

RECENTLY EMERGING LIVER DISEASE IN DOGS COPPER HEPATOPATHY

Over the past 5-7 years a condition affecting the canine liver has become more frequently identified. It often can remain undetected until patients become very ill. However, regular blood chemistry monitoring, such as is included in many annual wellness exams, can often identify increased liver enzymes, which is often an early sign of Copper Hepatopathy (CH) or Copper Storage Disease. The condition is ultimately diagnosed upon biopsy of the liver, microscopic examination of the biopsy and quantitation of the amount of copper within the liver

Copper is an element that, in trace amounts, is an essential part of our and our dog's daily diet. The liver plays a prominent role in metabolism, storage and excretion of copper. The liver is the principal recipient of absorbed copper, it has the highest stored content, delivers protein-bound copper to other tissues and is the principal organ of copper elimination when it is in excess. The liver's pivotal role in copper management makes it particularly vulnerable when the elimination processes fail.

Copper is absorbed through the gastrointestinal tract, approximately 40-60% is absorbed in the upper small intestine. It is then presented to the liver for utilization or excretion. Most canine diets are in excess of the required amount of copper. However, the liver regulates copper balance by excreting copper in the bile. The excess copper is then disposed of in the feces. This is the major route of copper excretion. Smaller amounts of copper are excreted through the urine.

Conditions that cause excessive amounts of normally vital substances, like copper, or metabolic by-products accumulate within the body are referred to as a storage diseases. Most storage diseases are the result of genetic or heritable metabolic defects. Storage Diseases result due to an error in metabolism causing substances to accumulate within specific tissues causing damage to the surrounding, normal tissues. Some storage diseases may be treated with medications and by limiting the patients exposure to the substance that is accumulating abnormally and others may be fatal.

Wilson's disease, an inherited condition in humans where copper accumulates within the brain, liver and other tissues was first documented in 1912, by a British neurologist, Samuel, Alexander Kinnier Wilson. Copper Storage disease affects many different species including humans and dogs. Some of the earliest studies identifying abnormal liver copper levels in dogs were published in the 1990's. However, it was not until later that we learned that Bedlington Terriers had a very similar condition to Wilson's disease with the genetic defect being identified within that breed. Subsequently similar conditions have been documented within the veterinary literature in Dobermans, Dalmatians, Labradors and West Highland White Terriers, to name a few. However, other than the Bedlington Terrier, the genetic link to copper storage within the liver has not been identified. This may also mean that the underlying cause for copper storage in other breeds of dogs may be distinctly different from the Bedlington Terrier.

Increased copper intake appears to be an uncommon cause of copper accumulation in the dog. Most commercial dog foods contain a copper content of 12-16 mg/kg dry matter. This is higher than the minimum daily requirement. Since exposure to elevated levels of copper is so common, it is unlikely this is a source of copper related hepatic disease in the dog. However, recent studies have considered a correlation between the changes in dog food formulations (elevated copper levels) and the increased frequency with which elevated hepatic copper has been appreciated in dogs. Further understanding of the exact etiology of the many breed related copper liver diseases may help substantiate this concern.

Over the past 5-7 years Copper Hepatopathy or Copper Storage Disease has become more frequently identified in dogs. Although Bull Terriers are not among the breeds currently reported within the literature, in my practice I have treated a number of different breeds of dogs and mixed breed dogs affected with this disease. I consider Copper Hepatopathy/Storage Disease an emerging condition and I think it is important that all dog breeders and enthusiasts should be aware of its existence.

Liver biopsy and microscopic evaluation of the liver as well as quantitation of copper content within the liver are key to achieving a diagnosis of Copper Hepatopathy. When a liver biopsy is examined microscopically, whether the copper accumulation is occurring in a Bedlington Terrier or

Labrador, the condition appears very similar. The copper accumulates within characteristic areas of the liver's microscopic architecture. The amount of copper within the liver can also be quantitated from a biopsy sample and this also aids in the diagnosis as well as identifying the magnitude of the copper storage. Unlike the Bedlington Terrier, we are uncertain why the other breeds are developing these excessive stores of copper. Some researchers have suggested that it may be a combination of excessive amounts of copper within the dogs diet coupled with a disfunction of the normal liver metabolism that may be occurring as a result of a genetic defect causing an error in normal metabolism.

Until we understand this condition better, there are no real preventative measures can be put in place to avoid Copper Hepatopathy/Storage other than selecting foods that are not in excess of the daily requirement of copper (0.1mg/kg/day, *Nutrient Requirements of Dogs and Cats*, 2006, National Academy of Sciences). Also, recognition as to whether you have a breed that has been documented as predisposed to the disease is important, since regular monitoring could aid in early identification of the illness.

At this time, the best plan is to have your dogs annual or semi-annual laboratory testing done and be sure that liver enzymes, renal function and a CBC are included in these tests. Be sure you discuss the results with your veterinarian. If there are abnormalities identified, make sure a diagnostic plan is created to pursue any irregularities. If your pet becomes ill and has even mildly elevated liver enzymes, be sure to pursue this further and monitor the liver enzyme values until they have returned to normal or, if they remain persistently elevated, additional tests are pursued. Additional blood tests, abdominal ultrasound and liver biopsy may be discussed with you. At my hospital we often perform ultrasound guided biopsies of the liver. This test is minimally invasive, performed under sedation and often the dogs return home the same day or the next morning.

In many cases Copper Hepatopathy/Storage Disease can be treated and managed very successfully. Hopefully, as we learn more, veterinarians can provide preventive measures to dog owners that will decrease the frequency and severity of this disease.