WHEN TO CONSIDER WILSON'S DISEASE

PROGRESSIVE MULTIORGAN DAMAGE, SIGNIFICANT PHENOTYPE VARIABILITY, WITH SYMPTOMS MOST OFTEN APPEARING BETWEEN THE AGES OF 5-35 YEARS, BUT > 8% AFTER THE AGE OF 40

Three main telltale disorders: hepatic (45%), neurological (35%), psychiatric (10%)

Clinical signs

Liver damage

Most common telltale sign in children at an average age of 10.5 years

Asymptomatic liver disease (biological **abnormality** discovered **by chance)**

Chronic hepatitis, fibrosis, cirrhosis, splenomegaly (portal hypertension)

Acute or fulminant hepatitis

Neurological impairment

On average around the age of 20

Generalised or focal **dystonia** including abnormal facial mimicry **(sardonic expressions), distal choreic movements**

Difficulty walking, unusual clumsiness, decline in educational achievement, dysarthria with **hypersalivation**

Cerebellar syndrome associated with postural and/or intentional tremors

Bilateral, symmetrical **Parkinsonian syndrome**, hypertonia that is mainly axial.

Possible epilepsy

Psychiatric disorders

Changes in personality and behaviour: frontal syndrome with attention deficit, **neuropsychiatric manifestations** (depression, addictions, even psychosis, etc.)

Other impairments

ophthalmological

in >95% of patients with neurological damage and in 50% of patients with liver damage

Kayser-Fleischer ring

Renal

Lithiasis, tubulopathy

Cardiac

Cardiomyopathy, rhythm disorders and dysautonomia

Gynaecological

Amenorrhoea or recurrent spontaneous miscarriage

Haematological

Coombs-negative haemolytic anaemia, isolated thrombocytopaenia, leukopaenia (signs of hypersplenism)

Osteoarticular

Osteoarticular pain, osteomalacia, osteopenia, osteoporosis, arthropathy

Specialist workup

Additional tests

Laboratory:

cytolysis, cholestasis,[1] sometimes with signs of hepatocellular insufficiency, +/- anaemia (particularly Coombs-negative haemolytic) isolated thrombocytopaenia, leukopaenia

Liver ultrasound:

steatosis, signs of cirrhosis (sometimes complicated by hepatocellular carcinoma) and signs of portal hypertension

Additional tests

Brain MRI (T1, T2 and FLAIR sequences): bilateral and symmetrical damage to the basal ganglia, dentate nuclei and substantia nigra, midbrain damage with "Face of the Giant Panda", and frequent diffuse cerebral atrophy

Additional tests

Eye examination with slit lamp: **Kayser-Fleischer ring**

Wilson's Disease?

Specialist medical opinion and reference laboratory

Specialist workup

Decrease in the ceruloplasmin level[2]

Increase in 24 hr urine copper

Decrease in overall copper level

Exchangeable copper assay (high[3])

Calculation of the ratio of exchangeable copper/ total copper in serum (REC) (high >15%)

→ **Confirmatory genetic analysis (*ATP7B* gene)** →

Urgent specialist advice from a Centre of Excellence:
https://www.crmrwilson.com
https://www.filiere-g2m.fr/annuaire/
https://www.filfoie.com/

Initial assessment, specialist care, specific treatment (indications, initiation) coordinated by a Centre of Excellence

Genetic counselling, family screening in a specialist centre

For more information: PNDS French National Authority for Health - Wilson's Disease (has-sante.fr)

[1] Normal liver function test results do not eliminate liver impairment: quietly-developing steatosis or fibrosis (thus the benefit of Fibroscan®).
[2] The level of ceruloplasmin may be normal, and decreases can occur in other circumstances (healthy heterozygotes, viral hepatitis, malnutrition, etc.).
[3] Sometimes exchangeable copper can be normal (especially in hepatic or asymptomatic forms).

Maladies rares Héréditaires du Métabolisme
Filière nationale de santé