Wilson's Disease Pathophysiology

Wilson disease is an autosomal recessive disorder due to a mutation in the ATP7B gene on chromosome 13, causing a failure to incorporate copper into ceruloplasmin and impaired copper excretion into bile. This disease is characterized by marked accumulation of copper in tissues and organs to toxic levels, icnlduing the liver, brain and eye. Normally, copper is absorbed in the small intestine and transported to the liver where it is incorporated into enzymes and bound to apoceruloplasmin to form ceruloplasmin. Ceruloplasmin can be secreted into the blood while excess copper is transported into bile to be excreted. A mutation in the ATP7B gene leads to a decrease in copper transport into bile, impairs its incorporation to ceruloplasmin, and also decreases ceruloplasmin secretion into the blood causing accumulation of copper in the liver and decreased ceruloplasmin levels. The excess copper in the liver causes toxic injury via the production of reactive oxygen species and non ceruloplasmin bound copper enters the systemic circulation and can cause hemolysis of red blood cells and pathologic changes in the brain, cornea, kidneys, and joints. Penicillamine is a copper chelator that can be used in the treatment of Wilson disease.

PLAY PICMONIC

Autosomal Recessive

Recessive-chocolate

This disease is inherited in an autosomal recessive fashion.

Mutation in ATP7B gene

A-Apple (TP) Toilet-paper 7 (B) Bee

A mutation in the ATP7B gene leads to a decrease in copper transport into bile and impairs its incorporation to ceruloplasmin. It also decreases ceruloplasmin secretion into the blood causing accumulation of copper in the liver and decreased ceruloplasmin levels.

Chromosome 13

Friday-the-13th-guy standing on Chromosome

ATP7B gene is located on chromosome 13.

Decrease in Ceruloplasmin

Down-arrow Cereal-plastic

A mutation in the ATP7B gene leads to a decrease in copper transport into bile and impairs its incorporation to ceruloplasmin, leading to decreased ceruloplasmin levels in the blood.

Inadequate copper excretion

Copper-cops

Normally, copper is absorbed in the small intestine and transported to the liver where it is incorporated into enzymes and bound to apoceruloplasmin to form ceruloplasmin. Ceruloplasmin can be secreted into the blood while excess copper is transported into bile to be excreted. A mutation in the ATP7B gene leads to a decrease in copper transport into bile and inadequate copper excretion.

Liver

Liver

Mutation of the ATP7B gene leads to toxic accumulation of copper in the liver, which produces reactive oxygen species leading to liver damage. The hepatic changes are variable and can range from fatty change to cirrhosis and massive liver necrosis.

Brain

Brain

In the brain, the toxic injury primarily affects the basal ganglia, especially the putamen. Involvement of the brain can cause neuropsychiatric manifestations including a Parkinson disease like syndrome.

Kidney

Kidney

Non ceruloplasmin bound copper can enter the systemic circulation and can cause pathologic changes in the kidney.

Cornea

Corn-eyes

Almost all patients with neurologic involvement develop characteristic eye lesions in the cornea called Kayser Fleischer rings which are brownish green deposits of copper in Descement's membrane of the cornea.

Joints

Smoking Joints

Non ceruloplasmin bound copper can enter the systemic circulation and can cause pathologic changes in the joints causing severe debilitating joint pain.

Treat with Penicillamine

Pencil-mine

Penicillamine is a copper chelator that can be used in the treatment of Wilson disease.