

For suspected patients with Wilson Disease (WD) perform the following:

- Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, total and conjugated bilirubin, complete blood cell count
- Serum ceruloplasmin (CP): [CERS/ Ceruloplasmin, Serum](#)
- Serum copper (Cu): [CUS1/ Copper, Serum](#)
- 24-Hour urine Cu: [CUU / Copper, 24 Hour, Urine](#)
- Slit-lamp exam for Kaiser-Fleischer (K-F) ring
- Brain MRI for neurologic symptoms

All siblings and first-degree relatives of affected patients

Neurological or psychiatric symptoms ± liver disease
Unexplained liver disease (elevated AST, ALT)

<ul style="list-style-type: none"> Normal CP and serum Cu Normal 24-hour urine Cu Normal liver function tests K-F ring absent 	<ul style="list-style-type: none"> Normal CP and serum Cu Increased 24-hour urine Cu K-F ring present 	<ul style="list-style-type: none"> Decreased CP and serum Cu Increased 24-hour urine Cu K-F ring absent 	<ul style="list-style-type: none"> Decreased CP and serum Cu Increased 24-hour urine Cu K-F ring present 	<ul style="list-style-type: none"> Normal CP and serum Cu Normal 24-hour urine Cu K-F ring absent
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Age ≥15 years → STOP WD excluded

Age <15 years → WNDZ / Wilson Disease, *ATP7B* Full Gene Sequencing with Deletion/Duplication, *Varies* OR Continue follow-up

Preferred → WNDZ / Wilson Disease, *ATP7B* Full Gene Sequencing with Deletion/Duplication, *Varies*

Not required for diagnosis → Diagnostic for WD, liver biopsy not required → Diagnosis established, Initiate treatment, Initiate family screening

Continue evaluation for alternative diagnosis

Disease-causing variants not detected → STOP WD excluded

WNDZ / Wilson Disease, *ATP7B* Full Gene Sequencing with Deletion/Duplication, *Varies*

Any of the following combinations:

- Two disease-causing variants detected
- Two disease-causing variants detected AND consistent histology regardless of Cu level
- Disease-causing variants not detected AND increased Cu >250 mcg/g dry weight and consistent histology in the absence of long-standing (>1 year) liver failure or obstruction

Diagnosis established, Initiate treatment, Initiate family screening

Liver biopsy with histology and Cu quantitation.

- If histology is required for confirmation
- If liver Cu quantitation is required

Disease-causing variants not detected AND Clinical picture consistent with WD → Liver biopsy with histology and Cu quantitation.

Disease-causing variants not detected AND Clinical picture supports an alternative → Continue evaluation for alternative diagnosis

Disease-causing variants not detected AND Cu <250 mcg/g dry weight and inconsistent histology → Continue evaluation for alternative diagnosis