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
- Normal liver function tests
- K-F ring absent

Age ≥15 years

No mutations

Wilson disease excluded

WDZ / Wilson Disease, Full Gene Analysis, Varies
OR
Continue follow-up

WDZ / Wilson Disease, Full Gene Analysis, Varies

Any of the following combinations:
- Two mutations identified
- Two mutations identified AND consistent histology regardless of Cu level
- No mutations identified AND increased Cu >250 mcg/g dry weight and consistent histology in the absence of long-standing (>1 year) liver failure or obstruction

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

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

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

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

Age <15 years

Not required for diagnosis

Diagnostic for WD, liver biopsy not required

Continue evaluation for alternative diagnosis

No mutations identified AND Clinical picture supports an alternative diagnosis

Liver biopsy with histology and Cu quantitation.

- No mutations identified AND Clinical picture consistent with WD

No mutations identified AND Clinical picture supports an alternative diagnosis

Continue evaluation for alternative diagnosis

Diagnosis established
- Initiate treatment
- Initiate family screening

Any of the following combinations:
- Two mutations identified
- No mutations identified AND increased Cu >250 mcg/g dry weight and inconsistent histology

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

No mutations identified AND Clinical picture consistent with WD

No mutations identified AND Clinical picture supports an alternative diagnosis

Continue evaluation for alternative diagnosis

Diagnosis established
- Initiate treatment
- Initiate family screening

Begin with:
- AST, ALT, ALP, total and conjugated bilirubin, albumin, CBC
- Serum ceruloplasmin (CP)
- Serum copper (Cu)
- 24-Hour urine Cu
- Slit-lamp exam for Kaiser-Fleischer (K-F) ring
- Brain MRI for neurologic symptoms

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