



## Copper hepatopathy - a breed-associated inherited disease of the liver.

Recently a liver biopsy was submitted from a 4-year-old Bedlington terrier with elevated liver enzymes. The liver was reported to be grossly normal.

On histologic examination of the [submitted liver sections](#) there was moderate, chronic hepatitis with moderate portal to dissecting fibrosis, biliary hyperplasia, and mild hepatocellular loss.

Hepatocytes also exhibited large amounts of intracytoplasmic granules (see H&E stained at left). Intra-hepatocellular granules can represent a number of different materials with varying significance including:

1. Lipofuscin (wear and tear pigment)
2. Iron (from erythrocyte break down)
3. Bile (from intrahepatic or extrahepatic biliary stasis)
4. Copper (primary storage hepatopathy or secondary to hepatitis)

The nature of the intracytoplasmic granules was investigated with additional histochemical stains and was shown to be consistent with copper (bright red granules in the image of Rhodanine Cu stained section at right).

Based on the histologically significant intrahepatic copper accumulation and the breed, the changes are consistent with a diagnosis of primary copper-associated hepatopathy. This hereditary, autosomal recessive disease has been well documented in Bedlington Terriers and is most commonly caused by a deficiency of a protein named COMMD1, caused by a deletion in the encoding gene. This deficiency in COMMD1 results in impaired biliary copper excretion and progressive copper accumulation within hepatocytes. Intrahepatocytic copper continues to accumulate throughout the life of the animal.

It is important to remember that most animals with accumulation of intrahepatic copper do not have a primary copper storage disease. Intrahepatocyte copper accumulation can also occur secondary to abnormal hepatic function with cholestasis and altered biliary copper excretion, or due to excess dietary copper intake in any species. Whatever the inciting cause of accumulation, free copper ions can catalyze the formation of free radicals leading to hepatocellular necrosis and hepatitis.

Sadly, most cases of primary copper hepatopathy in Bedlington terriers result in chronic progressive liver failure. In some cases, the disease presents with acute hepatic necrosis resulting in the release of large amounts of copper into the circulatory system, leading to a haemolytic crisis.