RIVER CITY
GASTROENTEROLOGY

Wilson's Disease

Understanding copper overload: diagnosis and lifelong management

WHAT IS WILSON'S DISEASE?

Wilson's disease is a rare inherited disorder in which copper accumulates in the body, primarily in the liver, brain, and eyes, because the body cannot properly excrete excess copper. Left untreated, copper accumulation progressively damages these organs, leading to liver disease, neurological problems, and psychiatric symptoms.[1,2]

Wilson's disease affects approximately 1 in 30,000 people worldwide and can present at any age, though most commonly between ages 5 and 35. It is caused by mutations in the ATP7B gene, which encodes a copper-transporting protein in liver cells. With early diagnosis and treatment, most people with Wilson's disease can live a normal lifespan.[1]

HOW DOES COPPER NORMALLY WORK?

Copper is an essential mineral obtained through food. Normally, the liver absorbs copper from the gut, uses what it needs, and excretes the rest through bile into the intestine. In Wilson's disease, this excretion pathway is impaired because the ATP7B protein is defective. Copper progressively builds up first in the liver, then spills into the blood and deposits in the brain, corneas (eyes), kidneys, and joints.

SYMPTOMS

Wilson's disease is highly variable in presentation. Some people present predominantly with liver disease; others present primarily with neurological or psychiatric symptoms. Some have a combination.[1,2]

Liver disease (hepatic Wilson's disease):

- Elevated liver enzymes found on routine blood tests
- Acute hepatitis with jaundice, fatigue, and abdominal pain
- Chronic hepatitis or cirrhosis
- Acute liver failure (in some young patients, a life-threatening presentation)

Neurological symptoms (neurological Wilson's disease):

- Tremor (particularly at rest or with movement)
- Dysarthria (slurred or difficult speech)
- Dysphagia (difficulty swallowing)
- Dystonia (abnormal muscle contractions causing twisting postures)
- Incoordination (cerebellar ataxia)
- Rigidity and mask-like facial expression (resembling Parkinson's disease)

Psychiatric symptoms:

- Personality changes, mood swings, or emotional instability
- Depression, anxiety, or psychosis
- Cognitive impairment or difficulty concentrating

Other features:

- Kayser-Fleischer rings: golden-brown rings visible at the outer edge of the cornea (seen in almost all patients with neurological involvement and in about 50% with liver disease)

- Haemolytic anaemia (red blood cells breaking down)
- Kidney problems (renal tubular acidosis)
- Joint pain and arthritis

DIAGNOSIS

Wilson's disease can be challenging to diagnose because its presentations mimic many other conditions. Diagnosis is based on a combination of blood tests, urine tests, slit-lamp eye examination, and liver biopsy:[1,2]

- **Serum ceruloplasmin**: a copper-carrying protein in the blood. Low ceruloplasmin (less than 0.20 g/L) is found in approximately 80-90% of patients with Wilson's disease, but can also be low in other liver diseases and malnutrition.
- **24-hour urine copper**: urine collected over 24 hours is tested for copper content. Elevated urinary copper (above 100 micrograms/24 hours) is a strong indicator of Wilson's disease. Can be elevated by other liver diseases.
- **Slit-lamp examination**: a detailed eye examination performed by an ophthalmologist to detect Kayser-Fleischer rings. Their presence, in combination with other abnormal tests, is strongly supportive of Wilson's disease.
- **Liver biopsy with hepatic copper quantification**: the definitive test when the diagnosis is uncertain. Elevated liver copper content (above 250 micrograms/gram dry weight) confirms Wilson's disease.
- **ATP7B genetic testing**: identifies the specific mutations causing Wilson's disease. Used to confirm the diagnosis and screen siblings.
- **MRI brain**: assesses the extent of copper deposition in the brain, which appears as characteristic changes on MRI in people with neurological Wilson's disease.

All siblings of someone diagnosed with Wilson's disease should be screened, as they have a 1 in 4 chance of also having the condition.

TREATMENT

Treatment aims to remove excess copper from the body, prevent further accumulation, and maintain copper balance lifelong. Treatment must never be stopped, as copper re-accumulates rapidly and can cause rapid deterioration.[1,2,4]

Copper chelating agents (copper removal)

- **D-penicillamine**: the traditional first-line treatment, which binds copper in the blood and increases its excretion in the urine. Effective but can cause significant side effects including kidney problems, bone marrow suppression, and autoimmune reactions. Blood and urine tests are required regularly during treatment.
- **Trientine (triethylene tetramine dihydrochloride)**: an alternative chelating agent with a better side effect profile than D-penicillamine. Now preferred as first-line in many centres. Available in Australia through special access schemes.

Zinc therapy (maintenance)

Zinc supplements taken at high doses block copper absorption from the gut by inducing the production of metallothionein (a protein that binds copper in gut cells). Zinc is effective for maintenance therapy in stable patients, particularly those with liver disease, and is the treatment of choice during pregnancy. It has fewer side effects than chelating agents but works more slowly.[1]

DIETARY ADVICE

During the initial treatment phase, a low-copper diet can help reduce copper intake. Although diet alone cannot control Wilson's disease, avoiding very high-copper foods is sensible:

- Avoid shellfish (especially oysters and crab), liver, and organ meats, which have the highest copper content
- Reduce nuts, seeds, chocolate, mushrooms, and legumes
- If your drinking water comes from copper pipes, let the tap run before drinking or use a filter
- Avoid vitamin and mineral supplements containing copper

MONITORING

Lifelong monitoring is essential:[1,2]

- 24-hour urine copper and serum ceruloplasmin every 6-12 months to guide treatment adequacy
- Liver function tests, full blood count, and kidney function regularly (side effect monitoring for chelation)
- Liver imaging (ultrasound or FibroScan) to monitor liver disease
- Neurological assessment if neurological symptoms are present or worsen
- Pregnancy: requires careful specialist management; treatment must continue through pregnancy with dose adjustments

RESOURCES AND SUPPORT

- **Australian Liver Association:** www.australianliver.com.au - Find a hepatologist specialising in rare inherited liver diseases
- **Liver Foundation Australia:** www.liver.org.au - Patient information and support for inherited liver conditions
- **Wilson's Disease Association (US, with resources relevant internationally):** www.wilsonsdisease.org - Comprehensive international patient resources for Wilson's disease

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