

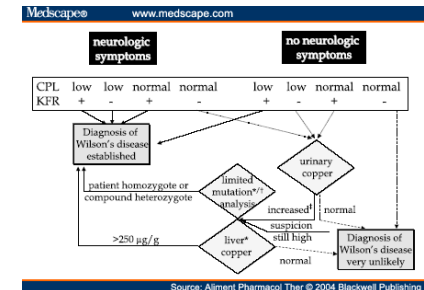
Wilson Disease

By xxxxx

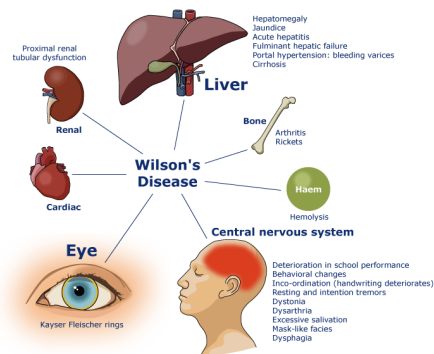
What is Wilson's disease?

- An **inherited** disorder
- Excessive amounts of **copper** accumulate in the body

- **liver**
- **brain**
- **eyes**



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Symptoms

- **Yellowing** of the skin or the whites of the eye (jaundice)
- **Fatigue**
- **Loss of appetite**
- **Abdominal swelling**
- **Psychiatric or nervous system problems in young adults**
- **Clumsiness, trembling, difficulty walking, speech problems, deteriorating school work, depression, anxiety, and mood swings**
- Copper deposits form a green-to-brownish ring, called the **Kayser-Fleischer ring**, around cornea (in eye)
- **Abnormalities in eye movements**

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Who is affected

- **1 in 30,000** individuals
- Signs and symptoms first appear between the ages of **6** and **40**, but most often begin during the **teenage years**

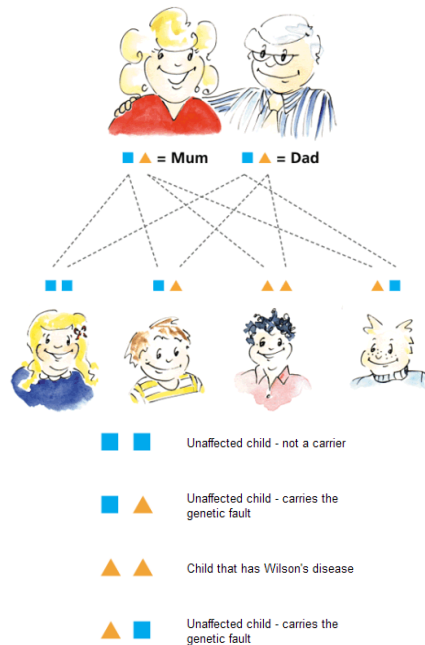
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How is it inherited?

- **Autosomal** recessive pattern
 - **both** copies of the gene in each cell have mutations.
 - Parents of an individual with an autosomal recessive condition **each** carry one copy of the mutated gene
 - They typically do **not** show signs and symptoms of the condition

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Mutations

- **Mutations** in the **ATP7B** gene cause this disease.
- Normal variations in the **PRNP** gene **modify** the course of Wilson disease.
- **The ATP7B gene**
 - provides **instructions** for making a **protein**
 - Plays a role in the **transport of copper** from the **liver** to other parts of the body.
 - Particularly important for the **elimination of excess copper** from the body.
 - Mutations in the ATP7B gene **prevent** the transport protein from functioning properly
 - Due to the shortage of functional protein, excess copper is **not removed** from the body.
 - Copper accumulates to **toxic levels** that can damage tissues and organs, particularly the liver and brain.
 - This explains why the symptoms occur
- A **normal variation** in the PRNP gene may **delay the age of onset of Wilson disease** and **affect the type of symptoms** that develop.

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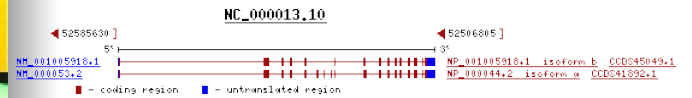
PRNP: More Details

- The **PRNP gene** provides instructions for making **prion protein**, which is active in the brain and other tissues.
- **Transferring copper**
 - Studies have focused on the **effects** of a PRNP gene variation that affects the prion protein at position 129.
 - At this position, the protein building block (amino acid) **methionine** or **valine** is used.
- Onset of symptoms of Wilson disease is delayed by several years if person has **methionine** (instead of valine) at **position 129** in the **prion protein**.
 - Also may **increase** symptoms that affect the **nervous system** (tremors).
- Larger studies needed to establish effects of this PRNP variation

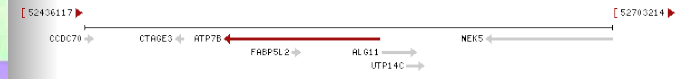
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Charts

■ Genomic regions, transcripts, and products



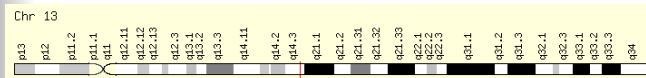
■ Genomic context



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Chromosome

- **Chromosome: 13**
- **Location: 13q14.3**



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NCBI links, etc

- Link for the gene, ATP7B:
 - http://www.ncbi.nlm.nih.gov/gene/540?ordinalpos=2&itool=EntrezSystem2.PEntrez.Gene.Gene_ResultsPanel.Gene_RVDocSum
- Link to FASTA for one of the two sequences
 - http://www.ncbi.nlm.nih.gov/nuccore/NM_001005918.1?report=fasta
 - That's for NM_001005918.1. The other is NM_000053.2.
 - Protein sequence:
 - [http://www.ncbi.nlm.nih.gov/protein/119722350?report=fasta&log\\$=seqview](http://www.ncbi.nlm.nih.gov/protein/119722350?report=fasta&log$=seqview)
- Involved in the **export of copper out of the cells**

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Animal to study

- This disease can be studied in **rats**
- The e-value is **$2e-13$**
- When you compare the protein sequences using **BLAST**, you find that the human protein sequence is **homologous** with the sequence in rats
- Although this is not very low of a value, the sequences are **95% identical**, which makes me confident that this would be an appropriate test animal
- The reason the e-value is so low is because the **protein sequence is short**

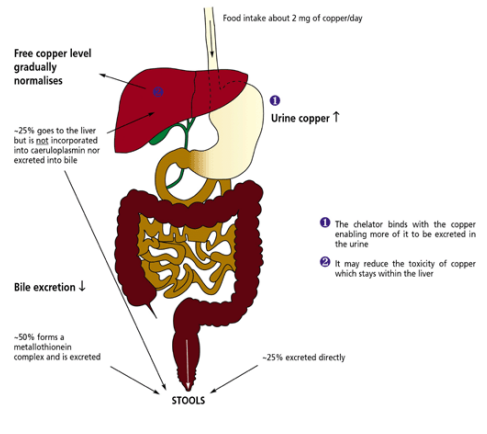
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Diagrams

- Provided by <http://www.hcforum.fr/eurowilson/?page=0&langue=it>

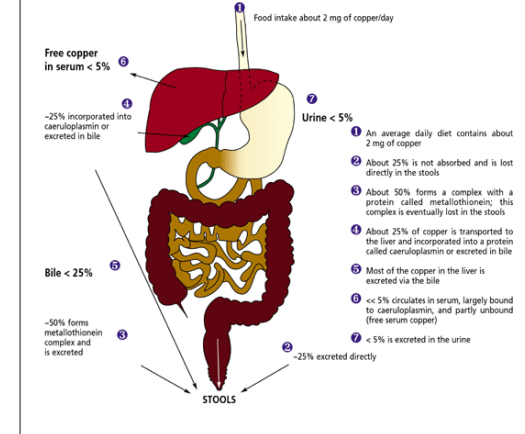
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Diagram IV: Wilson's disease patients on chelator therapy: enhanced urinary excretion of copper



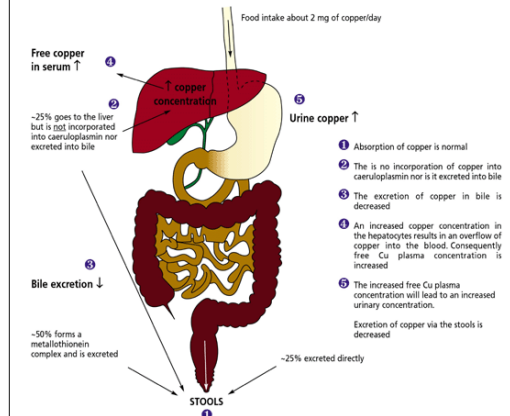
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Diagram I: healthy subjects: intake and excretion is well balanced



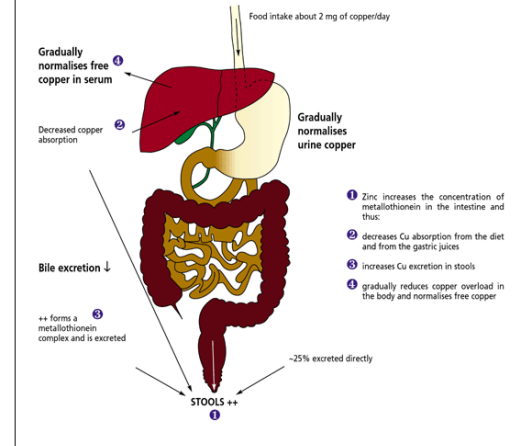
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Diagram II: Wilson's disease patients before treatment: reduced excretion and retention of copper



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Diagram III: Wilson's disease patients on zinc therapy: enhanced faecal excretion of copper



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More information:

- Treatment
 - American Association for the Study of Liver Disease: [Diagnosis and Treatment of Wilson Disease](#)
 - Gene Reviews
 - MedlinePlus Encyclopedia: [Wilson's disease](#)
- MedlinePlus - Health information (2 links)
- Additional NIH Resources - National Institutes of Health (3 links)
- Educational resources - Information pages (8 links)
- Patient support - For patients and families (5 links)
- Gene Reviews - Clinical summary
- Gene Tests - DNA tests ordered by healthcare professionals
- ClinicalTrials.gov - Linking patients to medical research
- PubMed - Recent literature
- Online Books - Medical and science texts
- Scriver's Online Metabolic and Molecular Bases of Inherited Disease (OMMBID): [Disorders of Copper Transport](#)
- OMIM - Genetic disorder catalog
- More questions?
 - See [How can I find a genetics professional in my area?](#) in the Handbook.
 - Ask the [Genetic and Rare Diseases Information Center](#).
 - Submit your question to [Ask the Geneticist](#).
 - What does it mean if a disorder seems to run in my family?
 - What are the different ways in which a genetic condition can be inherited?
 - If a genetic disorder runs in my family, what are the chances that my children will have the condition?
 - Why are some genetic conditions more common in particular ethnic groups?
 - Genetics and health
 - Resources for Patients and Families
 - Resources for Health Professionals

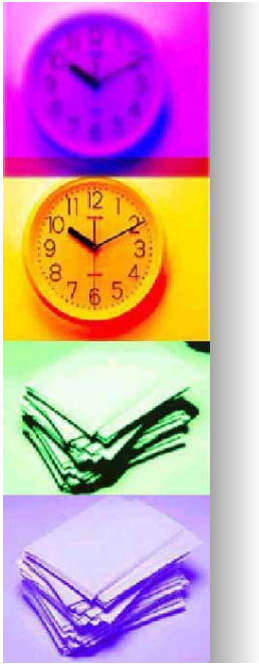
Links provided by Genetics Home Reference

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Bibliography

- <http://www.ncbi.nlm.nih.gov/>
- <http://www.hcforum.fr/eurowilson/?page=0&langue=it>
- <http://ghr.nlm.nih.gov/>
- <http://www.genecards.org/>

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The End!

