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)

Normal CP and serum Cu
- Normal 24-hour urine Cu
- K-F ring absent

Age ≥15 years

Disease-causing variants not detected
- WNDZ / Wilson Disease, ATP7B Full Gene Sequencing with Deletion/Duplication, Varies
- Continue follow-up

Normal CP and serum Cu
- Increased 24-hour urine Cu
- K-F ring present

Age <15 years

Preferred

Decreased CP and serum Cu
- Increased 24-hour urine Cu
- K-F ring absent

Not required for diagnosis

Decreased CP and serum Cu
- Increased 24-hour urine Cu
- K-F ring present

Diagnostic for WD, liver biopsy not required

Normal CP and serum Cu
- Normal 24-hour urine Cu
- K-F ring absent

Continue evaluation for alternative diagnosis

Disease-causing variants not detected

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

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

Liver biopsy with histology and Cu quantitation.

Disease-causing variants not detected AND
- Clinical picture consistent with WD

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

Diagnosis established
- Initiate treatment
- Initiate family screening

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