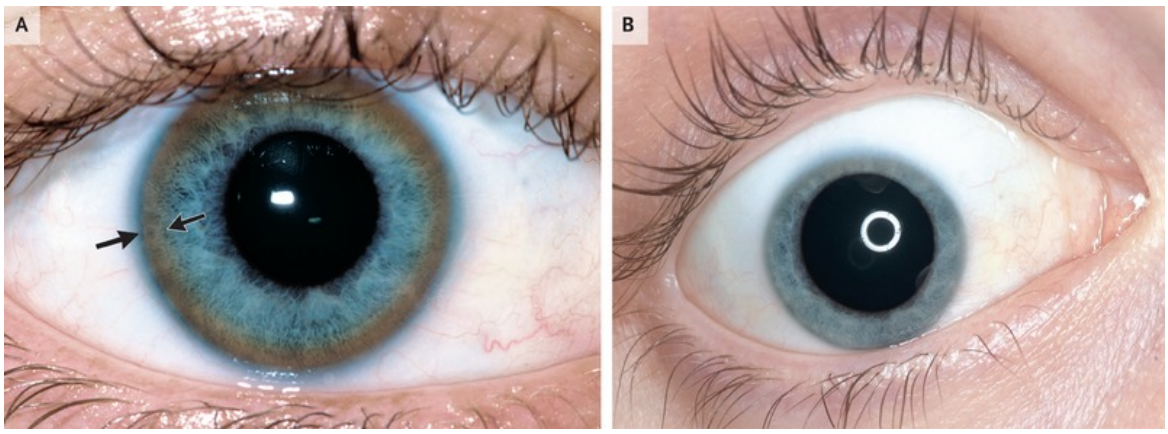
Wilson Disease is a genetic condition that causes the body to accumulate too much copper, which can affect the brain, liver, and eyes. The signs of Wilson disease often appear in the teenage years, and young adults with Wilson disease can develop problems with their nervous system, including issues with coordination, difficulty talking, impaired thinking, tremors, and psychiatric concerns (including mood disorders). Excess copper in the system can also damage the liver and can cause jaundice (yellowing of the skin and eyes) as well as fatigue.

Wilson disease can be diagnosed by measuring the amount of copper in the blood, urine, and liver. A characteristic sign of Wilson disease is a dark colored circle on the surface of the eye, called a Kayser Fleischer ring, caused by an accumulation of copper. The Kayser Fleischer ring does not hurt vision.



Source: N Engl J Med 2012; 366:e18

Genetics and Inheritance

Wilson disease is caused by mutations (or changes) in the *ATP7B* gene. This gene's function in the body is to help transport copper from the liver all around the body. It also is important to help the body get rid of excess copper. When this gene is not working properly and cannot get rid of extra copper in the body, it starts to build up and become toxic, which is what causes the signs and symptoms of Wilson disease.

Wilson disease is inherited in an autosomal recessive pattern. This means an individual who has Wilson disease has inherited two non-working copies of the *ATP7B* gene; the one they inherited from their mom is not working AND the one they inherited from their dad is not working. In the case of autosomal recessive conditions, if you inherit one working *ATP7B*

gene from a parent and one non-working *ATP7B* gene from a parent, you are called a 'carrier' for Wilson disease. Carriers do not have Wilson disease, and typically do not have signs or features of Wilson disease.

Diagnosing Wilson disease and genetic testing

Determining a diagnosis of Wilson disease can be complex and involve many different steps and types of testing, and should be done by a provider who is familiar with Wilson disease. The American Association for the Study of Liver Diseases (AASLD) published guidelines in 2008 that outline in detail the testing that is recommended to diagnose Wilson disease. Some findings that may raise the suspicion of Wilson disease are:

- Liver disease (recurrent jaundice, autoimmune-type hepatitis, or chronic liver disease)
- Neurological concerns (tremors, poor coordination, loss of fine-motor control, rigidity, gait disturbance, etc).
- Psychiatric concerns (depression, neurotic behaviors, personality disorganization, and intellectual deterioration.
- Kayser-Fleischer rings (copper deposits on the outside of the eye) occur in approximately 50-60% of people who have Wilson disease and liver disease, and in about 90% of people who have Wilson disease and neurologic or psychiatric concerns.

Genetic testing can also be helpful to establish the diagnosis of Wilson disease. Approaches may include:

- *Single site analysis*: Testing specific to a known mutation in the family
- *Full gene sequencing and rearrangement analysis*: Comprehensive testing to search for all currently detectable mutations in the *ATP7B* gene.
- *Gene panels*: A panel of genes that includes *ATP7B* and other genes that are suspected to be involved.

Treatment for Wilson disease

Treatment options for individuals with Wilson disease may vary, but in general would start with copper chelating therapy, which include medications that increase the body's ability to get rid of extra copper. Taking zinc supplements after this can help to interfere with the body's ability to absorb excess copper, which can further reduce many of the symptoms that affect someone with Wilson disease. There is also lab work (blood and urine) that is recommended to do one to two times per year. Individuals with Wilson disease should try to avoid foods that have high levels of copper (liver, brain, chocolate, mushrooms, shellfish,

and nuts), particularly at the start of treatment.

Click here to learn more about scheduling a genetic counseling appointment for pregnancy-related questions.

Click here to learn more about scheduling a genetic counseling appointment for infertility or preconception questions.

Click here to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

Resources

Wilson Disease Association

https://www.wilsonsdisease.org