CHRONIC ACTIVE HEPATITIS
(LONG-TERM, ON-GOING INFLAMMATION OF THE LIVER)

BASICS

OVERVIEW
• Long-term (known as "chronic"), ongoing (known as "active") inflammation of the liver (known as "hepatitis") associated with accumulation of inflammatory cells and progressive scarring or formation of excessive fibrous tissue (known as "fibrosis")

GENETICS
• Inherited copper-storage disease of the liver—Bedlington terriers; other breeds
• May play a role in chronic, active hepatitis seen in cocker spaniels, Doberman pinschers, Labrador retrievers

SIGNALMENT/DESCRIPTION of ANIMAL

Species
• Dog

Breed Predilections
• Bedlington terriers
• Doberman pinschers
• Cocker spaniels
• Labrador retrievers
• Skye terriers
• Standard poodles
• West Highland white terriers (?)

Mean Age and Range
• Mean age—6 years
• Range—2 to 10 years of age

Predominant Sex
• Many breeds—females may be at higher risk than males
• Cocker spaniels—more common in males

SIGNS/OBSERVED CHANGES in the ANIMAL
• Sluggishness (lethargy)
• Lack of appetite (known as "anorexia")
• Weight loss
• Vomiting
• Excessive urination (known as "polyuria") and excessive thirst (known as "polydipsia")
• Yellowish discoloration to gums, moist tissues of body (known as "mucous membranes") and other tissues (discoloration known as "icterus" or "jaundice")
• Fluid build-up in the abdomen (known as "ascites")
• Poor body condition
• Nervous system signs (such as dullness, seizures) caused by accumulation of ammonia in the system, due to inability of the liver to rid the body of ammonia (condition known as "hepatic encephalopathy")

CAUSES
• Infectious disease—canine hepatitis virus; leptospirosis; canine acidophil-cell hepatitis (viral infection hypothesized, but may be initiated by other infectious agents)
• Immune-mediated disease—autoimmune disease
• Toxic—copper-storage disease; drugs (such as anticonvulsants, trimethoprim-sulfa [antibiotic], dimethylnitrosamine, oxibendazole); environmental

RISK FACTORS
• Breed
• Age
• Gender
• Drugs, especially anticonvulsants

TREATMENT

HEALTH CARE

- Inpatient—for diagnostic testing and initiation of medical therapy in overtly ill dogs
- Outpatient—if condition is stable at diagnosis
- Depends on underlying condition
- Fluid therapy—balanced electrolyte fluids, supplemented appropriately with potassium and dextrose; electrolytes are chemical compounds (such as sodium, potassium, chloride) necessary for the body to function; restrict sodium if fluid build-up in the abdomen (ascites) is present
- B-vitamins
- Drugs to increase elimination of fluids from the body (known as "diuretics") are the first option to decrease fluid build-up in the abdomen (ascites)
- Tapping the abdomen to withdraw or drain excessive fluid (known as "abdominocentesis")—sterile procedure used when fluid build-up in the abdomen is causing problems with food intake and/or breathing or impairing sleep

ACTIVITY

- Keep patient warm, inactive, and hydrated
- Rest and inactivity may promote healing of the liver; normal blood glucose (sugar) levels (known as "euglycemia"), and elimination of fluid build-up in the abdomen (ascites)

DIET

- Adequate calories—maintain muscle mass and body weight; record body condition score
- Dietary protein—restrict only if animal has nervous system signs (such as dullness, seizures) caused by accumulation of ammonia in the system, due to inability of the liver to rid the body of ammonia (hepatic encephalopathy); feed balanced diet; with hepatic encephalopathy, avoid fish, meat, and egg-quality protein (dogs); cats are true carnivores and require meat-source protein
- Meal frequency—feeding several small meals per day improves use of nutrients by the body
- Sodium restriction—with fluid build-up in the abdomen (ascites) or severely low levels of albumin (a protein) in the blood (known as "hypoalbuminemia")
- Good-quality vitamin supplement (without methionine)—vitamin metabolism is disturbed with liver disease and vitamins are lost into the urine—the animal needs vitamin supplementation to counter the disturbed metabolism and loss of vitamins into the urine
- Thiamine
- Partial intravenous feeding (known as "parenteral nutrition")—recommended for short-term lack of appetite: give total parenteral nutrition if lack of appetite lasts more than 5 days

SURGERY

- Surgical repair of acquired portosystemic shunt (condition of abnormal blood flow in the liver due to high blood pressure in the portal vein, the vein carrying blood from the digestive organs to the liver)

MEDICATIONS

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive.

Diuretics (drugs to increase elimination of fluids from the body)

- For fluid build-up in the abdomen (ascites)—combination of furosemide and spironolactone; recheck and adjust dose at 4 to 7-day intervals

Drugs for Hepatic Encephalopathy (nervous system disorder with signs [such as dullness, seizures] caused by accumulation of ammonia in the system due to inability of the liver to rid the body of ammonia)

- Antibiotics
- Nonabsorbable-fermented carbohydrates (such as lactulose) to decrease production of ammonia and to decrease absorption of ammonia from the intestinal tract into the body
- Enemas to clean out the large bowel or colon
- Zinc supplementation
- Drugs to decrease swelling in the brain, if present; example, mannitol

Antioxidants

- Vitamin E—α -tocopherol
- *S*-adenosylmethionine (SAMe)
- Avoid vitamin C (ascorbate) with high tissue-copper or iron concentration—augments oxidant injury associated with transition metals

Zinc (Zinc Acetate)

- Antioxidant and antifibrotic effects ("antifibrotic" refers to stopping or preventing formation of excessive fibrous tissue [fibrosis])
- Blocks copper uptake from the intestinal tract

Copper Chelation (use of specific chemicals to tie up copper in the system and to allow it to be removed from the body)

- d-Penicillamine (first choice) or trientine
- d-Penicillamine chelates copper and promotes excretion of copper into the urine and is suspected to have other liver protective effects; treatment should be initiated in affected dogs having abnormal liver-copper concentrations
- Follow chelation therapy with long-term zinc supplementation

Immunomodulation (drugs that alter the immune response)

- Steroids, such as prednisolone or prednisone; if animal has fluid build-up in the abdomen (ascites), use dexamethasone to avoid steroid influence on sodium retention in the body (known as "mineralocorticoid effect") seen with prednisolone and prednisone
- Azathioprine—additional therapy for immune-mediated inflammation
- Mycophenolate mofetil (very limited experience)—for patients that do not tolerate azathioprine
- Microemulsified cyclosporine—option, but limited long-term experience
- Ursodeoxycholic acid—modifies the immune response; provides protective effect to liver; prevents formation of excessive fibrous tissue; antioxidant

Antifibrotics (drugs that prevent formation of excessive fibrous tissue [fibrosis])

- Polyunsaturated phosphatidylcholine (phosphatidylcholine lecithin)—steroid-sparing effect allows lower dosage of prednisolone for disease management; other effects: modifies the immune response; acts as an antioxidant; provides protective effect to the liver
- Colchicine—inhibits collagen production
- Silibinin—protects the liver from numerous toxins; has antifibrotic and antioxidant effects; promotes liver-cell regeneration; especially if toxin- or drug-mediated injury suspected

FOLLOW-UP CARE

PATIENT MONITORING

- At-home behavior
- Body condition and weight—adjust food intake to maintain weight
- Complete blood count (CBC), serum biochemistry profile, and urinalysis—look for signs of drug toxicity and disease remission
- Patients receiving azathioprine should be monitored by blood work (including complete blood count [CBC] and biochemistry profile) every 7 to 10 days for first month to ensure absence of bone-marrow, liver, and pancreatic toxicity; if sudden (acute) bone-marrow toxicity occurs, stop therapy, allow recovery, then reintroduce drug at lower dose; if long-term (chronic) bone-marrow toxicity (after many months) or sudden (acute) cholestatic liver disease (disease in which the flow of bile is decreased or stopped) or pancreatic injury are identified, discontinue therapy permanently
- Patients receiving mycophenolate mofetil should be monitored for bone-marrow toxicity (rare at recommended dose)
- Patients receiving colchicine should be monitored for bloody diarrhea and bone-marrow suppression (adverse side effects of the drug)

PREVENTIONS AND AVOIDANCE

- Maintain high vigilance for early signs of inflammation of the liver (hepatitis) in breeds that are more likely to develop liver disease than other breeds; early signs of liver inflammation include high liver-enzyme activity, as seen on blood work
- Determine diagnosis and initiate therapy early

POSSIBLE COMPLICATIONS

- Sepsis (presence of pus-forming bacteria and their poisons in the blood or tissues) secondary to the animal's inability to develop a normal immune response
- Nervous system signs (such as dullness, seizures) caused by accumulation of ammonia in the system, due to inability of the liver to rid the body of ammonia (hepatic encephalopathy)
- Blood-clotting disorder (disseminated intravascular coagulopathy or DIC)
- Intestinal ulceration
- Liver failure and death

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying disorder
- Long-term (chronic) disease; yellowish discoloration to gums, moist tissues of body (known as "mucous membranes") and other tissues (icterus or jaundice); and fluid build-up in the abdomen (ascites)—poorer prognosis
- Use of multiple drugs (known as "polypharmacy") and nutritional support extend quality survival, compared with untreated cases, but no long-term studies yet available
- Early diagnosis in Doberman pinschers, Bedlington terriers, and cocker spaniels appears to delay disease progression for years

KEY POINTS

- Medication is required for life; disease is cyclic
- Quarterly or biannual physical examinations and evaluations are needed
- Lack of long-term veterinary studies to prove effectiveness of single or multiple (polypharmacy) drug approaches; recommendations derived from (1) broad clinical experience, (2) retrospective and prospective studies in human beings, and (3) animal disease models