In the name of God

Wilson disease in children: monitoring & follow up

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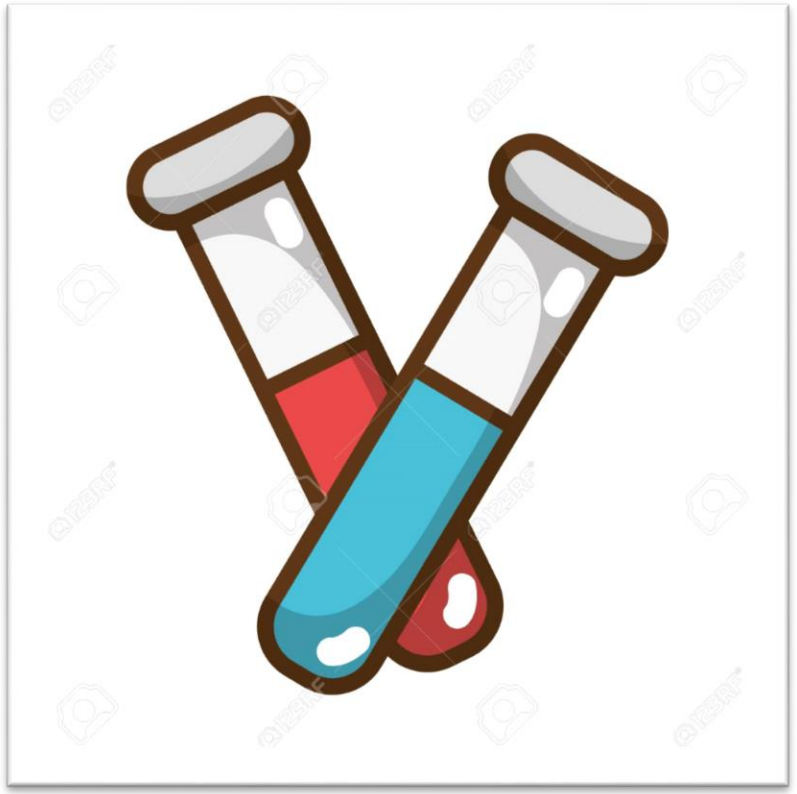
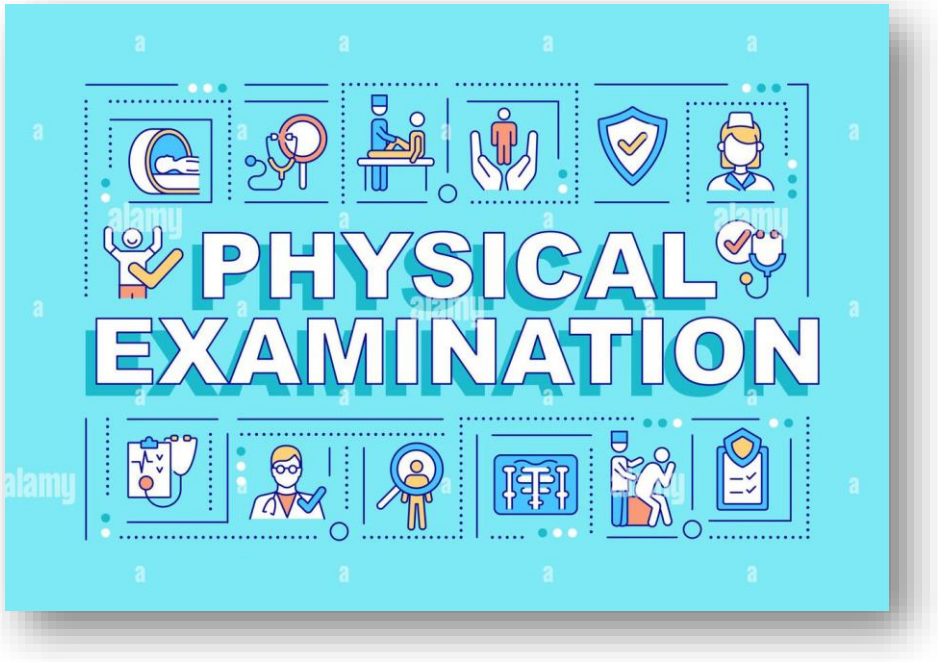
Goals of Monitoring:

- **Primary Goals**: Stabilize and improve symptoms, prevent disease progression
- **Secondary Goals**: Ensure medication adherence, monitor for side effects

Clinical Examination & Laboratory Tests:

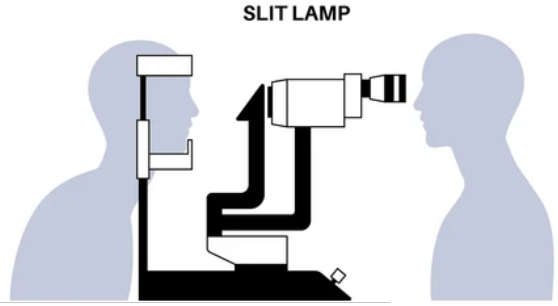




Clinical Examination & Laboratory Tests:

- During the 1st m of D-penicillamine Rx, the patient should be monitored weekly for fever/rash.
- CBC, U/A, renal and liver blood tests should be obtained each 1-2 weeks.
- Checking for symptoms of liver, neurological, or psychiatric disease, side effects of treatment
- If the patient responds appropriately with resolution of symptoms and normalization of liver blood tests, monitoring: every 1-3 months for the 1st year, and ideally every 6 months thereafter.
- Abnormalities in AST, ALT, and GGT may persist for at least a year of treatment
  - the trend should be toward improvement within the first six months of therapy.
- An annual 24-hour urinary copper excretion
- Non-ceruloplasmin-bound copper should normalize with effective therapy.
  - NL: 5–15 µg/dL during effective therapy.
  - > 20 µg/dL : Noncompliance
  - <5 µg/dL copper deficiency: ↓ dose of penicillamine: gradually by 25%

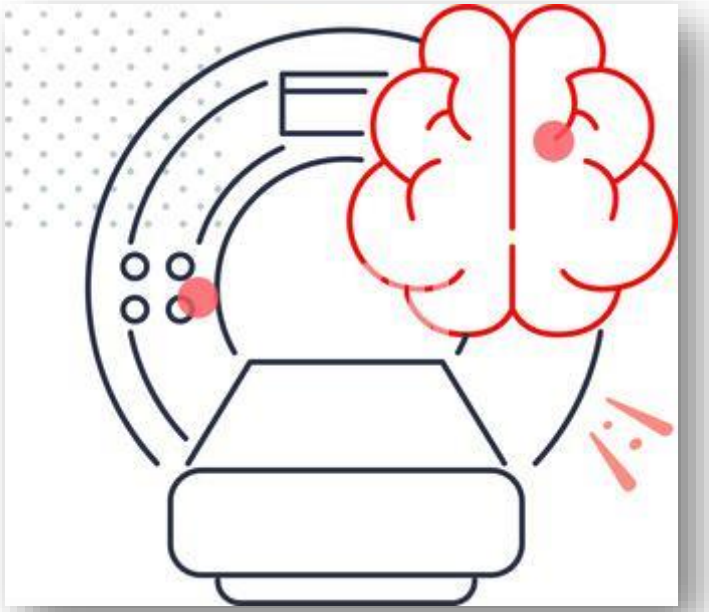
Ophthalmologic evaluation:

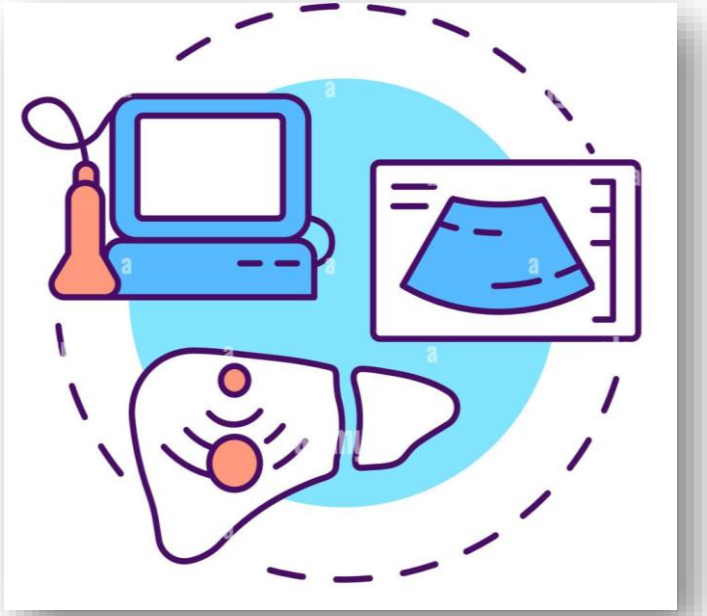


- K-F rings +ve: serial annual ophthalmologic examinations are helpful in documenting disappearance or significant reduction of these lesions with adequate copper chelation.
- Disappearance of KF rings following successful treatment of Wilson disease is typically a slow process that occurs over years: 6m -12 yr
- The lateral and medial portions of the ring disappear first, leaving superior and inferior crescents.
- May also be useful in patients without K-F rings: development or rings: indicate poor compliance.

Imaging and Other Tests:

- **Imaging**: Ultrasound, MRI of the brain if needed
- **Purpose**: Assess liver disease progression, detect neurological involvement



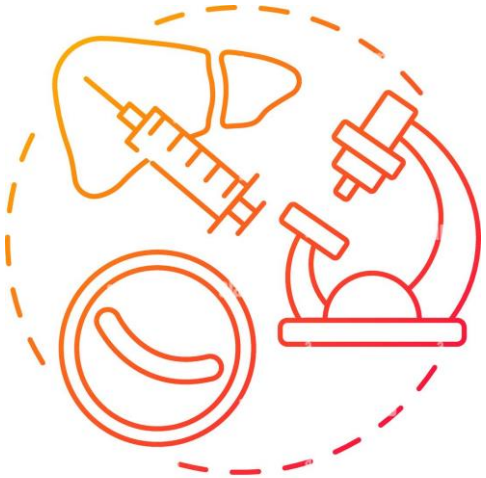


Medication Adherence/Follow-Up Visits:

- **Importance**: Lifelong adherence to medication and diet is crucial
- Uninterrupted lifelong therapy is mandatory (unless the patient has a liver transplant).
- If compliant, D-penicillamine therapy will maintain the asymptomatic patient in good health.
- A yearly discussion with the patient and family should reinforce the importance of adherence.
  - should be reminded of the possible fatal consequences of discontinuing this therapy suddenly.
- 8 of 11 patients who discontinued therapy died of acute liver failure within 2.6 years.
- Progressive liver disease may also occur unbeknownst to the poorly adherent patient.

Others:

- The effect of D-penicillamine therapy on psychiatric disturbances is difficult to predict, although improved school performance is commonly observed in treated children.
- Patients with psychiatric disturbances require not only copper chelation therapy, but also psychotherapy and appropriate psychotropic medications. Patients with significant neurologic symptoms require brain MRI imaging and evaluation by a movement disorder neurologist.



- Liver dysfunction generally improves rapidly (by 2-6 months) with D-penicillamine therapy however, if overt fibrosis and cirrhosis are present, the signs of portal hypertension show little response although histology may gradually improve.
- Hepatic copper content generally decreases but may remain quite elevated despite years of therapy and clinical improvement.

Special Circumstances

surgery

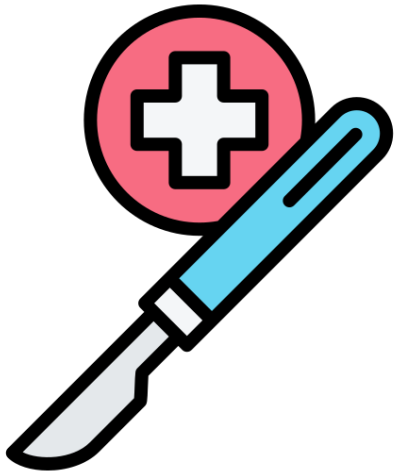
Pregnancy

Pregnancy:

- Fertility?
- During pregnancy it is advisable to continue D-penicillamine or trientine during the 1st and 2nd trimester at a reduced dose of 750–1,000 mg/day
  - one authority advises discontinuation during the first twelve weeks of gestation, if possible.
- Several patients who have discontinued therapy for longer periods during pregnancy: acute hemolysis or acute hepatic failure.
- D-penicillamine has been administered to over 150 pregnant: two cases of neonatal transient cutis laxa.
  - one infant developed a connective tissue defect, the mother treated with penicillamine for cystinuria.
- Trientine and zinc therapy are probably equivalent to D-penicillamine
- All children fathered by patients with WD have been normal.
- The risk to mother and infant of discontinuing copper-chelation therapy appears to be greater
- If Cesarean section is anticipated: reducing the dose of D-penicillamine to 250mg/day 6 weeks prior to delivery: wound healing.
- Women taking D-penicillamine or trientine should be advised not to breast feed: secreted in breast milk and could potentially be harmful to the infant causing copper deficiency

Surgery

- D-penicillamine has inhibitory effects on collagen crosslinking.
- In order to prevent interference with wound healing, it is recommended that, when patients with Wilson disease undergo scheduled surgery, the dose of D-penicillamine should be reduced, but not stopped, for 10 to 14 days post-operatively.



Review Article

Wilson disease in children and young adults - State of the art

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Abstract Wilson disease (WD) is an autosomal recessive disorder caused by mutations of the *ATP7B* gene, with a reported prevalence of 1:30,000–50,000. *ATP7B* encodes an enzyme called transmembrane copper-transporting ATPase, which is essential for copper incorporation into ceruloplasmin and for copper excretion into the bile. A lack or dysfunction of this enzyme results in a progressive accumulation of copper in several organs, especially in the liver, the nervous system, corneas, kidneys, and heart. Children with WD can present with asymptomatic liver disease, cirrhosis, or acute liver failure, with or without neurological and psychiatric symptoms. Approximately 20%–30% of WD patients present with ALF, while most of the other patients have chronic progressive hepatitis or cirrhosis if untreated. Although genetic testing has become a more important diagnostic tool for WD, the diagnosis remains based on both clinical features and laboratory investigations. The aims of treatment are to reduce copper levels and prevent its accumulation in the liver and other organs, especially in the central nervous system. Liver transplantation in WD is a life-saving option for patients presenting with liver failure and encephalopathy. For WD patients treated with chelating agents, adherence to the therapy is essential for long-term success. In this review, we also address specific issues in young adults as compared to children.

Keywords: Acute hepatic decompensation, chelating agents, chronic liver disease, copper metabolism, fulminant hepatic failure, liver transplantation, Wilson disease

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