Wilson Disease

Recognition, diagnostic workup, chelation/zinc therapy, monitoring, and management in special clinical situations including ALF, transplant, and pregnancy.

2022 AASLD Practice Guidance
Diagnosis and Management of Wilson Disease
Schilsky et al. · Hepatology 2023;77:1428–1455

FORMAT *38 numbered guidance statements — narrative consensus format (not GRADE-rated); grouped by clinical theme.*

1 Recognizing Wilson Disease

GS	STATEMENT
1	Consider WD in any individual with liver abnormalities of uncertain cause — age alone does not exclude the diagnosis
2	Must exclude WD in unexplained liver disease with neurological/psychiatric features; movement-disorder neurology and psychiatric evaluation may be needed
3	Suspect WD in ALF with nonimmune hemolytic anemia (incl. acute intravascular hemolysis) — urgent transplant evaluation required
4	Evaluate for WD in patients with recurrent self-limited nonimmune hemolysis
5	WD may involve renal, musculoskeletal, cardiac, or endocrine systems beyond liver and nervous system

2 Diagnostic Evaluation

GS	STATEMENT
6	History/exam plus baseline panel: liver biochemistries, CBC/INR, ceruloplasmin ± serum copper, basal 24-h urinary copper, slit-lamp/OCT for KF rings, neuro exam, ATP7B testing as logistics allow
7	Ceruloplasmin <5 mg/dL strongly suggests WD; a normal level does not exclude the diagnosis
8	24-h urinary copper typically >100 µg (symptomatic) or >40 µg (asymptomatic/children) suggests WD — requires clinical correlation
9	Liver biopsy aids diagnosis/staging and may reveal an alternative or concurrent liver disease
10	MRI brain (preferred) if neurological evaluation reveals abnormalities
11	ATP7B genetic testing may confirm diagnosis and is efficient for first-degree relative screening
12	Diagnostic scoring systems aid diagnosis in atypical presentations and for research purposes
13	Prognostic scoring systems (e.g., NWI), applied serially, help predict response to medical therapy
14	First-degree relatives of newly diagnosed patients must be screened for WD

3 Initial & Maintenance Therapy

GS	STATEMENT
15	All newly diagnosed patients start lifelong medical therapy; individualize timing in children <3y to degree of organ damage
16	Symptomatic patients: chelating agent (D-penicillamine or trientine) — trientine often better tolerated
17	Asymptomatic patients: lower-dose chelator or zinc
18	Transition to maintenance therapy after generally >1y with favorable clinical/biochemical response

4 Diet & Nutrition

GS	STATEMENT
19	Avoid high-copper foods/water, especially in year 1 of treatment; registered dietitian supervision helps prevent overly restrictive patterns
20	Patients unable to maintain adequate nutrition need supplement management that avoids excess copper — RD involvement recommended

5 Monitoring, Overtreatment & Adherence

GS	STATEMENT
21	Regular liver biochemistries/INR, CBC, urinalysis, and exam at least twice yearly (more often on chelation therapy)
22	24-h urinary copper yearly (more often if adherence uncertain or dose adjusted); track serum copper/ceruloplasmin trends
23	Overtreatment suggested by cytopenias, tissue iron retention, low serum copper + very low 24-h urinary copper (<100 µg on chelator, <20 µg on zinc) — reduce dose or hold therapy
24	Treatment failure: exclude concurrent disease/nonadherence, revise regimen; consider transplant if advanced disease
25	Adherence is critical to outcomes — team-based support and increased monitoring when nonadherence is suspected

6 Severe Disease, ALF & Transplant

GS	STATEMENT
26	Severe hepatic disease may respond to intensive combination regimen (chelator + zinc, temporally dispersed dosing); evaluate for transplant as backup
27	Advanced chronic liver disease failing/intolerant of medical therapy → prompt transplant evaluation
28	ALF due to WD → immediate transplant referral and evaluation
29	ALI due to WD may respond to medical therapy or progress to ALF — early transplant referral required
30	WD-specific medical treatment is unnecessary after liver transplantation
31	Liver failure and HCC are accepted transplant indications; isolated neurologic WD remains a controversial indication
32	Patients with cirrhosis or regressed cirrhosis should undergo HCC screening and surveillance

7 Pregnancy & Neuropsychiatric Care

GS	STATEMENT
33	Preconception counseling: genetic counseling plus medication safety discussion
34	Continue WD treatment in pregnancy; D-penicillamine is teratogenic (trientine data sparse) — reduced-dose chelation with trimester LFT monitoring, or zinc (established pre-conception), are options
35	Breastfeeding while on WD treatment: weigh infant risks/benefits individually
36	Effective restoration of copper balance may improve neurological/psychiatric features over time
37	Adjunctive medical treatment may alleviate parkinsonism, dystonia, and chorea
38	Persisting/severe psychiatric features despite adequate treatment may benefit from psychotropic medication or counseling

Schilsky ML, Roberts EA, Bronstein JM, et al. AASLD 2022 Practice Guidance on Wilson Disease. *Hepatology*. 2023;77(4):1428–1455.