

**Other Names:** Copper Hepatotoxicosis, Copper Storage Disease, Copper Storage Disease Modifier, Copper Storage Hepatitis, Copper-associated Hepatopathy, Hepatic Copper Toxicosis, Menkes Gene Disease Modifier, Wilson Disease

**Affected Genes:** ATP7B

**Inheritance:** Complex Inheritance

**Mutation:** Complex Rearrangement

## Common Symptoms

Copper toxicosis (Labrador retriever type) is an inherited metabolic disease affecting Labrador Retrievers, resulting in chronic liver failure. Dogs with copper toxicosis have a decreased ability to excrete dietary copper from the body resulting in excessive copper storage in tissues and organs, including the liver, which can result in liver damage and subsequent cirrhosis. Though the age of onset and speed of disease progression are variable, most affected dogs will present in middle age with non-specific signs of liver dysfunction including weight loss, lethargy, weakness, vomiting, diarrhea, and abdominal pain. In late stages of disease, affected dogs may develop signs of liver failure including abdominal swelling, jaundice, and neurological dysfunction. Dogs found to have one or two copies of the [Mutation](#) may benefit from certain therapies.

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## Breed-Specific Information for the Labrador Retriever

The [Mutation](#) of the *ATP7B* gene associated with copper toxicosis (Labrador retriever type) has been identified in the Labrador retriever, although its overall frequency in this breed is unknown.

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## Testing Tips

Genetic testing of the *ATP7B* gene in Labradors will reliably determine whether a dog is at increased risk of copper toxicosis (Labrador retriever type). Copper toxicosis (Labrador retriever type) is inherited in an autosomal incomplete dominant manner in dogs meaning that dogs only need to inherit one copy of the mutated gene to be at an increased risk of developing the disease. Though copper toxicosis is most commonly seen in dogs having two copies of the mutated gene,

[Carrier](#) dogs have a lower risk of copper toxicity than dogs with two copies of the [Mutation](#), but have a higher risk of developing the disease than dogs without the mutation. Thus, dogs that have one or two mutant copies of the gene are considered at risk for copper toxicosis. In addition, this disease seems to be sex-influenced in that female dogs inheriting one or two copies of the *ATP7B* mutation are at an increased risk of developing clinical disease compared to their male counterparts. Since there appears to be multiple genetic and environmental factors which play a role in causing copper toxicosis in dogs, a normal result in *ATP7B* does not exclude copper toxicosis in a pedigree and an at-risk result does not mean that a dog will develop copper toxicosis during its lifetime. Given the fact that the frequency of the *ATP7B* mutation appears to be relatively high among the Labrador samples submitted to PPG and that this mutation is only one of many factors contributing to the risk of developing copper toxicosis, it is recommended that dogs inheriting the *ATP7B* mutation be bred to dogs that have not inherited the *ATP7B* mutation rather than being removed from breeding programs. It is important to note that removal of all dogs with one or two copies of the *ATP7B* mutation from the gene pool would drastically reduce genetic diversity within the breed and potentially increase the risk of other genetic diseases in Labradors.

**\*Note:** A mutation present in the *ATP7A* gene has been shown to decrease copper accumulation in dogs that have inherited one or two copies of the *ATP7B* gene mutation associated with copper toxicosis (Labrador retriever type). The effect of the *ATP7A* gene mutation in preventing increases in total body copper is more effective in male dogs, though the mutation in *ATP7A* is not completely protective in either sex. Because there are multiple factors contributing to copper toxicosis, dogs inheriting the *ATP7A* mutation may still be at risk of copper toxicosis if they have also inherited the *ATP7B* gene mutation or other unknown mutations.

Genetic testing of the *ATP7A* gene in Labrador retrievers will reliably determine whether a dog is a genetic carrier of the copper toxicosis modifier (Labrador retriever type). The copper toxicosis modifier (Labrador retriever type) decreases the risk of excessive copper accumulation in an X-Linked incomplete dominant manner meaning that male dogs that are at risk for copper toxicosis due to inheritance of the associated mutation in the *ATP7B* gene only need to inherit one copy of the semi-protective *ATP7A* gene mutation to be at a decreased risk of disease. However, female dogs that are at risk for copper toxicosis due to inheritance of the associated *ATP7B* gene mutation and carriers of one copy of the semi-protective *ATP7A* mutation, may have a higher risk of developing copper toxicosis than male carriers due to the presence of another normal copy of the *ATP7A* gene in female dogs. Female dogs that inherit two copies of the *ATP7A*

mutation are more protected than those that inherit only one copy of the *ATP7A* mutation. In addition, male dogs inheriting one copy of the *ATP7A* mutation tend to accumulate less copper when inherited with the *ATP7B* mutation than their female counterparts. In general, dogs that are not at risk for copper toxicosis (Labrador retriever type) because they did not inherit the *ATP7B* gene mutation are not affected positively or negatively when they inherit one or two copies of the *ATP7A* gene mutation.

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**There may be other causes of this condition in dogs and a normal result does not exclude a different mutation in this gene or any other gene that may result in a similar genetic disease or trait.**

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## References

- Fieten H, Gill Yadvinder, Martin AJ, Concilli M, Dirksen K, van Steenbeek FG, Spee B, van den Ingh TSGAM, Martens ECCP, Festa P, Chesi G, van de Sluis B, Houwen RHJH, Watson AL, Aulchenko YS, Hodgkinson VL, Zhu S, Petris MJ, Polishchuk RS, Leegwater PAJ, Rothuizen J. The Menkes and Wilson disease genes counteract in copper toxicosis in Labrador retrievers: a new canine model for copper-metabolism disorders. *Dis Model Mech*. 2016 Jan;9(1):25-38. doi: 10.1242/dmm.020263. [[PubMed: 26747866](#)]
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