Wilson's Disease

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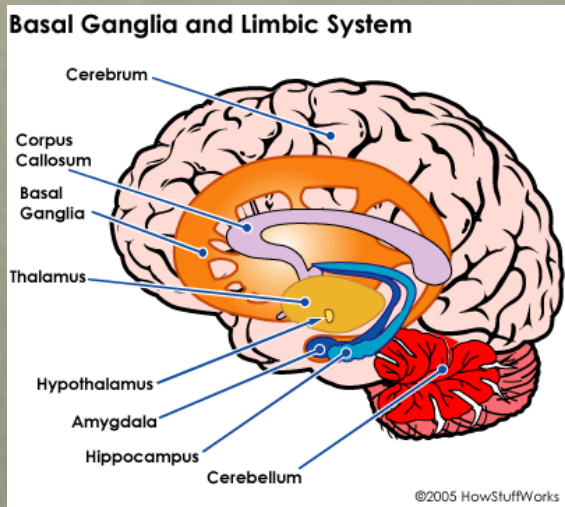
Biochem 118Q

What is Wilson's Disease?

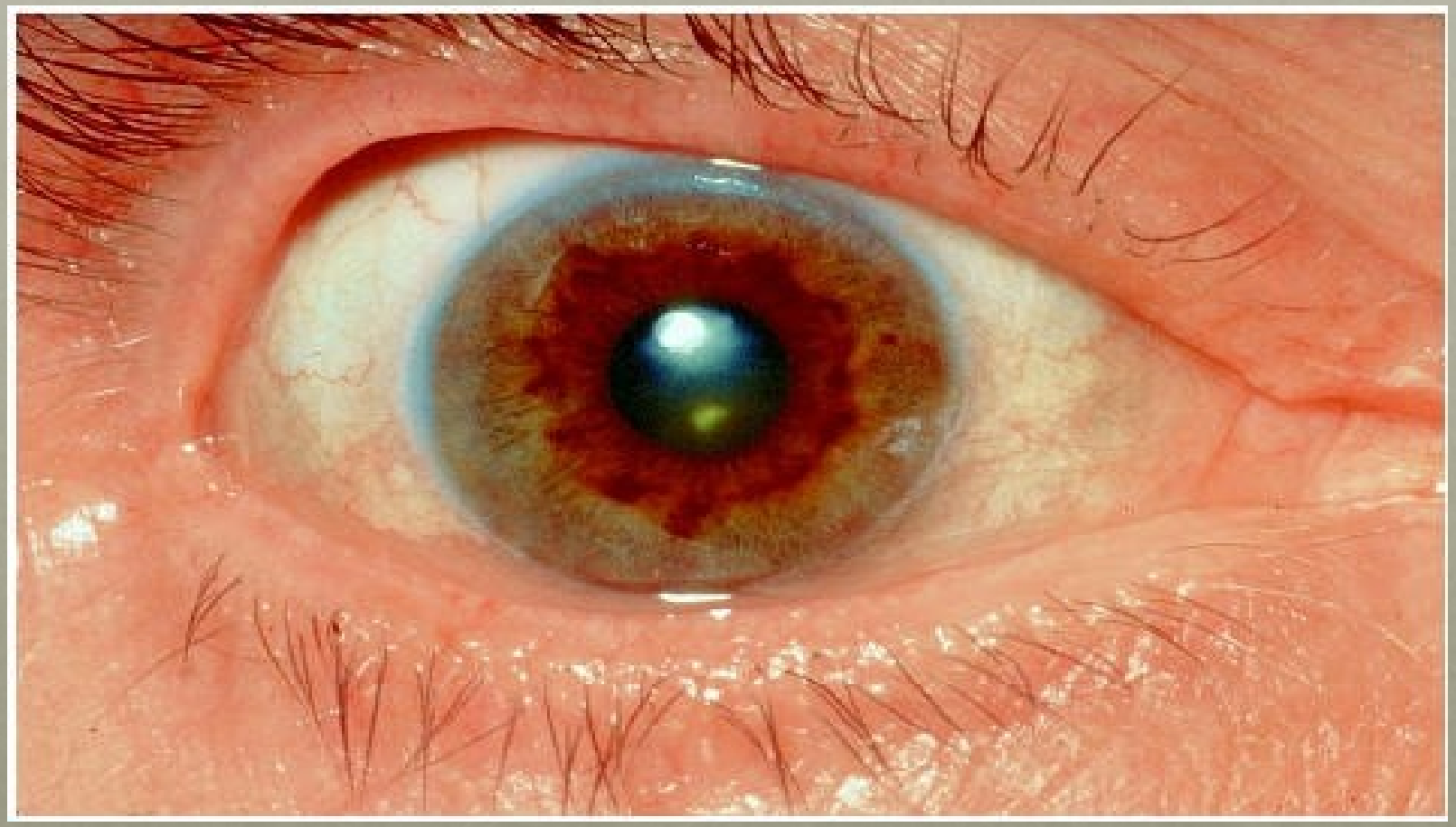
- A mutation in the ATP7B gene in chromosome 13 (13q14.3)
- The ATP7B gene encodes a transport protein, incorporates into ceruloplasmin (Cu protein)
- Copper builds up in the liver, brain, eyes, causes neurological damage
- Copper is necessary for bodily functions, many proteins require copper as a cofactor

Classical Symptoms

- the basal ganglia change in reaction to copper levels, ability to learn, action selection and execution, clumsiness
- The liver develops cirrhosis, inability to bind copper
- Children- liver disease, young adults- neurological problems, ataxia-coordination, dystonia-abnormal movement, seizures, migrane, psychosis
- Heart and kidney failure, heart muscle weakening, weakening of bones
  - -arthritis from copper buildup in synovial fluid,
  - cataracts

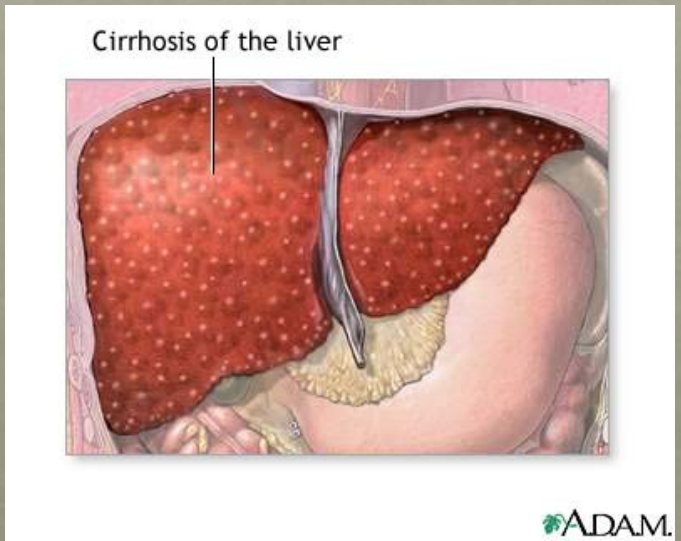


Kayser-Fleischer Ring



Classical Diagnosis

- Surefire- liver biopsy, 250 micrograms Cu per gram of liver tissue
- Ceruloplasmin (protein that carries copper and binds iron) is extremely low, >4/5 people
- Urine copper levels- 100 µmg/hour is definitive, 40µmg/hour

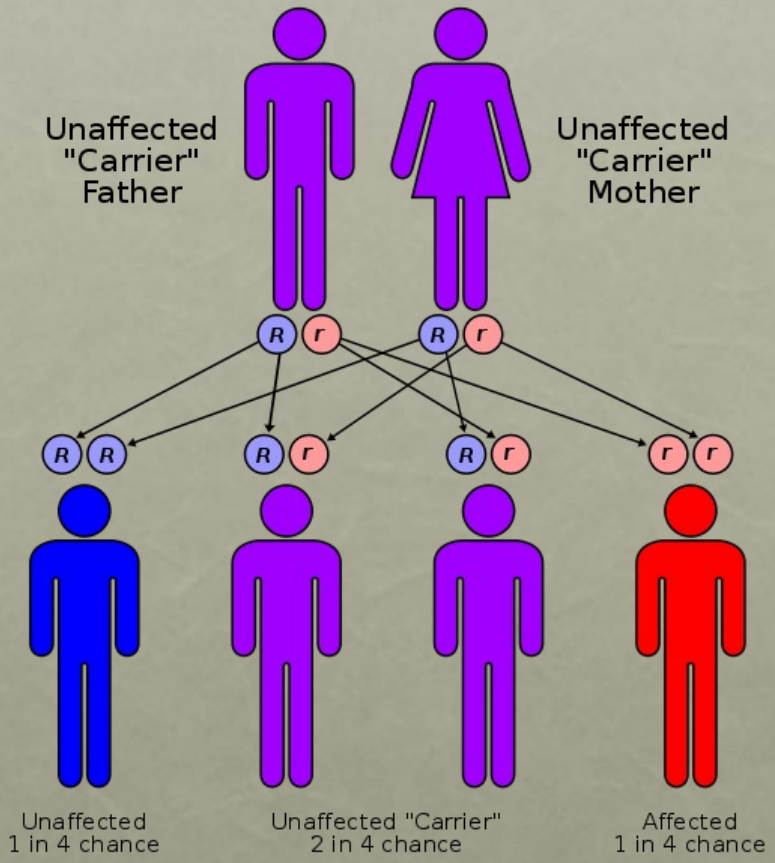


Classical Treatment

- Dietary changes- foods low in copper
- Zinc treatments- Metallothionein stimulation, urine excretion, clinical trials because not effective for all
- Penacillamine- binds copper, urine excretion
- Liver transplant surgery is effective in curing the disease, complications from surgery itself are a downside (transplant rejection)

Genetics

- Autosomal recessive, Mendelian
- 60% affected have homozygous genes, 30% have 1 bad copy (mild) and 10% have no detectable mutation but are slightly symptomatic
- Yang et al. (1997) stated that the full length ATP7B protein is 1465 amino acids long
- Without genetic testing, predisposition to the disease would not be known until symptoms developed



Genetic Diagnosis

- Inspection of ATP7B gene in Chromosome 13, Genetic analysis of ATP7B gene and others that code for copper binding proteins
- Over 300 different mutations in this gene
- Carrier testing, prenatal diagnosis, family planning and psychological support and counseling
- No genetic cure, diagnosis aids in treatment
- The introduction of functional ATP7B protein by recombinant adenovirus gene delivery

Genetic Frequencies

- Prevalence is 1 in 25,000 to 1 in 100,000, generally
- Carrier frequency is 1 in 90
- In China, Japan and Sardinia the frequency is as high as 1 in 10,000 (Sardinia, common DNA with a 15 base pair deletion)
- Two different mutations-**H1069Q (~40%)** common in European ancestry, **R778L (57%)** common in Asian ancestry

Works Cited

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