Wilson Disease

Genetics

-Gene: ATP7B (Copper-transporting ATPase 2; 13q14.3-q21.1)

-AR

Clinical findings/Dysmorphic features

-Disorder of copper metabolism; hepatic, neurologic, or psychiatric disturbances; 3-50 years

-Liver disease: recurrent jaundice, simple acute self-limited hepatitis-like illness, autoimmune-type hepatitis, hepatic failure, chronic liver disease

-Neurologic presentations: movement disorders (tremors, poor coordination, loss of fine-motor control, chorea, choreoathetosis) or rigid dystonia (mask-like facies, rigidity, gait disturbance, pseudobulbar involvement)

-Psychiatric disturbance: depression, neurotic behaviors, disorganization of personality

-Kayser-Fleischer rings: frequent, copper deposition in Descemet's membrane of the cornea

Etiology

-1:30,000; carrier frequency 1:90

Pathogenesis

-Copper-transporting ATPase 2: intracellular transmembrane copper transporter --> incorporating copper into ceruloplasmin and moving copper out of the hepatocyte into bile

-Tissue damage due to copper accumulation because of lack of copper transport from the liver

Genetic testing/diagnosis

-Diagnosis established by combination:

1) Biochemical (low serum copper and ceruloplasmin conc., inc. urinary copper excretion)

2) Clinical (Kayser Fleischer corneal ring)

3) Detection of biallelic ATP7B pathogenic variants

-ATP7B sequencing (98%) --> H1069Q (35-45% Europeans); R779L (57% Asians); H714Q and delC2337 (40% Russians)

Others

-Treatment: Chelating agents, liver transplant