal tracts and the terminal hepatic veins. Lymphatics that surrounded the terminal hepatic veins were often dilated. Atrophy of hepatocytes was evident, usually in the centrilobular (periacinar) areas, but nearly as often there was diffuse hepatocyte atrophy. In some instances, increased fibrosis and lymphatic distention in portal tracts and around terminal hepatic venules was detected in the biopsy specimens obtained 4 months after surgery.

**Treatment and outcome—**Six dogs were euthanatized at the time of initial diagnosis, and 1 dog was euthanatized within 5 months of initial diagnosis. Of the remaining 26 dogs that were discharged from the hospital, 3 received no treatment, 2 were treated surgically by banding the caudal vena cava, according to a published procedure,[9] and 21 were treated according to their clinical signs. Twenty-three dogs received a diet moderately restricted in sodium and protein,[b] including the 2 dogs treated surgically. Seven of 23 dogs received this diet as their only treatment. Additional treatment for other dogs included administration of furosemide or spironolactone (n = 7), metronidazole or cephalexin or neomycin and lactulose (7), antiulcer agents (cimetidine, 1; sucralfate, 1), and ursodiol[c] (2).

Of 26 dogs discharged from the hospital, outcome was determined for 19; 7 were lost to follow-up. Of the 19 dogs for which information was available, 4 were euthanatized because of factors related to persistent portal hypertension or portosystemic shunting (perforated duodenal ulcer, 3 dogs [2 to 4 weeks after diagnosis]; recurrent urate urolithiasis, 1 dog [2.5 years after diagnosis]). One dog died of unrelated illness, and 1 dog died of unknown cause. At the time of this report, 13 dogs had remained clinically normal for periods ranging from 5 months to 9 years (mean, 2.9 years; median, 2 years). Ascites resolved in 12 of 13 dogs but was difficult to control in 1 dog with a serum albumin concentration of 1.0 g/dl. In dogs that received drug treatment for ascites, hepatic encephalopathy, or both, owners suspended drug administration within 6 months of diagnosis because of perceived lack of necessity. Physical examination and clinicopathologic testing (CBC, serum biochemistry profile, urinalysis, serum bile acid concentrations determined after withholding of food and 2 hours after ingestion of a meal) were repeated serially in 8 of 13 dogs for as long as 6 years; results were unchanged from initial findings in 7 of 8 dogs. Serum bile acid concentration measured 2 hours after a meal 4 months after surgery in 1 of 2 dogs that underwent vena caval banding was improved (before surgery, 375 µmol/L; after surgery, 36 µmol/L); results were unchanged in the second dog. Abdominal ultrasonography was repeated 3 or 4 years after initial diagnosis in 5 of 8 dogs that were evaluated serially; results were unchanged from previous findings. Liver tissue was examined histologically a second time in 4 dogs (including 1 that underwent caudal vena caval banding) 2 weeks, 15 months, 20 months, and 4.5 years, respectively, after initial diagnosis. One dog died 2 weeks after the initial biopsy was performed. At necropsy, the liver from this dog had a substantial increase in fibrosis, compared with the initial biopsy specimen. Fibrosis expanded the portal tracts and central veins and dissected into the lobules, forming small nodular aggregates of hepatocytes. In the other 3 dogs from which biopsy specimens were obtained 15 months to 4.5 years after initial diagnosis, there was a consistent pattern of mild increase in portal tract and central vein fibrosis, and 1 dog had regenerative nodules. Diagnostic testing was not repeated in 5 dogs, but their owners were contacted by telephone or letter. Owners were happy with the quality of their pet's lives.

## Discussion

We believe that the condition described in the dogs of our report most closely resembles primary hypoplasia of the portal vasculature, as reported in 42 dogs in the Netherlands.[10] In that report, affected dogs were referred because of stunted growth or weight loss (69%), apathy (67%), intermittent vomiting, diarrhea, or both (38%), anorexia (33%), ascites (28%), and polydipsia (26%). More than 80% of the dogs were ≤ 2.5 years of age. In all dogs, serum biochemical test results were consistent with hepatic dysfunction. Abdominal fluid was not analyzed, but the gross description (clear and watery) was consistent with a pure transudate. Portal pressure was not measured in any dog, but in all dogs obvious multiple portosystemic collateral vessels, typical of the pattern associated with portal hypertension, were observed at surgery or necropsy. In most dogs, the liver had a slightly irregular surface and was judged to be small in half of the dogs. In 31% of the dogs, the extrahepatic portal vein was believed to be underdeveloped. Histopathologic

features in the livers of affected dogs[10] were quite similar to those in the dogs of our report. Thirty-nine dogs died naturally or were euthanatized because of disease progression. Long-term follow-up information was available for only 3 dogs that survived for up to 3 years. A protein-restricted diet was the only treatment. As part of their report, the authors reviewed 3 dogs reported as having hepatoportal fibrosis,[11] reconsidered the diagnosis, and concluded that the condition was actually portal vein hypoplasia.

Remarkable similarity in clinical description, diagnostic test results, and histopathologic findings in liver biopsy specimens from dogs reported to have hepatoportal fibrosis,[11,12] idiopathic hepatic fibrosis,[13] venoocclusive disease,[14] idiopathic chronic liver disease,[15] and nonfibrosing liver disease[16] strongly suggests that these liver disorders likely represent portal hypertension associated with the same underlying cause: intrahepatic portal vein hypoplasia. It seems possible that additional cases of intrahepatic portal vein hypoplasia may be detected in reports of dogs described as having portosystemic shunt, presumably of congenital origin.[17,18] Portal pressure was not measured in the dogs of the latter 2 reports, but 2 of 11 dogs had multiple portosystemic shunts,[17] and 3 of 6 dogs had ascites and multiple portosystemic shunts[18] consistent with high portal pressure. Portal pressure is within reference range in dogs with congenital portosystemic shunts.[19-21] In 2 more recent reports, it was concluded that the cause of portal hypertension and its sequelae (ie, ascites, signs consistent with hepatic encephalopathy, and portosystemic shunts) in 4 young male Doberman Pinschers[22] and in 13 of 32 dogs with a genetic storage disease[23] was a unique condition that resembled idiopathic noncirrhotic portal hypertension in human patients. Signs detected at referral, clinicopathologic findings, diagnostic imaging results, and histologic liver lesions in the dogs of these[22,23] and earlier reports[11-16] are virtually identical to those of the dogs of the study reported here; we believe that the cause of these findings was intrahepatic portal vein hypoplasia.

Noncirrhotic portal hypertension in human patients is the term ascribed to a spectrum of mostly nonprogressive hepatobiliary diseases characterized by intrahepatic presinusoidal portal hypertension, absence of extrahepatic portal vein obstruction, and relatively mild hepatic histologic changes.[24-27] Contrast studies of the extra- and intrahepatic portal vasculature often reveal dilation of the extrahepatic portal vein, collateral venous anastomoses, paucity of middle-sized intrahepatic portal vein branches, and abrupt cutoff of the peripheral venous branches.[28]

Microscopic examination of wedge liver biopsy specimens is vital in excluding other causes of intrahepatic portal hypertension in human patients with noncirrhotic portal hypertension.[29-33] Except for the finding of sclerosis of portal venules in human patients with noncirrhotic portal hypertension, the hepatic histopathologic findings in the dogs of the present report are remarkably similar. Investigators suspect that the histopathologic findings of nodular regenerative hyperplasia and incomplete septal cirrhosis in human patients with noncirrhotic portal hypertension reflect chronologic progression of a single disease.[26,32]

The importance of the fibrosis seen histologically in liver specimens from patients with noncirrhotic portal hypertension, in terms of either cause or effect, is unknown. Periportal fibrosis developed in rats repeatedly given lithocholate, a naturally occurring hepatotoxic bile salt, orally.[34] Increases in portal vascular resistance correlated with duration of lithocholate administration. It is possible that long-standing portosystemic shunting secondary to portal hypertension associated with congenital intrahepatic portal vein hypoplasia in the dogs of the study reported here resulted in repeated exposure to endogenous lithocholate, inducing periportal fibrosis. On the basis of this possible scenario, ursodiol was prescribed indefinitely for several dogs in our study.

Since noncirrhotic portal hypertension was first described in human patients in 1889,[35] efforts have been made to better characterize the disorder and identify underlying causes. Some investigators have speculated that because noncirrhotic portal hypertension is most often seen in patients from underdeveloped countries, gastrointestinal exposure to toxins or long-term absorption of bacterial products should be considered.[24-27] Proposed underlying causes have included exposure to trace metals such as arsenic and immune system dysregulation associated with certain infectious diseases such as schistosomiasis and malaria. Histologic liver lesions characteristic of noncirrhotic portal hypertension were induced in rabbits[36] and dogs[37] by intraportal injection of killed nonpathogenic *Escherichia coli*.

Two studies have investigated the prognosis for human patients with noncirrhotic portal hypertension, compared with that for cirrhosis.[d,38] In both studies, it was concluded that cirrhosis had a much worse prognosis than noncirrhotic portal hypertension. Review of results of our report and information in the veterinary literature concerning cirrhosis in dogs suggests the same general conclusion.

The histopathologic changes in the liver biopsy specimens of the dogs of our study were unlike those of cirrhosis as well as other generalized primary hepatopathies reported to cause intrahepatic portal hypertension in dogs. Congenital multiple microscopic arteriovenous fistulae were suspected to be responsible for portal hypertension that caused ascites, melena, and signs of hepatic encephalopathy in a 5-month-old female Miniature Poodle.[39] The presence of jaundice, diffuse infiltration of hepatic parenchyma with a mixed inflammatory cell population, severe lobular disorganization, and poor prognosis discriminates lobular dissecting hepatitis[40,41] from noncirrhotic portal hypertension.

Interestingly, the histologic liver lesions in the dogs reported here are indistinguishable from those in dogs with experimentally created portosystemic shunt[a] or naturally occurring congenital portosystemic shunt, even in dogs that are older than typical age at the time of diagnosis,[42,43] and from hepatic microvascular dysplasia.[44-46] This implies that the primary defect in noncirrhotic portal hypertension is localized to the smaller portal venules, and the remaining changes are consistent with longstanding portosystemic shunting and

portal blood deprivation. Portal hypertension is not a feature of created or congenital portosystemic shunts or of hepatic microvascular dysplasia. Of concern was some evidence of lesion progression in serial liver biopsy specimens from 4 dogs in our study, as indicated by increased amounts of fibrosis. Use of antifibrotic agents has been reported in a small number of reports. Gradual improvement in clinical signs and liver function test results were detected in 1 dog given colchicine (0.025 mg/kg [0.011 mg/lb] of body weight, PO, q 24 h) for 30 months.[12] Hepatic fibrosis did not appear to have progressed at the time of euthanasia because of nonhepatic illness. In another report, colchicine (0.025 mg/kg, PO, q 24 h) or prednisone (0.5 to 1.0 mg/kg [0.23 to 0.45 mg/lb], PO, q 24 h initially, then q 48 h) was given to modulate fibrosis in 2 and 6 dogs, respectively.[13] Although the number of treated dogs was small, the authors concluded that prednisone did little to modify the course of the disease.

Surgical management by use of vena caval banding, as an attempt to decrease portosystemic shunting and improve hepatic portal blood flow, was chosen for 2 dogs in our study, which was insufficient to draw meaningful conclusions. Varied success has been achieved with use of this procedure in dogs with hepatobiliary disease.[8,9,47] The earliest reference to success of vena caval banding claimed clinical improvement in > 60% of treated dogs.[9] In a report of 30 dogs with cirrhosis, 12 of which underwent vena caval banding, survival time was not different between dogs treated medically and dogs treated surgically.[9] Hepatic perfusion was not improved in dogs with experimentally induced severe hepatobiliary disease and portal hypertension that underwent vena caval banding.[47] These observations, combined with the fact that creation of portosystemic shunts, as opposed to reversal of portosystemic shunts, is considered a surgical remedy for human patients with noncirrhotic portal hypertension, extremely high portal pressure, and recurrent bleeding from esophageal varices,[48] suggest that vena caval banding cannot be recommended for treatment of dogs with noncirrhotic portal hypertension at this time.

Clinical signs of hepatic encephalopathy and ascites in the dogs of the study reported here were managed successfully, primarily by use of a protein- and sodium-restricted diet. More aggressive measures to control ascites (eg, administration of diuretics or therapeutic paracentesis) were needed only temporarily in most dogs. Among dogs that were discharged from the hospital and ultimately died of consequences related to portal hypertension, duodenal ulcer was the most common reason for death. Predisposition to gastrointestinal bleeding is common in dogs with intrahepatic portal hypertension and is likely associated with heightened susceptibility of the gastric and duodenal mucosa to injury, so indefinite use of antiulcer medication such as a histamine type-2 receptor antagonist is recommended. Polydipsia was probably related to a combination of factors, including low urea nitrogen content, psychogenic factors, and others,[49] so no particular treatment is warranted.

Idiopathic noncirrhotic portal hypertension is an infrequently reported cause of intrahepatic portal hypertension in dogs in the United States and appears to have a generally favorable prognosis. If the origin of portal hypertension has been localized to the liver and the histopathologic changes in liver wedge biopsy specimens are consistent with portosystemic shunt, then a diagnosis of idiopathic noncirrhotic portal hypertension can be made. Six dogs in the study reported here were euthanatized before a final diagnosis was reached because of the perceived poor prognosis. It is important to know that the clinical signs, clinicopathologic test results, portal pressure, and gross appearance of the liver of dogs with idiopathic noncirrhotic portal hypertension may be identical to those of dogs with more life-threatening hepatopathies. Only after liver biopsy results are available can an accurate diagnosis and prognosis be rendered. If a diagnosis of idiopathic noncirrhotic portal hypertension is made, we recommend treatment with a protein- and sodium-restricted diet, ursodiol, and a histamine type-2 receptor antagonist indefinitely. Colchicine may also be needed if a substantial amount of fibrosis is detected histologically. Because the prognosis for idiopathic noncirrhotic portal hypertension is generally favorable, owners of affected dogs should be discouraged from electing euthanasia.

[a]Courtesy of Laflamme D, Ralston Purina Company, St Louis, Mo, and Allen S, College of Veterinary Medicine, University of Georgia, Athens, Ga.

[b]Prescription diet k/d, Hill's Pet Products, Topeka, Kan.

[c]Actigall, Ciba Geigy Corp, Summit, NJ.

[d]Orozco H, Takahashi T, Garcia-Tsao G, et al. Idiopathic portal hypertension, portal vein thrombosis and cirrhosis. A comparative clinical study (abstr). *Gastroenterology* 1990;98:A618.

## References

1. Johnson SE. Portal hypertension. Part I. Pathophysiology and clinical consequences. *Compend Contin Educ Pract Vet* 1987;9:741–748.

2. Johnson SE. Portal hypertension. Part II. Clinical assessment and treatment. *Compend Contin Educ Pract Vet* 1987;9:917–928.

3. Hess PR, Bunch SE. Management of portal hypertension and its consequences. *Vet Clin North Am Small Anim Pract* 1995;25:461–483.

4. Twedt DC. Cirrhosis: a consequence of chronic liver disease. *Vet Clin North Am Small Anim Pract* 1985;15:151–176.

5. Calvert CA, Thrall DE. Treatment of canine heartworm disease coexisting with right-side heart failure. *J Am Vet Med Assoc* 1982;180:1201–1203.

6. Berg RJ, Wingfield W. Pericardial effusion in the dog: a review of 42 cases. *J Am Anim Hosp Assoc* 1984;20:721–730.

7. Fingland RB, Bonagura JD, Myer CW. Pulmonic stenosis in the dog: 29 cases (1975–1984). *J Am Vet Med Assoc* 1986;189:218–226.

8. Boothe HW, Howe LM, Edwards JF, et al. Multiple extrahepatic portosystemic shunts in dogs: 30 cases (1981–1993). *J Am Vet Med Assoc* 1996;208:1849–1854.

9. Breznock EM, Whiting PG. Portocaval shunts and anomalies. In: Slatter DH, ed. *Textbook of small animal surgery*. Philadelphia: WB Saunders Co, 1985;1156–1173.

10. Van den Ingh TS, Rothuizen J, Meyer HP. Portal hypertension associated with primary hypoplasia of the hepatic portal vein in dogs. *Vet Rec* 1995;137:424–427.

11. Van den Ingh TS, Rothuizen J. Hepatoportal fibrosis in three young dogs. *Vet Rec* 1982;110:575–577.

12. Rutgers HC, Haywood S, Batt RM. Colchicine treatment in a dog with hepatoportal fibrosis. *J Small Anim Pract* 1990;31:97–101.

13. Rutgers HC, Haywood S, Kelly DF. Idiopathic hepatic fibrosis in 15 dogs. *Vet Rec* 1993;133:115–118.

14. Rand JS, Best SJ, Mathews KA. Portosystemic vascular

shunts in a family of American cocker spaniels. *J Am Anim Hosp Assoc* 1988;24:265–272.

15. Laflamme DP. Heptoencephalopathy associated with multiple portal systemic shunts in a dog. *J Am Anim Hosp Assoc* 1989;25:199–202.

16. Hunt GB, Malik R, Chapman BL, et al. Ascites and portal hypertension in three young dogs with non-fibrosing liver disease. *J Small Anim Pract* 1993;34:428–433.

17. Cornelius LM, Thrall DE, Halliwell WH, et al. Anomalous portosystemic anastomoses associated with chronic hepatic insufficiency in six young dogs. *J Am Vet Med Assoc* 1975;167:220–228.

18. Meyer DJ. Liver function tests in dogs with portosystemic shunts: measurement of serum bile acid concentration. *J Am Vet Med Assoc* 1986;188:168–169.

19. Breznock EM. Surgical manipulation of portosystemic shunts in dogs. *J Am Vet Med Assoc* 1979;174:819–826.

20. Mathews K, Gofton N. Congenital extrahepatic portosystemic shunt occlusion in the dog: gross observations during surgical correction. *J Am Anim Hosp Assoc* 1988;24:387–394.

21. Swalec KM, Smeak DD. Partial versus complete attenuation of single portosystemic shunts. *Vet Surg* 1990;19:406–411.

22. DeMarco JA, Center SA, Dykes N, et al. A syndrome resembling idiopathic noncirrhotic portal hypertension in 4 young Doberman Pinschers. *J Vet Intern Med* 1998;12:147–156.

23. McEntee MF, Wright KN, Wanless I, et al. Noncirrhotic portal hypertension and nodular regenerative hyperplasia of the liver in dogs with mucopolysaccharidosis type I. *Hepatology* 1998;28: 385–390.

24. Sarin SK. Non-cirrhotic portal fibrosis. *Gut* 1989;30: 406–415.

25. Ludwig J, Hashimoto E, Obata H, et al. Idiopathic portal hypertension. *Hepatology* 1993;17:1157–1162.

26. Bioulac-Sage P, LeBail B, Bernard P-H, et al. Hepatoportal sclerosis. *Semin Liver Dis* 1995;15:329–339.

27. Wanless IR. Noncirrhotic portal hypertension. *Prog Liver Dis* 1996;14:265–278.

28. Futagaua S, Sukazawa M, Horisawa M, et al. Portographic liver changes in idiopathic noncirrhotic portal hypertension. *Am J Roentgenol* 1980;134:917–923.

29. Okuda K, Nakashima T, Okudaira M, et al. Liver pathology of idiopathic portal hypertension. Comparison with non-cirrhotic portal fibrosis of India. *Liver* 1982;2:176–192.

30. Terada T, Hoso M, Nakanumra Y. Microvasculature in the small portal tracts in idiopathic portal hypertension. A morphological comparison with other hepatic diseases. *Virchows Arch A Pathol Anat Histopathol* 1989;415:61–67.

31. Ohbu M, Okudaira M, Watanabe K, et al. Histopathological study of intrahepatic aberrant vessel in cases of noncirrhotic portal hypertension. *Hepatology* 1994;20:302–308.

32. Nakanuma Y, Hoso M, Sasaki M, et al. Histopathology of the liver in non-cirrhotic portal hypertension of unknown etiology. *Histopathology* 1996;28:195–204.

33. Oikawa H, Masuda T, Shin-Ichiro S, et al. Changes in lymph vessels and portal veins in the portal tract of patients with idiopathic portal hypertension: a morphometric study. *Hepatology* 1998;27: 1607–1610.

34. Shabayama Y, Nakata K. The relation of periportal fibrosis to portal hypertension. *J Hepatol* 1990;11:313–317.

35. Banthi G. Splenomegalie mit Leberzirrhose. Beitrage zur pathologischen. *Anat Allgemeinen Pathol* 1889;24:21–33.

36. Kono K, Ohnishi K, Omata M, et al. Experimental portal fibrosis produced by intraportal injection of killed non-pathogenic Escherichia coli in rabbits. *Gastroenterology* 1988;94:787–796.

37. Sugita S, Ohnishi K, Iida S, et al. Histological changes in the liver and portal hypertension subsequent to repeated intraportal injections of killed *E coli* in the dog. *Liver* 1988;8:1–9.

38. Okuda K, Kono K, Ohnishi K, et al. Clinical study of eighty-six cases of idiopathic portal hypertension and comparison with cirrhosis with splenomegaly. *Gastroenterology* 1984;86:600–610.

39. Schermerhorn T, Center SA, Dykes NL, et al. Suspected microscopic hepatic arteriovenous fistulae in a young dog. *J Am Vet Med Assoc* 1997;211:70–74.

40. Bennett AM, Davies JD, Gaskell CJ, et al. Lobular dissecting hepatitis in the dog. *Vet Pathol* 1983;20:179–188.

41. Van den Ingh TS, Rothuizen J. Lobular dissecting hepatitis in juvenile and young adult dogs. *J Vet Intern Med* 1994;8:217–220.

42. Johnson SE, Crisp SM, Smeak DD, et al. Hepatic encephalopathy in two aged dogs secondary to a presumed congenital portal-azygous shunt. *J Am Anim Hosp Assoc* 1989;25:129–137.

43. Cape L, Panciera DL, Partington B, et al. Glomerulonephritis and a congenital portocaval shunt in a seven-year-old dog. *J Am Anim Hosp Assoc* 1992;28:419–424.

44. Schermerhorn T, Center SA, Dykes NL, et al. Characterization of hepatoportal microvascular dysplasia in a kindred of Cairn terriers. *J Vet Intern Med* 1996;10:219–230.

45. Phillips L, Tappe J, Lyman R, et al. Hepatic microvascular dysplasia in dogs. *Prog Vet Neurol* 1996;7:88–96.

46. Allen L, Stobie D, Mauldin GN, et al. Clinicopathologic features of dogs with hepatic microvascular dysplasia with and without portosystemic shunts: 42 cases (1991–1996). *J Am Vet Med Assoc* 1999;214:218–220.

47. Butler-Howe LM, Boothe HW Jr, Boothe DM, et al. Effects of vena caval banding in experimentally induced multiple portosystemic shunts in dogs. *Am J Vet Res* 1993;54:1774–1783.

48. Sharma BC, Singh RP, Chawla YK, et al. Effect of shunt surgery on spleen size, portal pressure and oesophageal varices in patients with non-cirrhotic portal hypertension. *J Gastroenterol Hepatol* 1997;12:582–584.

49. Grauer GF, Pitts RP. Primary polydipsia in three dogs with portosystemic shunts. *J Am Anim Hosp Assoc* 1987;23:197–200.