Wilson's Disease

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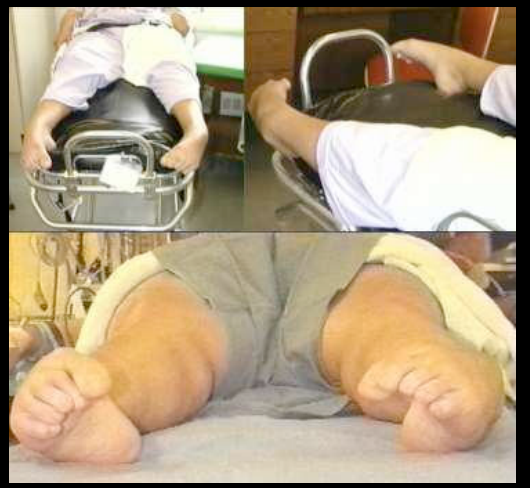
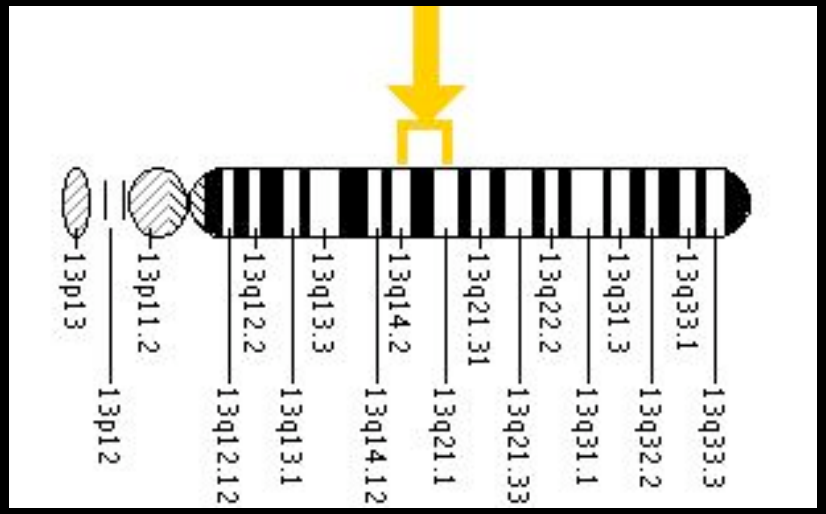
General Information

- Autosomal recessive
- Hepatolenticular Degeneration
- Copper Metabolism
- Liver, Brain, Eyes, Kidneys
  - Toxic
- Menkes Disease
- Frequency: 1/30,000 in most populations
  - 1/10,000 in China, Japan, and Sardinia



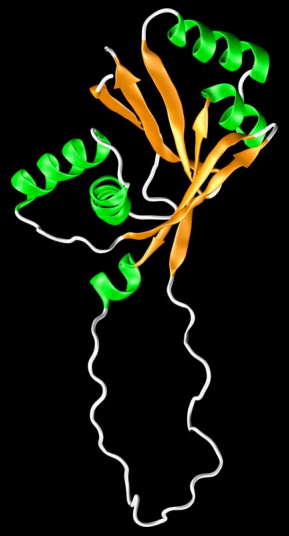
Genetics

- Gene is ATP7B
- Chromosome 13
  - base pairs 51,404,805 to 51,483,630
- ATPase family
- Protein: copper-transporting ATPase 2
  - Exports copper from cells



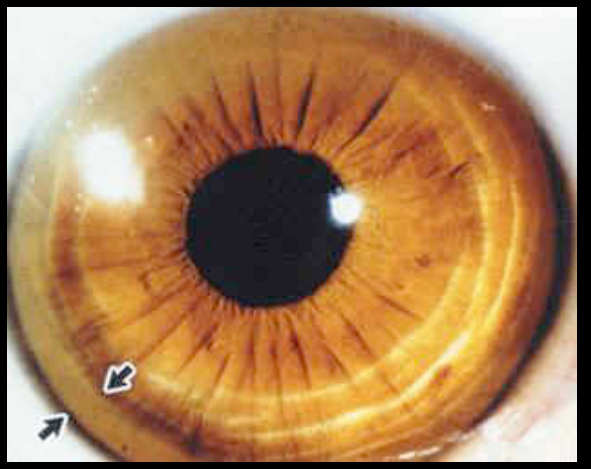
Mutations

- Complete Gene Sequencing: mutations in 98% affected
- +260 mutations cause Wilson's
- H1069Q- mutation found in 45% affected Europeans
- R778L- mutation found in 57% affected Asians
- Common in exons 8, 12, 14, and 18



Classical Diagnosis

- Low serum and ceruloplasmin
- 24-hr urinary copper excretion text
  - + if >100mg
- Kayser- Fleischer rings
  - Slit lamp
  - 50-60% liver disease,
  - 90% neurological/psychiatric signs
- Liver Biopsy
  - +250 µg/g dry weight
  - Confirms diagnosis

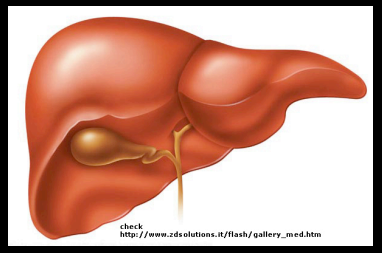


Symptoms

- Most common in kids: liver disease
- Most common in adults: neurological disease
- Mainly hepatic, neurologic, hematologic, or psychiatric signs
  - Enlarged abdomen
  - Jaundice
  - Fatty liver
  - Weakness
  - Arm/hand tremors
  - Abnormal arms/leg posture/movements
  - Slow movements/facial expressions
  - Speech impairment
  - Depression
  - Dementia
  - Aggression
  - Hemolytic Anemia
  - Autoimmune hepatitis
  - Vomiting Blood
  - Arthritis
  - Stiffness

Classical Treatment

- Lifelong, including during pregnancy
- Zinc acetate
- Copper Chelating agents
  - Penicillamine, trientine (better)
    - Use with antioxidants to avoid tissue damage
- Low-Copper Diet
  - Mushrooms, nuts, chocolate, dried fruit, liver, shellfish, tap water
- Orthotopic Liver Transplant

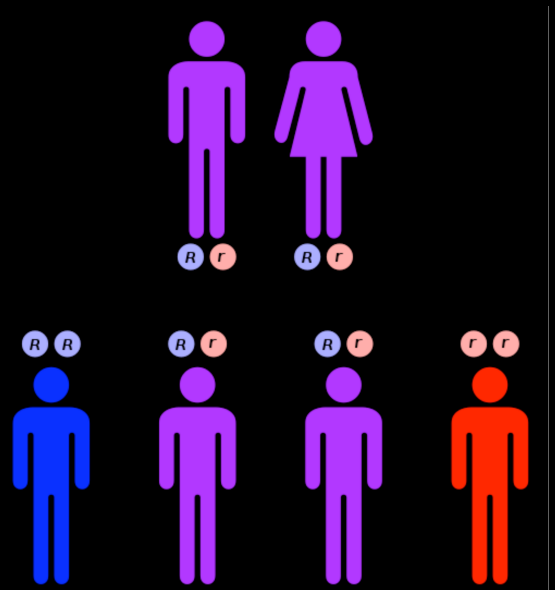


With Gene Discovery

- Diagnosis primarily biochemical
- Genetic testing available
  - Recommended since have treatment
- Can do confirmatory diagnostic, predictive testing, carrier testing, prenatal diagnosis
  - Prenatal possible if mutation has been identified in family
- Test methods:
    - Targeted mutation analysis
    - Sequence analysis/mutation scanning of exons
    - Sequence analysis of coding region
    - Deletion/duplication testing

Further Treatment

- Genetic testing allows therapies to start before symptoms
- Heterozygotes
  - Do not have clinical symptoms but may test positive or borderline for tests
  - Genetic test confirms if just a carrier or if affected
- Under investigation: ammonium tetrathiomolybdate



Sources

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