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Comprehensive review of hepatitis in canines: Etiology, pathogenesis, diagnosis, treatment and management

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Abstract
The present review aims to provide a comprehensive understanding of hepatitis in dogs by detailing its etiology, pathogenesis, diagnostic approaches, treatment strategies, and preventive measures. The primary objective is to consolidate available scientific knowledge on various forms of canine hepatitis, including acute and chronic hepatitis, infectious canine hepatitis (ICH), bacterial hepatitis, and toxin-induced hepatic disorders. Information was compiled from documented outbreaks, histopathological investigations, laboratory diagnostic findings, and therapeutic protocols reported in veterinary literature. The methodology involves an analytical synthesis of data regarding viral behavior, bacterial involvement, toxicological influences, clinical manifestations, and organ-specific pathological changes. The review highlights that ICH, caused by Canine Adenovirus-1, remains a significant concern in young or unvaccinated dogs and can lead to severe hepatic necrosis, vasculitis, coagulopathy, and high mortality. Bacterial and toxic hepatitis also contribute substantially to hepatic disease burdens, presenting diagnostic challenges due to overlapping clinical and histological features. Management relies heavily on supportive therapy, correction of metabolic and coagulation imbalances, and targeted antimicrobial use when indicated. The findings emphasize that preventive vaccination, strict hygiene measures, early diagnosis, and standardized histopathological interpretation are essential for reducing disease incidence and improving clinical outcomes in canine populations.

Keywords: Canine hepatitis, CAV-1, liver pathology, diagnosis, treatment, prevention

Introduction
Hepatitis in dogs refers to inflammation of the liver, a condition that represents a broad clinical syndrome rather than a single disease entity. This inflammation may occur abruptly as acute hepatitis or may progress gradually over months, resulting in chronic hepatitis. Although hepatitis in humans has been extensively researched, canine hepatitis remains less clearly understood due to limited studies and the frequent absence of an identifiable cause in many canine cases. Because the underlying triggers are often unknown, veterinary diagnosis and treatment usually rely on the microscopic appearance of liver tissue, especially patterns of degeneration, inflammation, fibrosis, and necrosis. For this reason, consistent and standardized interpretation of liver histopathology is crucial. Standardized reporting helps avoid misinterpretation, reduces contradictory diagnoses, and supports effective communication among veterinary professionals. It also improves collaboration across research centres working to better define and classify liver disorders in dogs.
The WSAVA Liver Diseases and Pathology Standardization Research Group is currently leading efforts to unify the classification of canine liver diseases. Their work includes the refinement of terminology related to parenchymal liver disorders and the development of internationally accepted diagnostic criteria. Establishing uniform definitions for the various forms of canine hepatitis is a key foundation for advancing research, identifying new causes, and developing improved treatments.

Stages of Hepatitis in Dogs
Hepatitis in dogs can progress through several stages, ranging from a sudden onset of inflammation to long-standing liver damage. The main forms include acute hepatitis, chronic hepatitis, and cirrhosis, each presenting distinct pathological features and clinical implications.

Acute Hepatitis

A rapid onset of liver inflammation characterizes acute hepatitis. Microscopically, it typically includes: inflammatory cell infiltration, Hepatocellular necrosis or programmed cell death, and Early attempts at tissue regeneration.

The severity and distribution of liver cell injury vary depending on the cause, the dog's immune response and the duration of the condition. Identifying the type and extent of inflammation and necrosis is essential for diagnosis and guiding treatment. A particularly severe form, known as fulminant hepatitis, involves extensive and sudden destruction of liver tissue, resulting in acute liver failure. In such cases, dogs may deteriorate rapidly—sometimes fatally—within as little as 48 hours after clinical signs appear.

Chronic Hepatitis

Chronic hepatitis develops when liver inflammation persists over an extended period. It is typically marked by: Ongoing hepatocyte apoptosis or necrosis, Mononuclear or mixed inflammatory infiltrates, Attempts at regeneration, varying degrees of fibrosis. The activity of the disease reflects the level of inflammation and ongoing cell death, while the stage refers to the degree of fibrosis and architectural disruption of the liver.

Severe fibrosis may progress to cirrhosis, where normal liver architecture is replaced by nodules and scar tissue, leading to irreversible liver dysfunction. The pattern of fibrosis—whether patchy, bridging or diffuse—affects both prognosis and treatment planning.

Infectious Canine Hepatitis (ICH)

Infectious Canine Hepatitis (ICH) is a viral disease that primarily targets the liver and is caused by Canine Adenovirus Type 1 (CAV-1). Although it shares the name "hepatitis," it is unrelated to the hepatitis viruses that infect humans; therefore, infected dogs pose no risk to people or to human health. CAV-1 can infect domestic dogs as well as certain wild canids such as wolves, foxes and coyotes, and occasionally other species like bears. Once a dog becomes infected, the virus replicates in the tonsils and lymphoid tissues before spreading to the liver, kidneys, and the lining of blood vessels.

The incubation period generally ranges from 4 to 9 days. While many dogs are protected through routine vaccination, outbreaks can still occur, especially among puppies, unvaccinated dogs, or animals imported from regions with inadequate vaccination protocols.

The replacement of early CAV-1 vaccines with the safer CAV-2-based vaccine, which offers cross-protection, has greatly reduced vaccine-related reactions and lowered the prevalence of ICH worldwide. However, severe disease can still emerge in unvaccinated populations. ICH can progress from mild to life-threatening. Some dogs recover fully from the acute infection, while others may develop chronic active hepatitis, potentially leading to cirrhosis as the liver becomes heavily scarred.

Clinical Presentation Dogs affected by ICH may show a variety of signs depending on disease severity, including: Fever and lethargy Vomiting and diarrhoea, Abdominal discomfort, Inappetence, Widespread haemorrhages, Respiratory difficulty (less common).

A classic but not universal sign is "blue eye," a temporary corneal opacity that occurs due to immune-complex deposition, typically 1-3 weeks after recovery from the acute illness.

Transmission

The virus is shed in Urine, Feces, Saliva, and Nasal secretions. Transmission occurs through direct contact or exposure to contaminated environments. Notably, infected dogs can continue shedding the virus in their urine for months after clinical recovery. Treatment Overview Management focuses on supportive care and liver-protective therapies, such as: Fluid therapy Medications to support liver function (e.g., SAMe, milk thistle, ursodiol) Vitamin supplementation Management of complications such as vomiting, ocular inflammation, or coagulopathies.

Epidemiology

Infectious Canine Hepatitis (ICH) Although routine vaccination has significantly reduced the global incidence of Infectious Canine Hepatitis, outbreaks continue to be reported most commonly in shelters, breeding facilities, stray populations, and environments where vaccination practices are inconsistent. Several well-documented outbreaks illustrate how quickly CAV-1 can spread, especially among young or immunologically naïve dogs.

Outbreak 1: Brindisi Province, Italy (February 2001) In early 2001, a large shelter in southern Italy housing over 250 dogs reported a sudden onset of systemic illness in young puppies. About twenty puppies aged 2-3 months developed: High fever, Respiratory difficulty, Mucopurulent eye discharge, Vomiting, Neurological symptoms, including tremors and seizures. Eleven puppies died, and several survivors later developed unilateral or bilateral corneal opacity ("blue eye"). Older dogs in the shelter showed milder signs, such as conjunctivitis and occasional neurologic abnormalities. Diagnostic samples collected from affected animals confirmed infection with canine adenovirus.

Outbreak 2: Matera Province, Italy (October 2001) A second outbreak occurred in another large shelter containing approximately 300 dogs. Vaccination and sanitation protocols were unclear. Twenty-two dogs ranging from 2 months to 2 years of age became ill, with six fatalities. Affected dogs primarily showed: Fever, Severe weight loss, Vomiting and diarrhea. Rectal swabs from recovered dogs later tested positive for CAV-1.

Outbreak 3: Valenzano, Apulia Region (November 2004). Even shelters with established vaccination programs may experience isolated infections. In this case, four vaccinated puppies aged 3-9 months developed Depression, Fever, Hemorrhagic diarrhea. All four deteriorated rapidly, with three deaths occurring within three days of symptom onset. Post-mortem examinations revealed widespread organ damage typical of acute CAV-1 infection.

Outbreak 4: Bari Veterinary Clinic (January 2006) Two recently imported puppies—one Labrador Retriever and one Beagle—presented with severe illness shortly after arrival from a pet shop. Although they had received some vaccinations in Hungary and Italy, both displayed classical

signs of ICH. The Labrador succumbed to seizures and hemorrhagic gastroenteric signs, while the Beagle exhibited neurological symptoms and urinary incontinence but eventually recovered. Samples (including urine, swabs, and post-mortem tissues) confirmed CAV-1 infection.

The incidence of CHV in domestic and colony-bred dogs has been found in serologic studies. In England, 45.8% of dogs tested positive for antibodies, whereas 39.3% of dogs in the Netherlands tested positive. Serologic research in Italy has found that the frequency is higher in kennelled dogs (27.9%), whereas it is lower in pets (3.1%).

Host Range and Global Distribution While domestic dogs are the primary hosts, CAV-1 infects a variety of wild carnivores, including Red foxes, Wolves, Coyotes, Bears Mustelids (e.g., weasels, martens, otters). Seroprevalence varies widely by region.

Studies have shown up to 97% prevalence in isolated red-fox populations. Antibodies in several North American carnivores, including polar bears and sea lions A fatal case in a Eurasian river otter. High environmental resistance of the virus enables prolonged persistence in contaminated areas, contributing to ongoing risks in wildlife and unvaccinated domestic dogs.

Pathogenesis

The development of Infectious Canine Hepatitis follows a predictable sequence beginning with viral entry and culminating in widespread organ damage. Understanding this progression helps explain the wide variety of clinical signs and the rapid deterioration that can occur in severe cases.

1. Entry and Initial Replication The CAV-1 virus typically enters the body when a dog inhales or ingests contaminated secretions such as urine, feces, saliva, or nasal discharge. After entry, the virus first multiplies in the tonsils. It then spreads to nearby lymphoid tissues. From there, it enters the bloodstream, producing viremia. This early replication phase allows the virus to disseminate quickly throughout the body.
2. Target Organs and Tissue Damage Once circulating in the bloodstream, CAV-1 shows a strong preference for several tissues, notably: Liver (hepatocytes), Kidneys (particularly renal tubular and glomerular cells), Spleen, Endothelial cells lining blood vessels. Because the virus attacks the lining of blood vessels, it often causes vasculitis, leading to hemorrhage and swelling in multiple organs. Hepatocellular injury results in inflammation and necrosis, which are the hallmark features of ICH.
3. Viral Replication and Shedding CAV-1 replicates extensively in infected tissues, releasing large numbers of viral particles back into circulation. Infected dogs shed virus through: Urine (for months), Feces, Saliva, Ocular and nasal secretions. This prolonged shedding contributes significantly to environmental contamination and transmission.
4. Immune Response and Secondary Injury The dog's immune system attempts to contain the infection by generating antibodies and activating inflammatory pathways. However, the immune response itself may worsen tissue damage. In some dogs, immune-complex deposition leads to corneal edema ("blue eye"). Delayed immune reactions contribute to chronic liver disease and fibrosis. Thus, both viral destruction and immune-mediated processes play important roles in disease progression.
5. Clinical Consequences The severity of illness varies, but common clinical outcomes include: Fever, Lethargy, and anorexia. Vomiting or diarrhea, Abdominal pain, Jaundice from hepatocellular damage, Hemorrhages due to vasculitis and coagulopathy Neurological signs when the CNS or vasculature is affected. Without prompt intervention, severe cases can progress to acute liver failure or disseminated intravascular coagulation (DIC).

Clinical Findings

Dogs infected with CAV-1 may present with a wide spectrum of clinical signs, ranging from mild, transient illness to rapidly progressive, life-threatening disease. The variability depends on factors such as age, immune status, viral load, and concurrent infections.

1. General Systemic Signs These are often the first abnormalities noticed: High fever — one of the earliest signs Profound lethargy — dogs become inactive or weak Loss of appetite — may progress to complete anorexia
2. Gastrointestinal Signs As the virus affects the liver and gastrointestinal tract, dogs may develop: Vomiting, sometimes containing bile or foam Diarrhea, which may be watery, mucous-filled, or blood-tinged Abdominal discomfort, demonstrated by posture changes, whining, or sensitivity to touch
3. Liver-Related Signs Damage to liver tissue and bile flow leads to: Jaundice, visible in the gums, sclera ("whites of the eyes"), and skin Dark urine from elevated bilirubin levels Coagulopathy, as the liver fails to produce essential clotting factors
4. Hemorrhagic Manifestations Because CAV-1 targets blood vessel endothelium, many dogs exhibit signs of bleeding: Petechiae — pinpoint red spots on skin or mucous membranes, Ecchymoses — larger bruised areas, Internal bleeding, which may present as bloody diarrhea, nosebleeds, or anemia
5. Ocular Signs ("Blue Eye") A characteristic feature in some dogs is: Corneal edema, giving the eye a cloudy or bluish hue. This results from immune-complex deposition in the cornea and usually appears 1-3 weeks after clinical recovery.
6. Respiratory and Neurological Involvement. In more advanced or severe infections, Dyspnea or increased respiratory effort may occur. Neurological signs, such as Seizures, Ataxia (uncoordinated movement), Disorientation, Depression, or coma in severe cases. Neurological involvement is often linked to severe vasculitis, liver-related toxin buildup, or brain inflammation.
7. Variability in Disease Severity. Not all infected dogs show obvious signs: Some may present with only mild fever or lethargy. Others may remain completely asymptomatic. Severe cases can deteriorate rapidly due to acute hepatic failure or DIC. Early recognition and supportive care greatly improve survival outcomes.

Diagnosis

Diagnosing ICH requires combining clinical observations with laboratory testing and, when necessary, histopathology. Because early signs can resemble other infectious or

inflammatory diseases, a systematic diagnostic approach is essential—particularly in young, unvaccinated dogs showing fever, gastrointestinal disturbances, or ocular changes.

1. Clinical Suspicion Veterinarians should immediately consider ICH in: Puppies and dogs under one year of age, Animals with uncertain or incomplete vaccination histories, Dogs presenting with fever, gastrointestinal signs, respiratory issues, or corneal edema. Cases with hemorrhages or neurologic abnormalities. Early suspicion guides further testing and isolation measures.
2. Necropsy and Histopathology Post-mortem examination remains one of the most definitive tools for diagnosis. Characteristic findings include: Intranuclear viral inclusion bodies in hepatocytes and Kupffer cells, Centrilobular necrosis of liver tissue, Edematous and thickened gallbladder wall, considered a suggestive gross lesion, Widespread hemorrhage in lymph nodes, lungs, kidneys, and serosal surfaces. While inclusion bodies provide strong evidence, their absence does not rule out infection, especially in chronic or late-stage disease.
3. Hematology (CBC Findings) The complete blood count often reveals multiple abnormalities: Leukopenia early in the disease. First, a lymphopenia, followed by neutropenia. Thrombocytopenia contributes to bleeding tendencies. Anemia, sometimes accompanied by increased nucleated red blood cells, Band neutrophilia and toxic changes in severe cases. Leukocytosis may appear during recovery.
4. Serum Biochemistry Biochemical changes typically reflect liver dysfunction: Marked increases in ALT and ALP (often > 1000 U/L), Hyperbilirubinemia, Hypoglycemia Hypoalbuminemia. Dogs with neurologic signs may also show elevated blood ammonia, suggesting hepatic encephalopathy.
5. Urinalysis Common urinary abnormalities include: Proteinuria, Hematuria, Bilirubinuria, and Hyaline and granular casts. These changes reflect renal involvement and impaired liver clearance.
6. Coagulation Testing CAV-1 frequently compromises the liver's ability to produce clotting factors. Findings may include: Prolonged prothrombin time, Elevated activated partial thromboplastin time (6-7× normal), Hypofibrinogenemia, Increased fibrin degradation products, Impaired platelet adhesion, Indicators of DIC (disseminated intravascular coagulation)
7. Diagnostic Imaging Although imaging is not diagnostic, it can support clinical suspicion: Radiographs may show a normal or mildly enlarged liver. Poor abdominal detail due to effusion. Ultrasound findings are variable and often nonspecific
8. Microbiologic and Molecular Testing: Virus Isolation CAV-1 can be isolated from many tissues during acute infection. Despite its diagnostic value, viral culture is not routinely available in most veterinary laboratories. Serology Tests, such as SN, ELISA, and HI, can detect antibodies. Limitations include: Dogs may die before producing detectable antibodies. Recent vaccination complicates interpretation. Diagnosis often relies on a fourfold rise in titer in paired samples. PCR Testing Conventional PCR assays can detect CAV-1 DNA in tissues or swabs (blood, nasal, rectal, ocular). Limitations: Real-time PCR specific for CAV-1 may not be commercially available in all regions. Persistent urinary shedding can cause ambiguous results
9. Pathologic Findings (Gross & Microscopic) Gross Pathology Dogs that succumb to ICH often show: Blood-tinged abdominal fluid Slightly enlarged, mottled liver Notably thickened gallbladder wall Enlarged, edematous lymph nodes Subserosal hemorrhages in multiple organs Splenomegaly Multifocal lung consolidation Histopathology Microscopic lesions include: Hepatocellular necrosis Intranuclear inclusion bodies in hepatocytes and Kupffer cells Mixed inflammatory infiltrates Interstitial nephritis Hemorrhage and thrombosis due to DIC Inclusion bodies in endothelial cells of various tissues Immunohistochemistry helps confirm the presence of viral antigen.

Treatment

There is no antiviral medication that directly eliminates CAV-1; therefore, treatment focuses on supportive care, stabilization, and management of complications. The intensity of therapy depends on how severely the liver and other organs are affected. Early intervention greatly increases the likelihood of recovery.

1. Supportive and Stabilizing Care Fluid Therapy: Maintaining hydration and correcting electrolyte imbalances are essential. Dogs with vomiting or diarrhea may require: Intravenous crystalloids, Addition of glucose and electrolytes when necessary Blood products to address anemia or coagulopathy. Because vascular permeability is often increased, fluid administration must be closely monitored to prevent overload. Nutritional Support: Severely ill dogs may not tolerate oral feeding, requiring assisted feeding or Partial or complete parenteral nutrition. Providing energy helps minimize catabolism and support liver repair.
2. Management of Gastrointestinal and Hepatic Symptoms Dogs frequently require medications to protect the gastrointestinal tract and support liver function: Antiemetics to control vomiting, Antacids and sucralfate to minimize gastric irritation Milk thistle, SAMe, ursodiol, and vitamin E to support hepatic regeneration. In severe hepatic injury, medications that reduce inflammation and oxidative stress may also be considered.
3. Treatment of Coagulation Problems Coagulopathies are common due to impaired liver synthesis of clotting factors. Plasma transfusions can provide clotting proteins. Heparin may be required when DIC is suspected. Whole blood transfusions may be needed for dogs with active bleeding
4. Treatment of Secondary Infections Because ICH weakens the immune system and damages mucosal barriers, secondary bacterial infections can occur. In such cases, Broad-spectrum antibiotics (e.g., ampicillin) may be administered parenterally. Antibiotics are especially indicated if hemorrhagic gastroenteritis or bacteremia is suspected
5. Management of Neurological Signs. Some dogs develop hepatic encephalopathy due to toxin buildup. Treatment may include: Lactulose (oral or enema) to reduce ammonia absorption, Antibiotics with poor intestinal absorption to modify gut flora Control of seizures if present

6. Ocular Treatment ("Blue Eye") When immune-complex deposition leads to corneal edema: Topical corticosteroids, Atropine to control uveitis and prevent secondary glaucoma. These treatments are only used when no corneal ulcer is present.
7. Isolation and Environmental Management ICH is highly contagious; therefore, Affected dogs must be isolated. Surfaces, bedding, and bowls require thorough cleaning and disinfection. Viral shedding in urine can continue for months, so long-term precautions are needed.
8. Prognosis Outcome depends on: Extent of liver involvement, Strength of the dog's immune response, Presence of complications (e.g., DIC, neurological signs). Dogs that survive the acute phase often recover fully, but some may later develop Chronic hepatitis or Chronic glomerulonephritis
9. Immunity and Vaccination Long-lasting immunity typically develops after natural infection. Vaccination with CAV-2-based vaccines provides strong protection and avoids adverse effects associated with older CAV-1 vaccines. Puppies should receive: First dose at 6 weeks, Boosters every 3-4 weeks until 16 weeks, followed by regular adult boosters. Because vaccinated dogs may temporarily shed CAV-2, herd immunity is further enhanced within communities.

Prevention

Preventing ICH relies heavily on effective vaccination programs and appropriate management practices, especially in environments with high animal density. Because CAV-1 is highly contagious and environmentally resilient, proactive prevention is far more effective—and far safer—than treating the disease after exposure.

1. Vaccination Vaccination is the primary defense against ICH. Modern canine vaccines use Canine Adenovirus Type 2 (CAV-2), which provides reliable cross-protection against CAV-1 while avoiding side effects seen with earlier CAV-1 vaccines. Puppy vaccination schedule: First dose at 6 weeks of age, Booster every 3-4 weeks, Final dose at 16 weeks or older. Adult dogs should receive periodic booster vaccinations to maintain strong immunity. Because vaccinated dogs may shed attenuated CAV-2 briefly from the respiratory tract, unvaccinated dogs in the vicinity may develop immunity indirectly—an effect that has contributed to a significant decline of ICH in well-vaccinated regions.
2. Shelter and Kennel Management Outbreaks often occur in densely housed or poorly managed facilities. Key preventive measures include: Strict hygiene protocols, Regular disinfection of kennels, bowls, bedding, and equipment, Quarantine of new or unvaccinated animals, reducing overcrowding, ensuring dogs are vaccinated before entering group settings Immediate isolation of symptomatic animals. These practices are particularly important in shelters with high animal turnover.
3. Environmental Control CAV-1 can survive for extended periods in the environment, especially in cooler conditions. Therefore, High-quality disinfectants effective against non-enveloped viruses should be used. Outdoor areas contaminated with urine require special attention. Shared resources (water troughs, food bowls) should be sanitized frequently. Proper sanitation reduces viral load and prevents indirect transmission.
4. Avoiding Exposure to Wild Carnivores Because CAV-1 circulates among wild canids—including foxes, wolves, and coyotes—contact between domestic dogs and wildlife should be minimized. This is particularly important in rural, suburban, or wooded areas where wildlife activity is common.

Canine Hepatitis Caused by Intrahepatic Bacteria

Canine hepatitis may also arise from bacterial infiltration of liver tissue, either as a primary infection or secondary to biliary, gastrointestinal, or systemic disease. When bacteria invade the hepatic parenchyma, they trigger varying degrees of inflammation, which can resemble other forms of hepatitis but require different diagnostic and therapeutic approaches. Veterinary pathologists classify these bacterial-associated liver diseases under categories such as: Acute hepatitis, Chronic hepatitis, Granulomatous hepatitis (GH), Pyogranulomatous inflammation, Cholangiohepatitis, Lobular dissecting hepatitis. These conditions are recognized in the histologic classification system established by the World Small Animal Veterinary Association (WSAVA).

Etiology

A wide range of bacteria have been implicated in canine hepatic inflammation. They may originate from the intestine, biliary system, bloodstream, or adjacent organs. Common Enteric Bacteria. These are frequently found in dogs with bacterial hepatitis: *Escherichia coli*, *Enterococcus* spp. *Bacteroides* spp. *Streptococcus* spp. *Clostridium* spp. *Helicobacter canis* Non-enteric Bacteria. Less common but clinically significant pathogens include: *Leptospira* spp. *Bartonella* spp. *Clostridium piliforme* (Tyzzer's disease) *Mycobacterium* spp. These organisms may reach the liver through hematogenous spread, biliary reflux, or systemic infection.

Clinical Findings

Dogs with bacterial hepatitis often show non-specific systemic signs that overlap with other liver diseases. Typical clinical features include: Lethargy and weakness, reduced appetite or complete anorexia, Vomiting, Abdominal discomfort or palpable abdominal tension Fever (pyrexia). Common laboratory abnormalities include neutrophilia, thrombocytopenia, Hypoalbuminemia, Hyperglobulinemia, and Elevated alkaline phosphatase (ALP), often greater than ALT elevations. These patterns may suggest cholestasis or a mixed inflammatory disease, rather than pure hepatocellular necrosis. Granulomatous or pyogranulomatous inflammation may coexist with biliary involvement, and identifying specific bacterial organisms can be challenging. Some dogs show bacterial morphology consistent with Helicobacter or Leptospira, though confirmatory testing may not always support infection.

Diagnosis

Accurate diagnosis requires combining clinical data, imaging, cytology, culture, and molecular techniques. Diagnostic considerations include: Ultrasound changes may overestimate liver echogenicity due to surrounding mesenteric inflammation or abdominal fluid. Bile cultures are often more frequently positive than liver tissue cultures, especially in cases of cholangitis or bile duct obstruction. Bacteria frequently isolated include *E. coli* and

Enterococcus spp., correlating with organisms identified histologically. The presence of bacteria in both liver and spleen suggests bacteraemia and hematogenous spread.

Additional diagnostic tools

Fluorescence in situ hybridization (FISH) can pinpoint bacteria within inflammatory lesions. 16S rRNA sequencing: identifies bacterial species when culture is inconclusive.

Histopathology: demonstrates the relationship between bacteria and inflammatory infiltrates. A major limitation is that not all cases undergo advanced testing due to sample availability or financial constraints.

Treatment

Bacterial hepatitis can be life-threatening; empirical antimicrobial therapy is initiated while awaiting culture results. Broad-spectrum coverage may include: Fluoroquinolones, Doxycycline or other tetracyclines, Chloramphenicol, Amoxicillin-Agents targeting atypical bacteria such as Bartonella or Mycobacterium when clinically indicated. Therapy may continue for 4-8 weeks, depending on response, severity, and culture findings.

Additional considerations:

Dogs may show ultrasonographic features suggestive of pancreatitis, but confirmatory testing may be negative. Concurrent diseases (e.g., bile duct obstruction) must also be treated to prevent recurrence. Overall, treatment success depends on identifying the bacterial source, relieving biliary obstruction if present, and providing adequate antimicrobial courses.

Canine Hepatitis Caused by Toxins and Chemicals

Certain toxins, chemicals, and metabolic abnormalities can trigger liver inflammation in dogs. These non-infectious forms of hepatitis vary widely depending on the type of toxin, the dog's genetic predisposition, and the duration or intensity of exposure. Some breeds are more susceptible to toxin-associated hepatitis due to inherited deficiencies in copper metabolism or other metabolic pathways.

1. Breed Predispositions Several dog breeds display a higher-than-average incidence of chronic hepatitis, likely due to underlying genetic factors: Cocker Spaniels (American and English), West Highland White Terriers, Skye Terriers, Dalmatians, Labrador Retrievers, Doberman Pinschers, Bedlington Terriers.

Conversely, some breeds, such as Beagles, rarely develop chronic hepatitis. Copper-Associated Hepatitis. In certain breeds, abnormal copper metabolism contributes significantly to chronic liver disease: Bedlington Terriers. Copper toxicosis is linked to a deletion in exon 2 of the MURR1 gene. West Highland White Terriers, Dalmatians, Skye Terriers, and Labradors may also develop copper accumulation due to genetic predispositions. Excess copper in hepatocytes leads to oxidative damage, cell death, and chronic inflammation. Alpha-1 Antitrypsin-Associated Hepatitis In English Cocker Spaniels, elevated levels of intracellular alpha-1 antitrypsin contribute to chronic hepatitis. Similar to affected humans, defective secretion of this protein results in its accumulation within the hepatocyte endoplasmic reticulum, eventually causing cell injury and chronic inflammation.

2. Toxic Liver Injury: The liver is particularly vulnerable to toxins because it: Receives blood directly from the gastrointestinal tract, is responsible for metabolizing drugs, chemicals, and xenobiotics, and converts certain substances into more reactive or harmful metabolites. Dogs and cats are especially sensitive to toxic injury due to relatively low levels of protective antioxidants such as glutathione.

Common Categories of Hepatotoxins Drugs (e.g., acetaminophen, chemotherapy agents) Environmental chemicals Plants and fungi (e.g., aflatoxins, certain mushrooms) Idiosyncratic reactions where liver injury occurs unpredictably in a small number of exposed animals Mechanisms of Toxicity Toxins can injure the liver through several pathways: Direct cellular injury (e.g., acetaminophen damaging hepatocyte proteins) Oxidative stress and formation of free radicals Disruption of RNA/DNA synthesis, such as: RNA polymerase inhibition (mushroom toxins) DNA alkylation (cyclophosphamide) Lysosomal dysfunction Cholestasis caused by impaired bile flow Interference with protein synthesis

3. Pathogenesis of Toxic and Chemical Hepatitis. Toxic injuries primarily trigger: Hepatocellular swelling, Steatosis (fat accumulation), Necrosis, often in specific lobular zones such as: Centrilobular, Midzonal, Periportal, Panlobular.

Secondary effects may include: Inflammation, Cholestasis, Fibrosis. A major challenge is that many toxins produce overlapping histological patterns, making it difficult to determine the exact cause based solely on tissue appearance. Acute injuries dominated by necrosis may lack significant inflammation early on, while chronic injuries typically involve fibrosis, persistent inflammation, and architectural distortion.

4. Infectious Disease Interaction Some infectious agents produce hepatic necrosis that closely mimics toxic injury. Examples include: Canine and feline herpesviruses, Clostridium piliforme (Tyzzer's disease), Toxoplasma, Neospora, Sarcocystis, and FIP virus in cats. These conditions often result in widespread necrosis with minimal inflammation early, making differentiation from toxic hepatitis challenging.

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