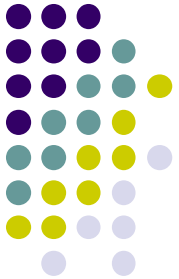
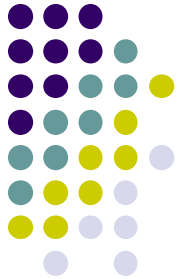


COPPER

COPPER

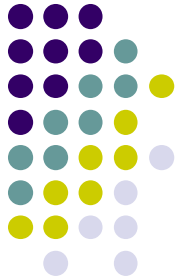


Total body copper content 100-150mg

Distribution

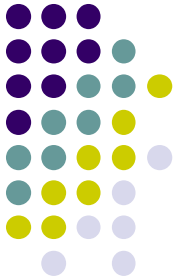
- **liver**
- **muscles**
- **bones**
- **brain**
- **kidney**
- **heart**

Copper containing enzymes and functions



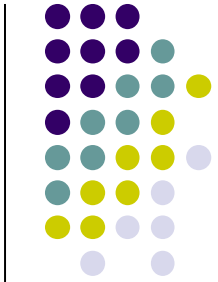
- **ALA Synthase- heme synthesis**
- **Ceruloplasmin- iron binding to transferrin**
- **Lysyl oxidase-collagen maturation**
- **Tyrosinase-melanin synthesis**
- **Cytochrome oxidase, cytochrome c- ETC**
- **Monoamine oxidase-catecholamine breakdown**
- **Superoxide dismutase-free radical scavenging**

Role of copper in Hb synthesis



- **integral part of ALA sythase**
- **uptake of iron by normoblasts**
- **Facilitate mobilization & utilization of iron**
- **Microcytic normochromic anemia in deficiency**

Copper containing non enzyme proteins



- **Hepatocuprein - liver – storage form**
- **Cerebrocuprein – brain**
- **Hemocuprein - RBC**
- **Erythrocuprein – bone marrow**

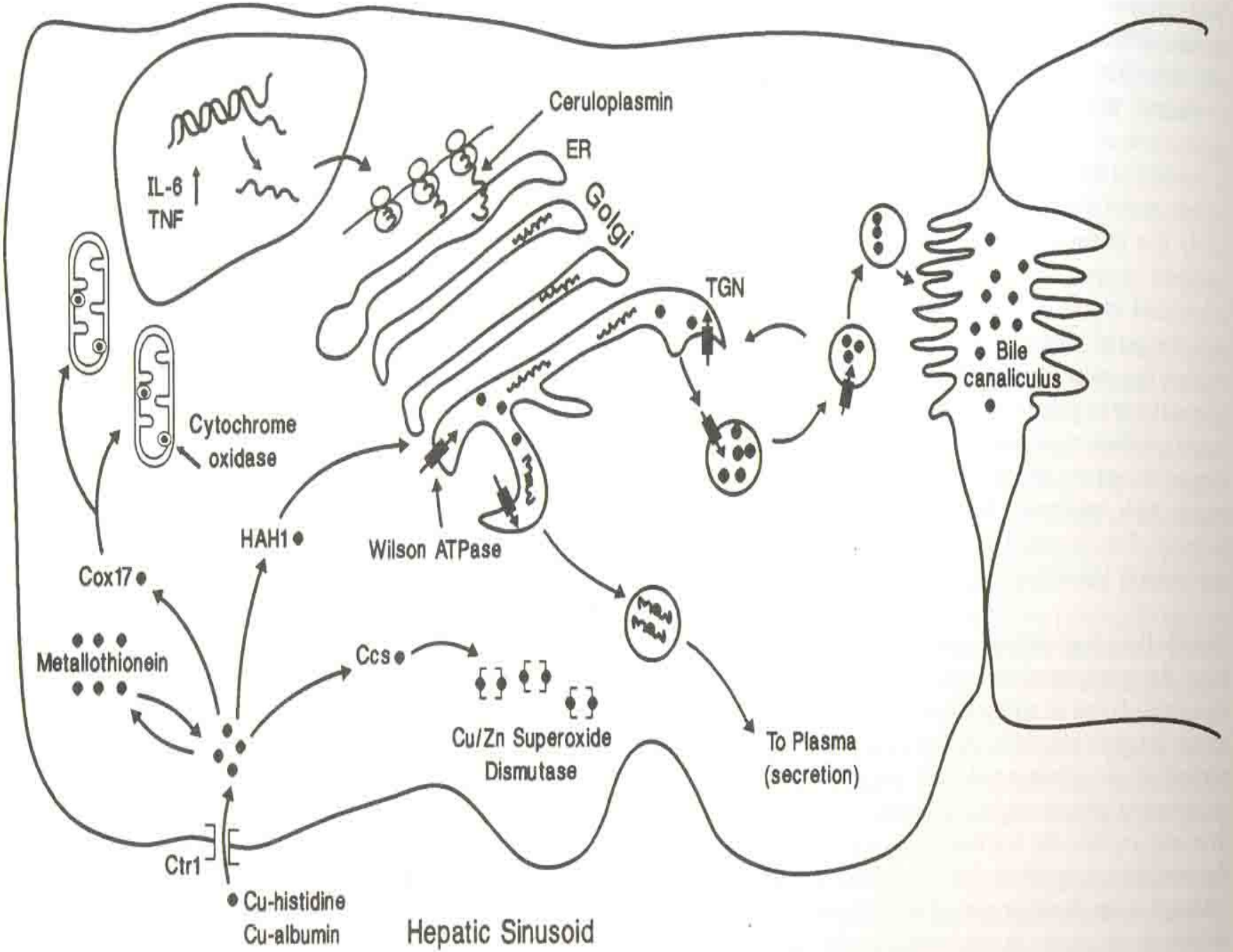
sources

- **Cereals,**
- **meat**
- **Green leafy vegetables**
- **nuts**
- **Milk poor source**
- **Daily requirement – 1.5 -3 mg**

absorption

- **Duodenum**

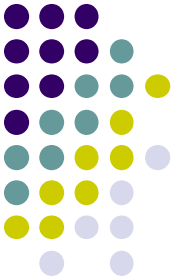
- **Excretion**
- **Through *BILE***


Ceruloplasmin
ER
Golgi
IL-6
TNF
TGN
Bile
canaliculus
Cytochrome
oxidase
HAH1
Wilson ATPase
Cox17
Metallothionein
Ccs
Cu/Zn Superoxide
Dismutase
To Plasma
(secretion)
Ctr1
Cu-histidine
Cu-albumin
Hepatic Sinusoid

in plasma copper is

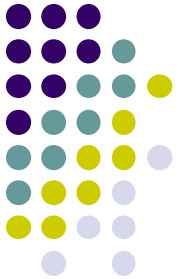
- *Loosely bound to albumin (10%)*
- *Tightly bound to ceruloplasmin (90%)*

Ceruloplasmin



- Imp Cu containing protein in plasma
- Alpha 2 globulin, synthesized in liver
- Carries 90% of Cu in plasma
- Since tightly bound, not released easily
- 1 molecule binds to 6-8 Cu atoms

Ceruloplasmin



- **Ferroxidase activity, oxidizes ferrous to ferric (helps to incorporate Fe in transferrin)**
- **Decreased in Wilson's disease, cirrhosis, nephrosis, malnutrtion.**
- **Increased in infection & inflammation.**
- *Normal serum ceruloplasmin is 25 - 50mg/dl*

Abnormal metabolism of copper

1. Wilson's disease

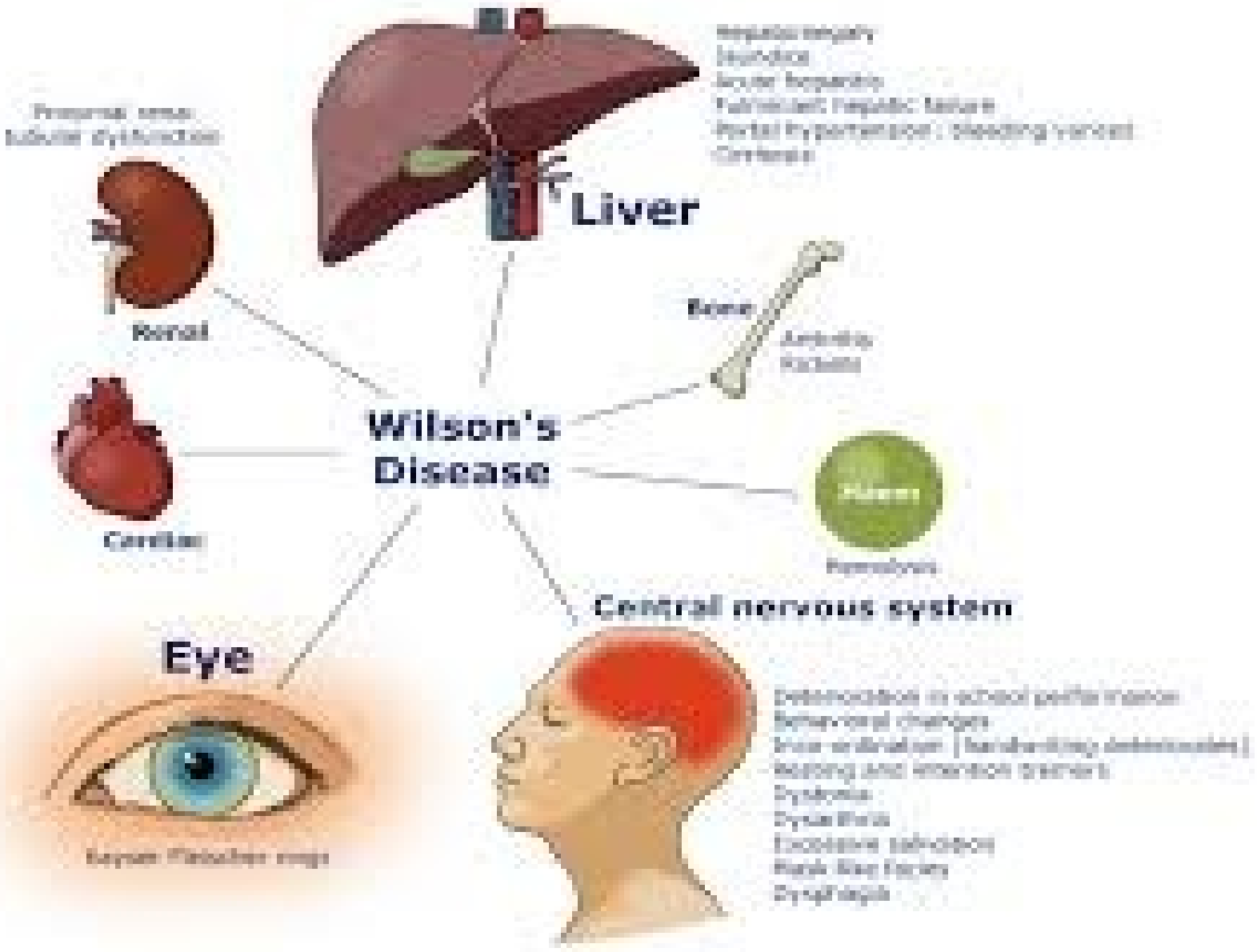
- **Wilson's hepatolenticular degeneration**
- **autosomal recessive**
- **Mutation in gene coding copper binding ATPase**
- **Enzyme involved in excretion of copper from liver cells**
- **So impaired ability of liver to excrete cu^{++} into bile**

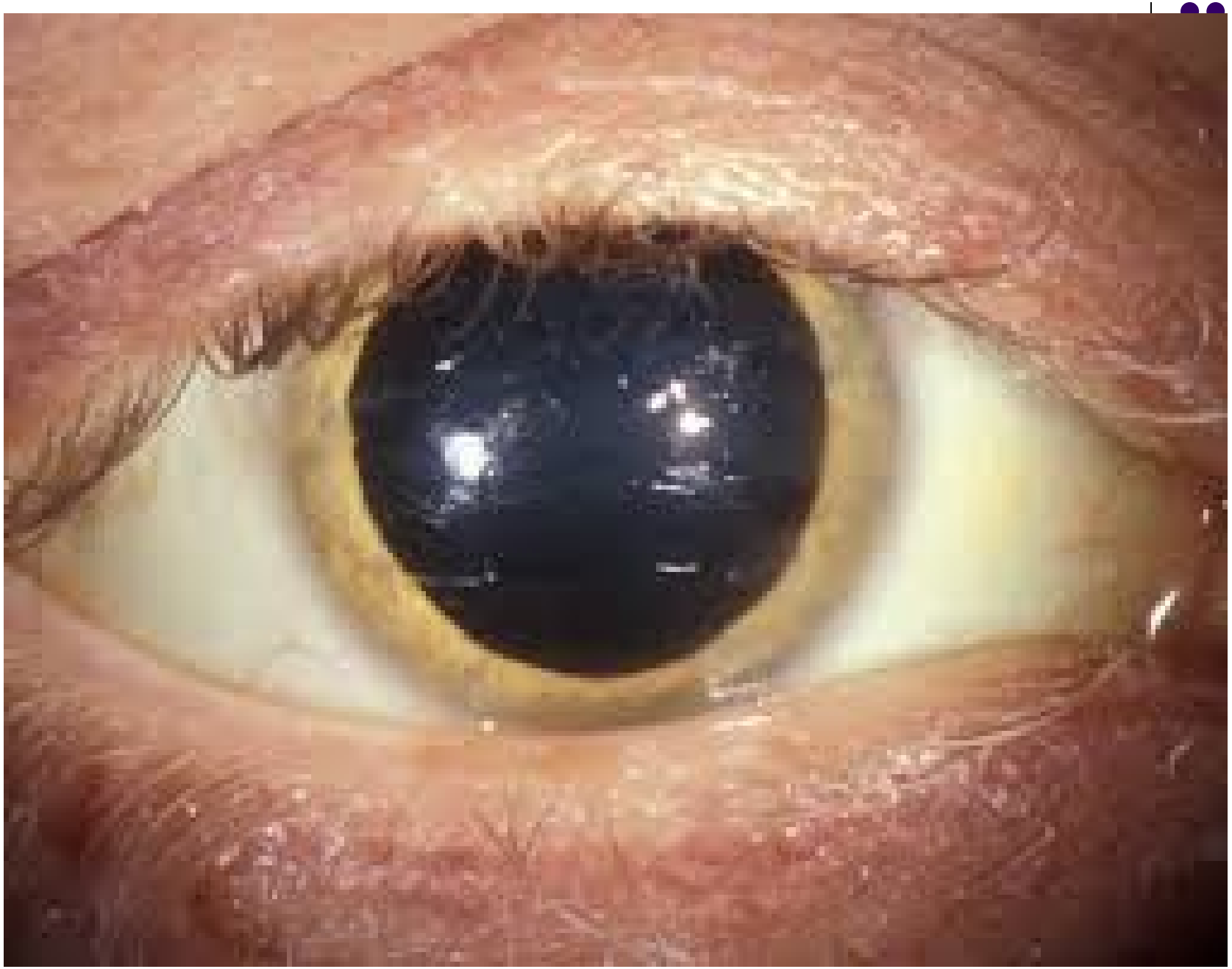
Wilson's disease

- Cu accumulation in liver, brain
- Defect in the incorporation of cu^{++} in to apoceruloplasmin
- So low levels of ceruloplasmin in plasma

C/F:

- Liver — cirrhosis
- Brain — lenticular degeneration
- Cornea — *Kayser - Fleischer* ring (green pigment ring around cornea)


Liver
Renal
Bone
Wilson's Disease
Cardiac
Central nervous system
Eye

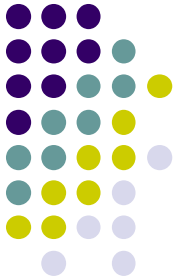


Treatment

- Diet low in copper
- Chelating agent - penicillamine – chelates copper, excreted in urine
- Zn – ↓ Cu absorption

Abnormal metabolism of copper

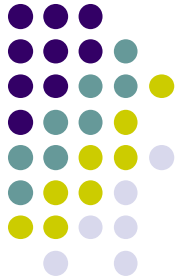
2. Aceruloplasminemia



- **Genetic disorder**
- **Ceruloplasmin level very low**
- **Low *Ferroxidase* activity**
- **Failure of release of iron from cells**
- **Iron accumulates – brain, liver & pancreas**
- **C/F – severe neurologic signs**

Abnormal metabolism of copper

3. Copper deficiency

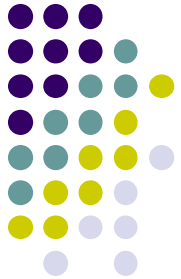


a. Anemia

- **Cu - integral part of ALA synthase – Heme synthesis**
- **Cu helps uptake of iron by normoblasts**
- **Cu def. – Microcytic normochromic anemia - RBC count ↓ , cell size small, Hb – near normal , if associated with Fe def. , hypochromic anemia seen**

Abnormal metabolism of copper

3. Copper deficiency

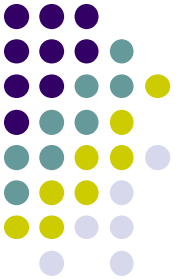


b. Cardiovascular diseases

- **Cu – constituent of lysyl oxidase - reaction involved in making cross linkages in Elastin**
- **Elastin abnormal – weakening of walls of major blood vessels – fatal rupture of wall of aorta**
- **Fibrosis of myocardium – cardiac failure**

Abnormal metabolism of copper

4. Menkes disease (kinky or Steely hair syndrome)



- **X linked disorder – only males affected**
- **Mutation in gene coding copper binding ATPase**
- **Involved in efflux of Cu from cells**
- **Transport across serosal surface of int epithelial cell defective**
- **Incorporation of Cu into apoenzymes requiring Cu is defective, so Cu-dependent enzyme activity low.**

- Cu accumulation in cells – not available for metabolism
- Defective cross linking of Connective tissue
- Cu required for Tyrosinase - melanin

- **Clinical features**

  Abnormal hair , flag type of hair growth with alternate white patches

  growth retardation

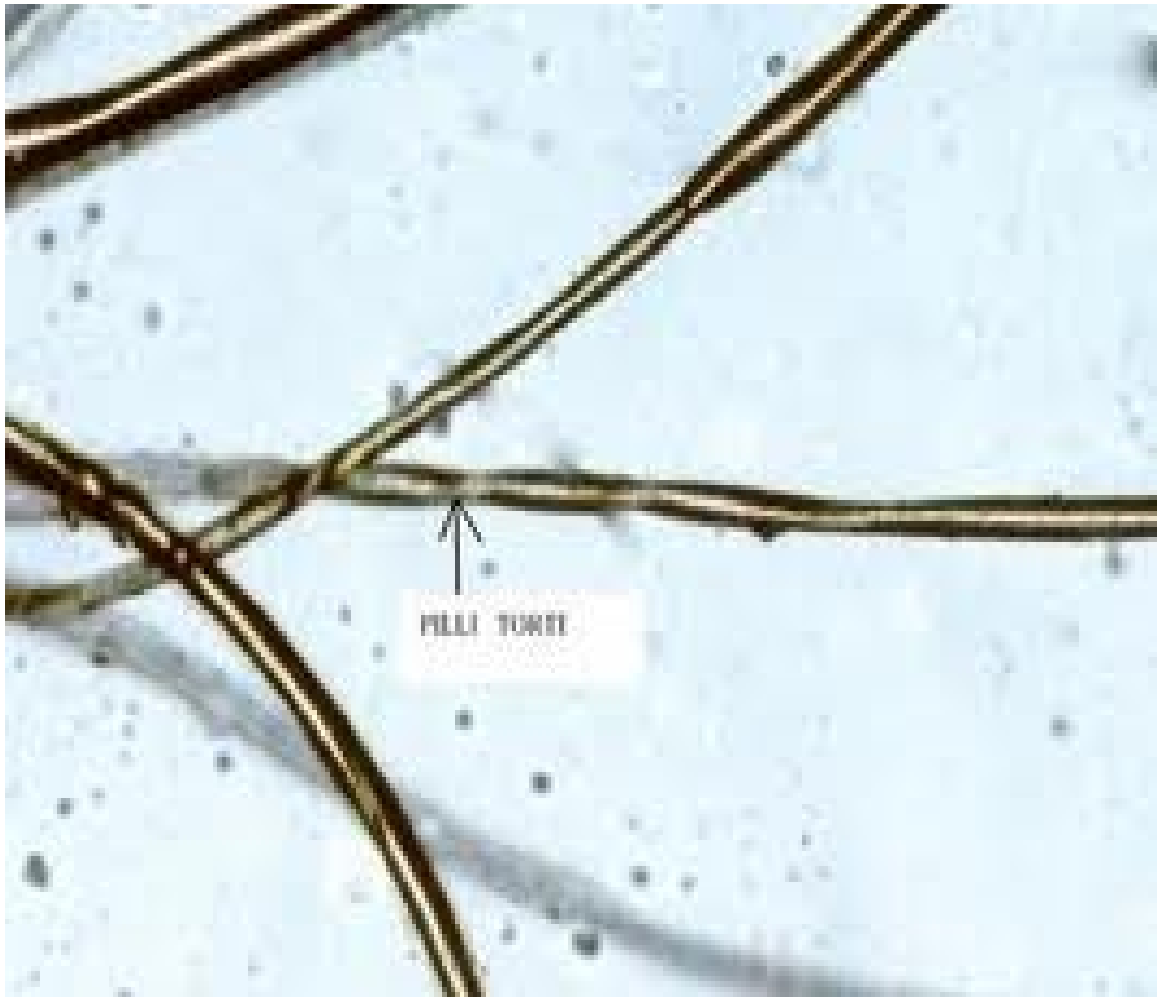
  mental retardation

  hypo pigmentation

  early death

Lab finding -

Low serum Cu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