Wilson’s Disease

•***DR.WAFAA MANSOR***

Wilson's Disease

- Rare Autosomal recessive disease
- Mutation of Wilson disease protein gene (ATP7B)
- Excessive Copper accumulation in the liver or brain
- Leads to Hepatitis, Psychiatric or Neurological symptoms
- Affects 1-4 out 100,000 people
- Fatal disease if not diagnosed early
- Disease usually manifest between ages 4 and late teens

Discovery

- First described in 1912 by a British neurologist

Samuel Alexander Kinnier Wilson (1878-1937)

Copper in the body

- Copper is as essential as any other vitamins and is present in most food
- Required by the body for different functions
- Most people have more cooper than they need, healthy people are able to excrete copper
- At birth people with Wilson's disease begin to accumulate copper and are unable to excrete it

Copper in the body

- Copper is utilized as a cofactor for different enzymes such as

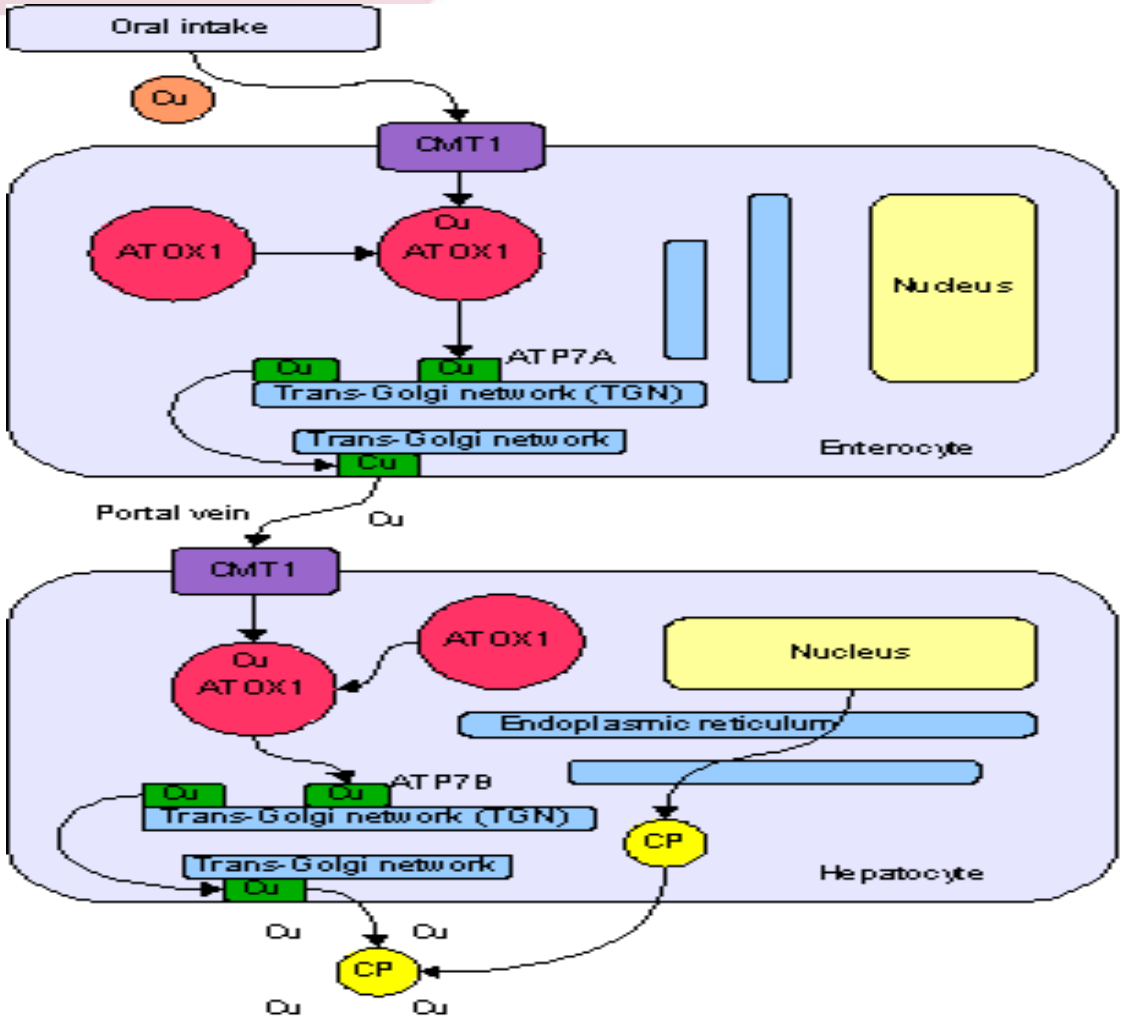
Cerloplasmin and cytochrome C

- Copper membrane transporter 1(CMT1) carries copper into the cells.
- Binds to a protein known as ATOX1 in golgi apparatus

Copper in the Liver – ATP7B

- Increasing levels of copper causes ATP7A (an enzyme) to release copper into portal vein to the Liver
- ATP7B binds copper to Cerluplasmin in the liver and releases it into the blood stream
- ATP7B also removes excess copper into bile
- Mutation of ATP7B in Wilson's disease impairs these functions

Copper metabolism

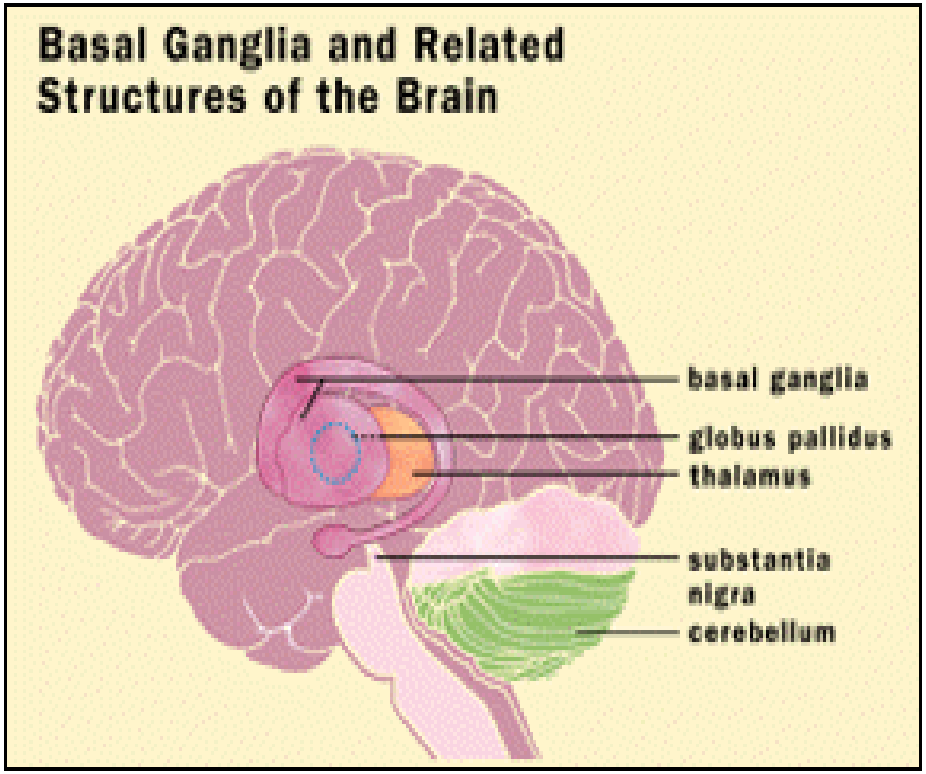


Impairment of ATP7B

- Impairment of ATP7B causes copper to accumulate in the liver – (it does not bind to cerluoplasmin)
- High levels of copper in the liver causes oxidative damage through a process known as Fenton's Chemistry
- Oxidative damage in the liver leads to Chronic Active Hepatitis

Impairment of ATP7B

- Unbound copper is released into the bloodstream and deposits at different organs such as
- Kidney
- Eyes
- Brain



Copper in the Brain

- Copper is deposited in the basal ganglion and the Putamen.
- These structures plays a role in coordination of movement and mood regulation

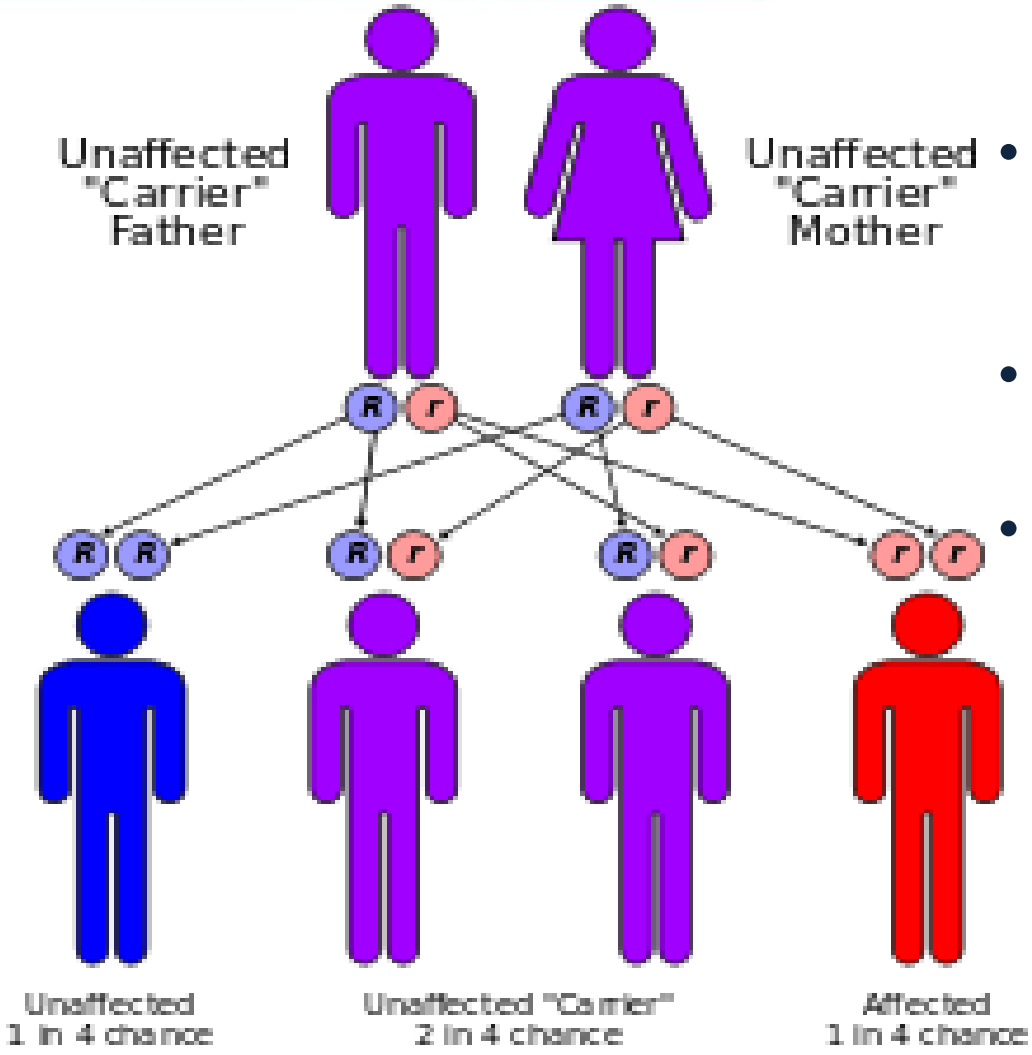
ATP7B in Wilson's Disease

- ATP7B mapped to chromosome 13, found in the liver, kidney and placenta
- Gene codes for P-type ATPase binds copper to cerluoplasmin
- Mutation of this gene impairs the function of ATP7B enzyme
- Mutation can be detected in 90% of Wilson's Disease sufferers

ATP7B in Wilson's Disease

- There are 300 mutation types of the ATP7B gene
- Most common mutation occurs at position 1069 – substitution of histidine to glutamine (common in western population)
- In China mutation occurs at position 778 - substitution of arganine to leucine. Mutation very uncommon

Autosomal Recessive Disorder



People at Risk

- People with parent that are carriers of the defective gene
- 25% chance in each pregnancy
- Most commonly found in Eastern European people and south Italian descent

Symptoms

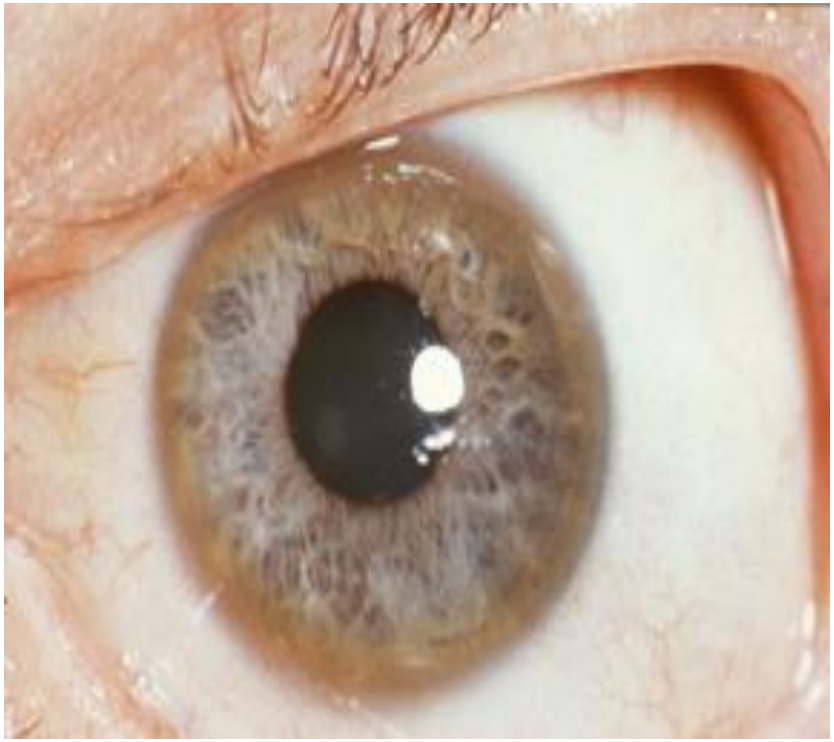
Neuropsychiatric Symptoms

- Clumsiness
- Behavioral changes
- Hand tremor
- Slurred speech
- Seizures
- Front lobe disorders- Impaired judgment, promiscuity, Dementia
- Depression
- Anxiety

Hepatic Symptoms

- Tiredness
- Portal hypertension
- Chronic active hepatitis
- Jaundice

Symptoms



Copper in the Eye

- Kayser-Fleischer rings brown ring on the edge of the iris.
- Accumulation of cooper in the eye.

Treatment

- Medications that remove excess cooper
- Liver transplant is usually needed in cases of severe damage.

Reference

- http://www.mayoclinic.com/health/wilsons-disease/DS00411
- http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001789/
- http://www.rightdiagnosis.com/w/wilsons_disease/intro.htm
- http://www.wilsonsdisease.org/about-wilsondisease.php