Wilson Disease Testing Algorithm

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

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

WDZ / Wilson Disease, Full Gene Analysis

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

Age <15 years

No mutations

Preferred

Normal liver function tests

WDZ / Wilson Disease, Full Gene Analysis

Normal liver function tests

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
- K-F ring absent

Not required for diagnosis

Diagnostic for WD, liver biopsy not required

No mutations identified AND Clinical picture supports an alternative diagnosis

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

Liver biopsy with histology and Cu quantitation.

- Diagnosis established
- Initiate treatment
- Initiate family screening

No mutations identified AND
- Cu <250 mcg/g dry weight and inconsistent histology

Continue evaluation for alternative diagnosis

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

No mutations identified AND
- Clinical picture consistent with WD

Continue evaluation for alternative diagnosis

If liver Cu quantitation is required

Diagnosis established
- Initiate treatment
- Initiate family screening

Continue evaluation for alternative diagnosis

No mutations identified AND
- Liver biopsy not required

Continue evaluation for alternative diagnosis

No mutations identified AND
- Continue follow-up

Wilson disease excluded

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

Liver biopsy with histology and Cu quantitation.

- Diagnosis established
- Initiate treatment
- Initiate family screening

Continue evaluation for alternative diagnosis