

About Wilson's Disease

Wilson's Disease is a genetic disorder that is fatal unless detected and treated before serious illness from copper poisoning develops. Wilson's Disease affects approximately one in 30,000 people worldwide. The genetic defect causes excessive copper accumulation in the liver or brain.

Small amounts of copper are as essential as vitamins. Copper is present in most foods (see [Copper Content of Various Foods](#)), and most people have much more copper than they need. Healthy people excrete copper they don't need but Wilson's Disease patients cannot.

Copper begins to accumulate immediately after birth. Excess copper attacks the liver or brain, resulting in hepatitis, psychiatric, or neurologic symptoms. The symptoms usually appear in late adolescence. Patients may have jaundice, abdominal swelling, vomiting of blood, and abdominal pain. They may have tremors and difficulty walking, talking and swallowing. They may develop all degrees of mental illness including homicidal or suicidal behavior, depression, and aggression. Women may have menstrual irregularities, absent periods, infertility, or multiple miscarriages. No matter how the disease begins, it is always fatal if it is not diagnosed and treated.

The first part of the body that copper affects is the liver. In about half of Wilson's Disease patients the liver is the only affected organ. The initial physical changes in the liver are only visible under the

microscope. When hepatitis develops, patients are often thought to have infectious hepatitis or infectious mononucleosis when they actually have Wilson's Disease hepatitis. Testing for Wilson's Disease should be performed in individuals with unexplained, abnormal liver tests.

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How is Wilson's Disease Diagnosed?

The diagnosis of Wilson's Disease is made by relatively simple tests. The tests can diagnose the disease in both symptomatic patients and people who show no signs of the disease. These tests can include:

- Ophthalmologic slit lamp examination for Kayser-Fleischer rings
- Serum ceruloplasmin test
- 24-hour urine copper test
- Liver biopsy for histology and histochemistry and copper quantification
- Genetic testing, haplotype analysis for siblings and mutation analysis.

It is important to diagnose Wilson's Disease as early as possible, since severe liver damage can occur before there are any signs of the disease. Individuals with Wilson's Disease may falsely appear to be in excellent health. For additional information, refer to the Boston University Medical Campus website at www.bumc.bu.edu or consult with your physician.

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How is Wilson's Disease Inherited?

Wilson's Disease is an autosomal recessive disease, which means it is not sex-linked (it occurs equally in men and women). In order to inherit it, both of ones parents must carry a gene that each passes to the affected child. Two abnormal genes are required to have the disease. At least one in 30,000 people of all races and nationalities has the disease.

The responsible gene is located at a precisely known site on chromosome 13. The gene is called *ATP7B*. Some cases of Wilson's Disease occur due to spontaneous mutations in the gene. Most are transmitted from generation to generation.

Most patients have no family history of Wilson's Disease. People with only one abnormal gene are called carriers. Carriers (heterozygotes) may have mild, but medically insignificant, abnormalities of copper metabolism. Carriers do not become ill and should not be treated.

More than 200 different mutations of *ATP7B* have been identified thus far. Therefore, it has been difficult to devise a simple genetic screening test for Wilson's Disease. However, in a particular family, if the precise mutation is identified, a genetic diagnosis is possible by haplotype analysis. This requires a blood sample from both the patient and a relative. The samples are compared to each other. Haplotype testing helps to find symptom-free siblings who have the disease so that they may be treated before they become ill.

Someday a genetic test may help in genetic screening and prenatal diagnosis. However, at this time, there is no available test for these purposes.

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What is the Likelihood of Inheriting Wilson's Disease?

One in 100 individuals in the general population carries one abnormal copy of the Wilson's Disease gene. Carriers have one normal and one abnormal gene. All (100%) children of those afflicted with Wilson's Disease receive at least one abnormal copy of the Wilson's Disease gene. One half (50%) of a carrier's children receive at least one abnormal copy of the Wilson's Disease gene.

Siblings of Wilson's Disease patients have a 1 in 4 chance of having the disease. Since both of a siblings' parents are carriers, 1/4 of the siblings' children have the disease, 1/2 are carriers, and 1/4 are disease free with no Wilson's Disease gene.

Children of patients have a 1 in 200 chance of having the disease. A child of a Wilson's Disease patient has a 100% chance of getting one abnormal gene. The patient's spouse has a 1 in 100 chance of

carrying the abnormal Wilson's Disease gene and half the time he or she will pass it on.

Grandchildren of patients have a 1 in 400 chance of having the disease. A grandchild of a Wilson's Disease patient has a 50% chance of getting one abnormal gene, since each a patient's child is a carrier. From the other parent, a grandchild has a 1 in 200 chance of getting the gene ($1/2$ times $1/200$, or $1/400$).

Nieces and Nephews of patients with siblings who do not have Wilson's Disease have a $1/600$ chance of having the disease. Two-thirds of unaffected siblings carry the gene. The risk both parents being carriers is $2/3$ times $1/100$, or 1 in 150. The risk of each of their children having the disease is 1 in 600 ($1/4$ times $1/150$).

Cousins of Wilson's Disease patients have a 1 in 800 chance of having the disease. Fifty percent of aunts and uncles are carriers. The risk of both parents of a cousin carrying the abnormal gene is $1/2$ times $1/100$, or 1 in 200. Since 1 in 4 children of two Wilson's Disease patients is afflicted, the overall risk of a cousin of a Wilson's Disease patient being afflicted is $1/4$ times $1/200$, or $1/800$.

All siblings and children of Wilson's Disease patients should be tested for Wilson's Disease. Other relatives who have had symptoms or laboratory tests that indicate liver or neurological disease also should be tested for Wilson's Disease.

People with Wilson's Disease may not have any signs, symptoms, or evidence of illness. However, people with mild or non-apparent Wilson's Disease will become seriously ill and eventually die if they are not treated.

Testing is simple and safe. There are excellent treatments available. Failure to treat Wilson's Disease causes severe disability and eventually death.

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How is Wilson's Disease Being Treated?

Wilson's Disease is a very treatable condition. With proper therapy, disease progress can be halted and oftentimes symptoms can be improved. Treatment is aimed at removing excess accumulated

copper and preventing its reaccumulation. Therapy must be lifelong. Patients may become progressively more sick from day to day, so immediate treatment can be critical. Treatment delays may cause irreversible damage.

The newest FDA-approved drug is zinc acetate ([Galzin™](#)). (To link to a page about Galzin, [CLICK HERE](#).) Zinc acts by blocking the absorption of copper in the intestinal tract. This action both depletes accumulated copper and prevents its reaccumulation. Zinc's effectiveness has been shown by more than 30 years of considerable experience overseas. A major advantage of zinc therapy is its lack of side effects.

Other drugs approved for use in Wilson's Disease include penicillamine ([Cuprimine](#), Depen) and trientine ([Syprine](#)). (To link to a page about Cuprimine and Syprine, [CLICK HERE](#).) Both of these drugs act by chelation or binding of copper, causing its increased urinary excretion.

Tetrathiomolybdate is another chelating drug that is under investigation for initial treatment of Wilson's Disease. Thus far, it has not caused the neurological worsening often associated with penicillamine and even with trientine.

Patients with severe hepatitis or liver failure may require liver transplant. Patients being investigated or treated for Wilson's Disease should be cared for by specialists in Wilson's Disease or by specialists in consultation with their primary physicians.

Stopping treatment completely will result in death, sometimes as quickly as within three months. Decreasing dosage of medications also can result in unnecessary disease progression.

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Who Can I Contact for Help?

There are healthcare professionals in a variety of countries ready to assist you in diagnosing and treating Wilson's Disease.

For a listing of physicians and institutions familiar with Wilson's Disease and/or that accept Wilson's Disease patients, [CLICK](#)

[HERE.](#)

For a listing of WDA Centers of Excellence, **[CLICK HERE.](#)**

For a listing of individuals who can offer support to Wilson's Disease patients and families, **[CLICK HERE.](#)**

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