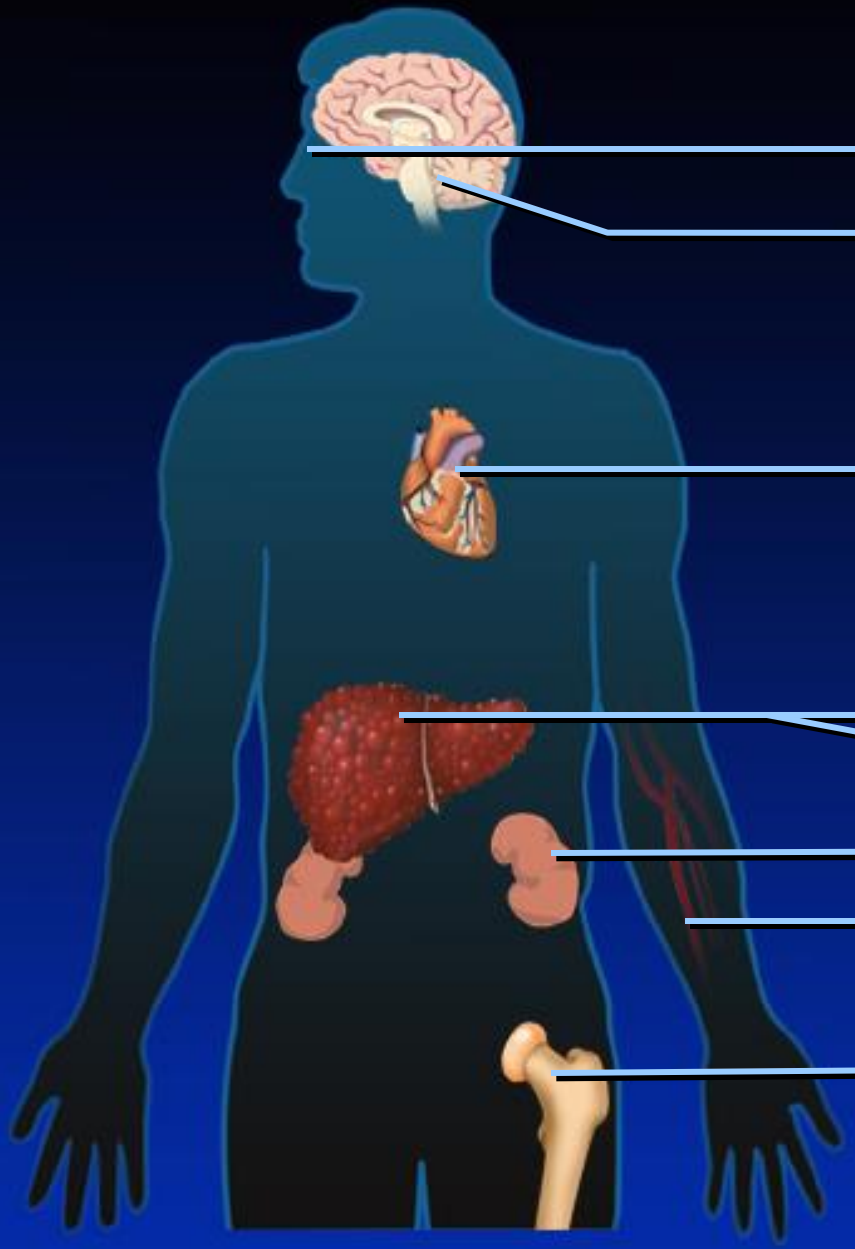
Genetic Diseases – Wilson's Disease



Kayser-Fleischer rings

Neuropsychiatric disorders

Cardiomyopathy

Hepatitis

Cirrhosis

Fanconi syndrome

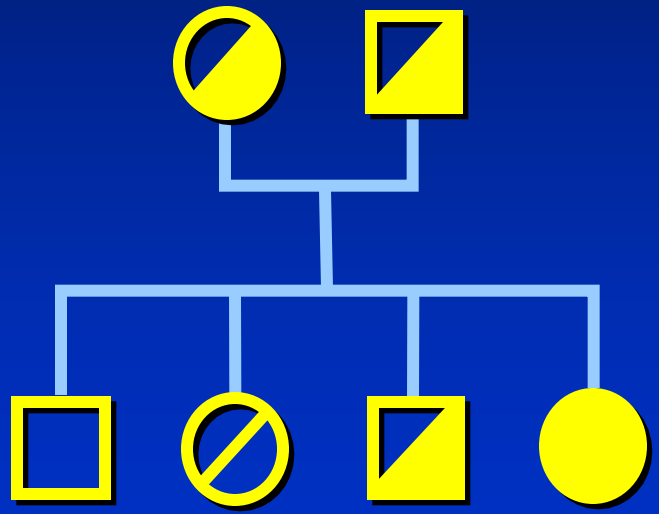
Hemolysis

Osteoporosis and arthropathy

Copper Overload Disorders

Primary

Wilson's Disease

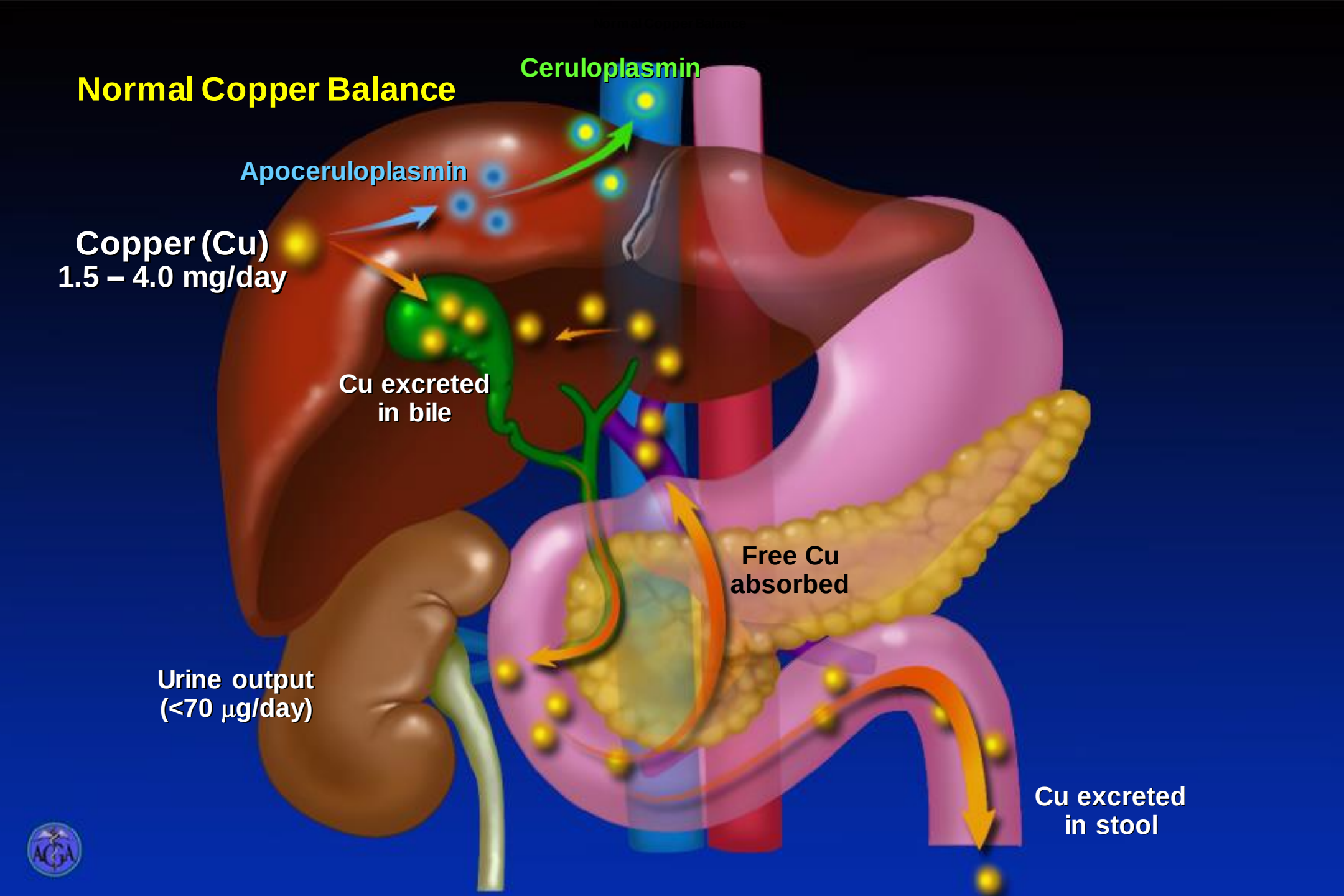


Autosomal recessive inheritance

Secondary

Chronic cholestasis

- Primary biliary cirrhosis
- Byler's syndrome


Normal Copper Balance
Ceruloplasmin
Apoceruloplasmin
Copper (Cu)
1.5 – 4.0 mg/day
Cu excreted
in bile
Free Cu
absorbed
Urine output
(<70 μg/day)
Cu excreted
in stool

Ceruloplasmin

A blue α_2 globulin

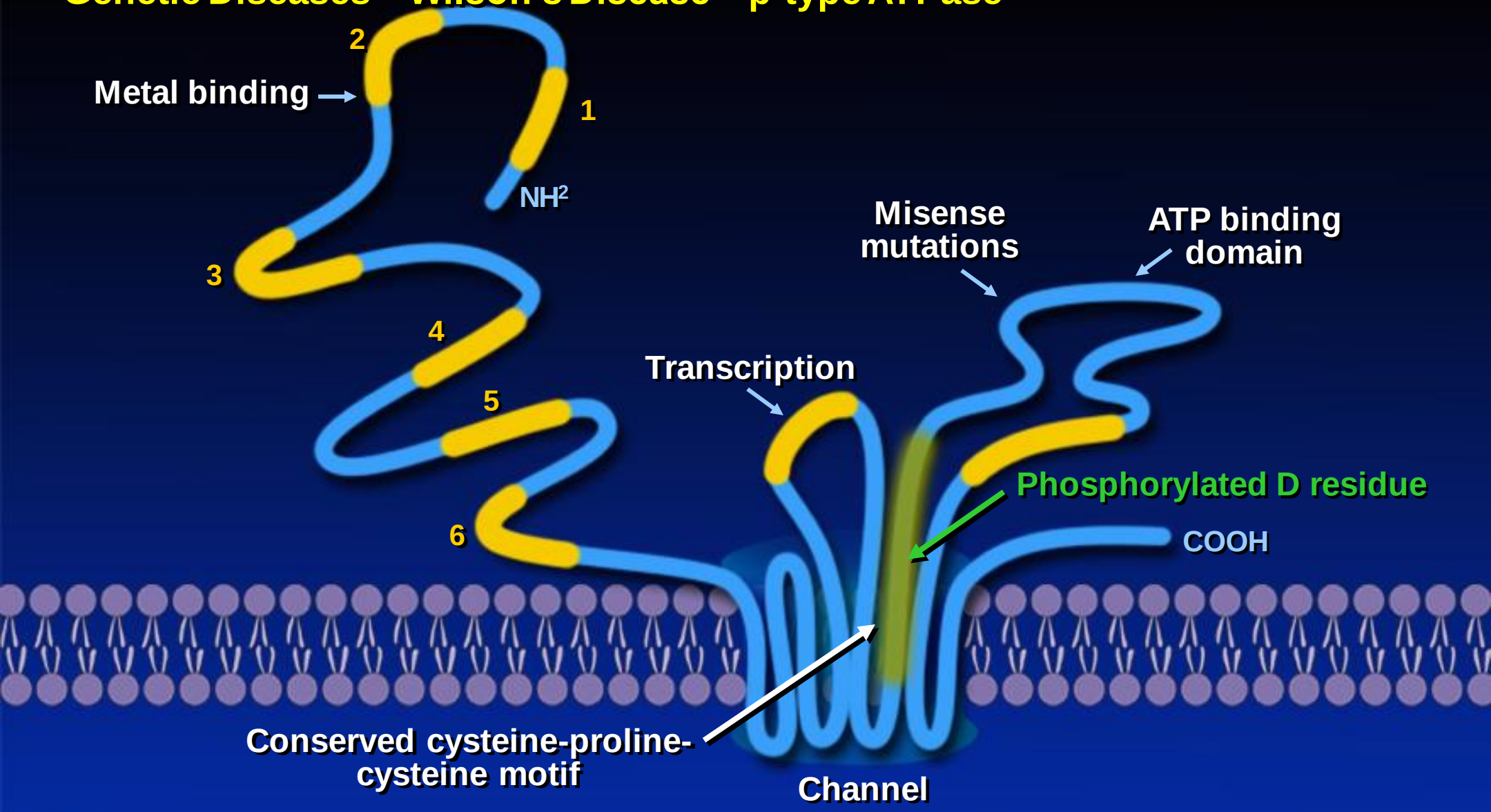
Binds copper irreversibly

Normal serum level = 20-40 mg/dL

Decreased serum ceruloplasmin is seen in:

- Wilson's disease
  - 95% of homozygotes
  - 20% of heterozygotes
- Protein loss
- Hepatic failure
- Menkes syndrome

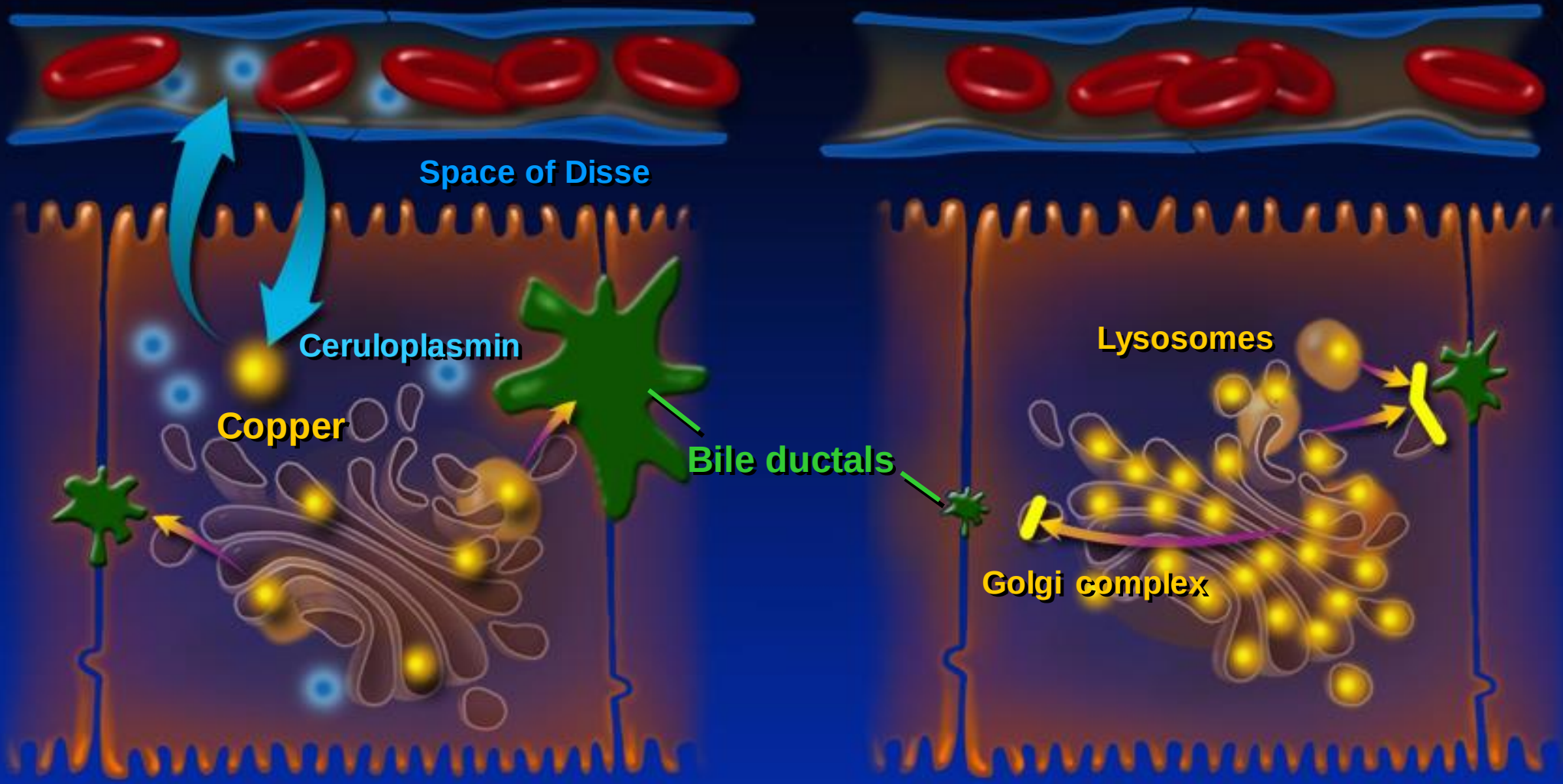
Genetic Diseases – Wilson's Disease – p-type ATPase



Genetic Diseases – Wilson's Disease

Normal Copper Balance

Abnormal Copper Balance



Copper build-up leads to cell stress and death

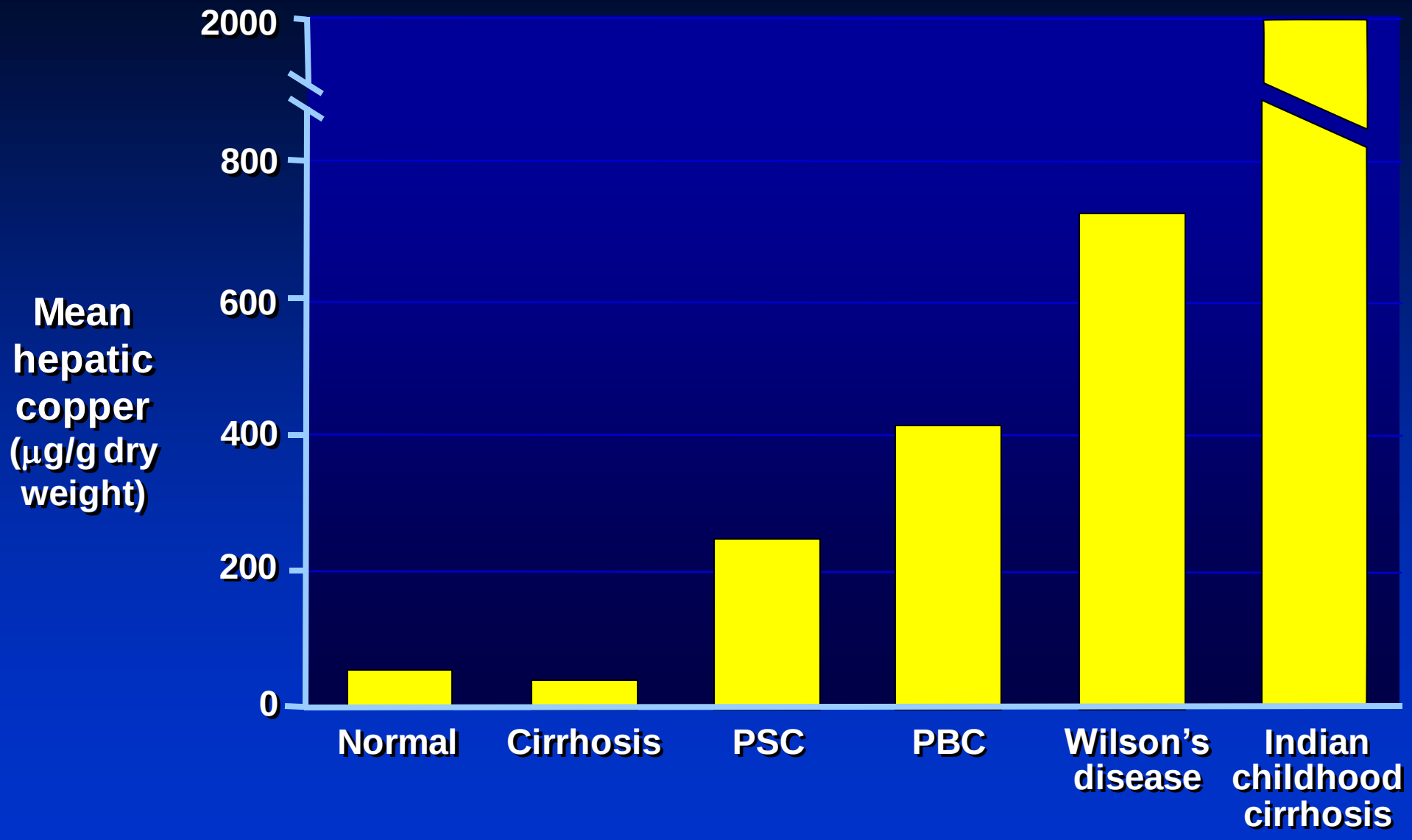
Genetic Diseases – Wilson's Disease

Usual Features in Homozygotes	Usual Features in Heterozygotes
Ceruloplasmin <20 mg/dl	Rarely
Urine copper >100 mg/day	Rarely
Kayser-Fleischer rings	Never
Hepatic histology abnormal	Never
Hepatic copper >250 mg/g	Rarely

Indications for Testing

- Liver disease in children, adolescents, young adults
- Hemolysis with liver disease
- Neurologic disease in the young
  - Parkinsonian tremor
  - Gait disturbance
  - Psychosis or other mental disorders
- Fanconi syndrome
- Hypouricemia
- Kayser-Fleischer rings
- Sunflower cataracts
- Siblings of affected patients

Genetic Diseases – Wilson's Disease



Genetic Diseases – Wilson's Disease

Presentations

Liver	Abnormal liver tests Acute hepatitis Acute hepatic failure Liver disease with hemolysis Chronic hepatitis Cryptogenic cirrhosis
CNS	Parkinson-like disorders Psychiatric disorders
Eye	Kayser-Fleischer rings Sunflower cataracts
Kidney	Fanconi syndrome with hypouricemia

Genetic Diseases – Wilson's Disease

Diagnostic Testing

Ceruloplasmin
Slit lamp examination
Urine copper

Ceruloplasmin <20 mg/dL
(5% of Wilson's patients have normal ceruloplasmin levels)
Kayser-Fleischer rings
Urine copper >100 μg/24 hr

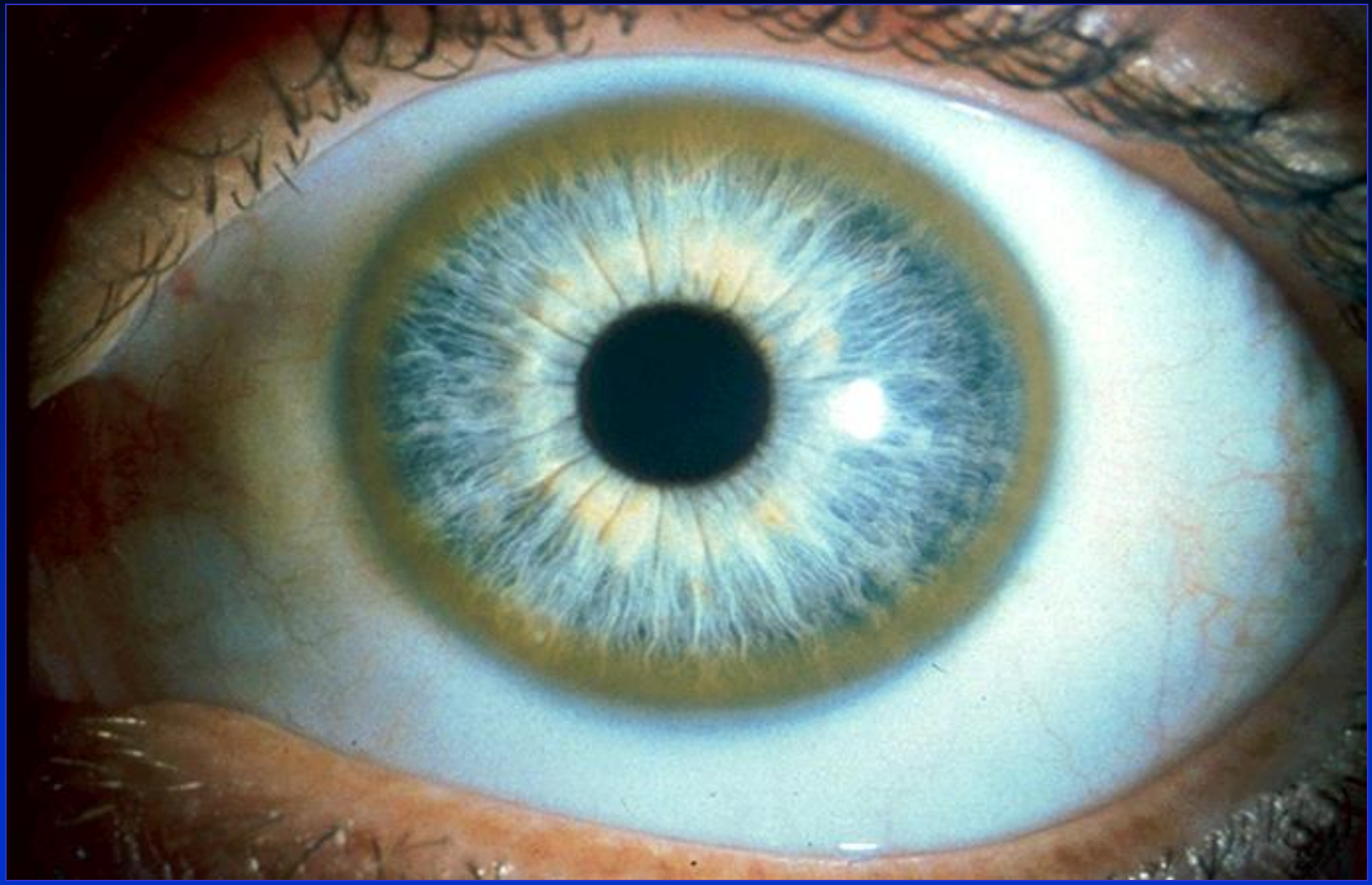
Liver biopsy with quantitative copper determination confirms diagnosis

Genetic Diseases – Wilson's Disease

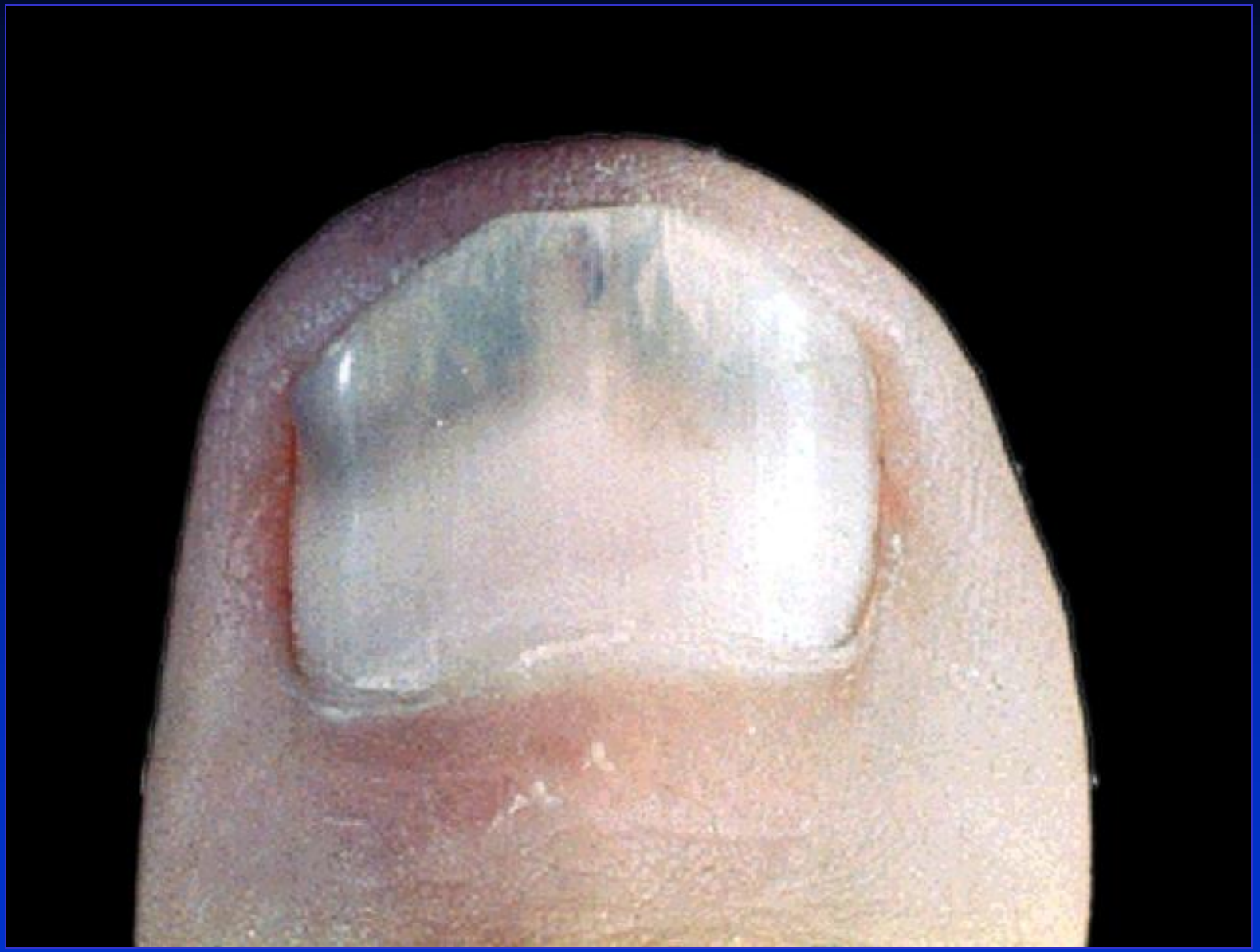
Management

Therapy	Chelation + pyridoxine Zinc Avoid high copper foods Transplantation in selected cases Family screening
Monitoring	Urine copper Non-ceruloplasmin copper Do NOT monitor Kayser-Fleischer rings
Results	Treatment prevents disease Improves liver and CNS disease Prolongs life

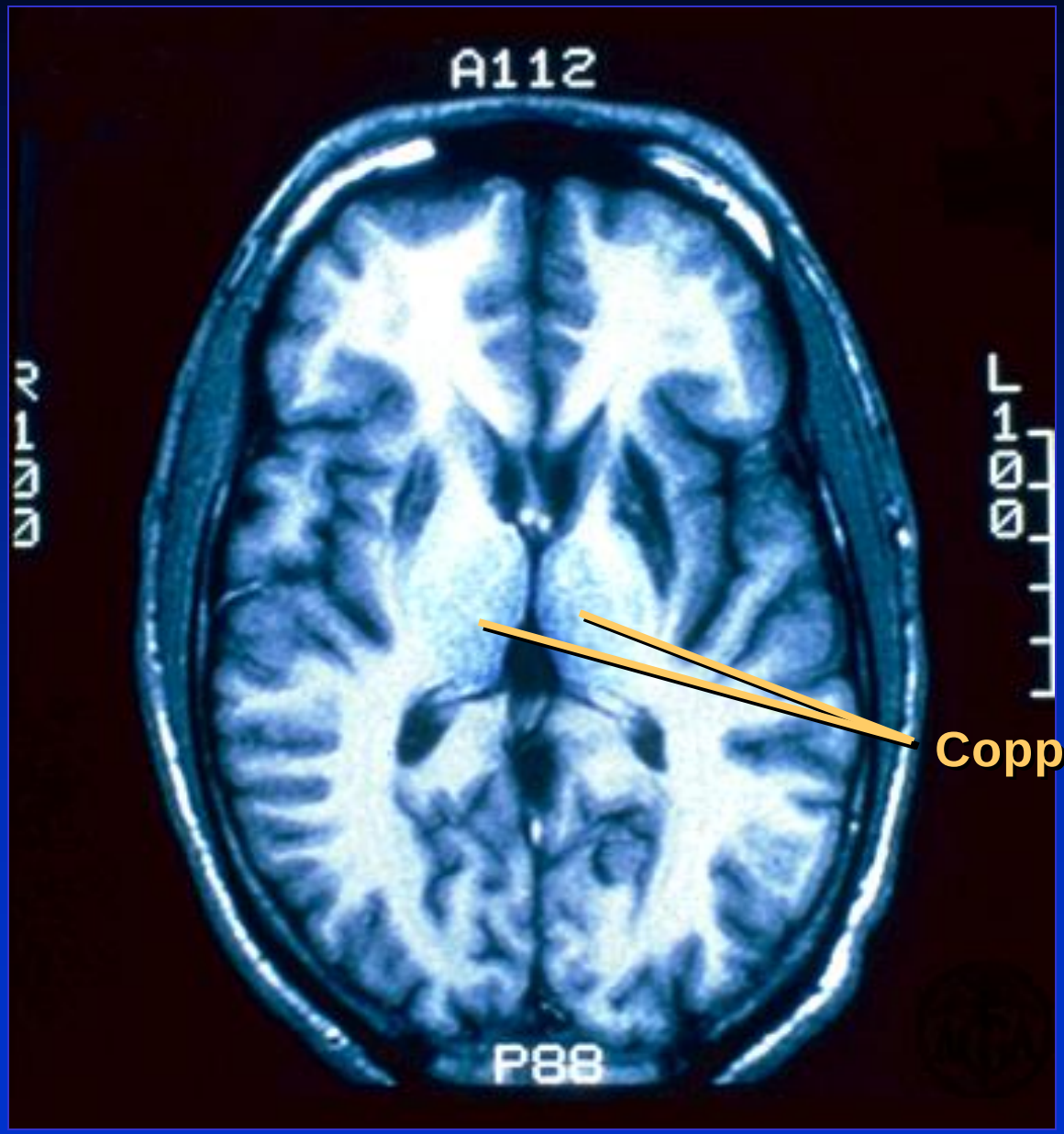
Genetic Diseases – Wilson's Disease



Genetic Diseases – Wilson's Disease

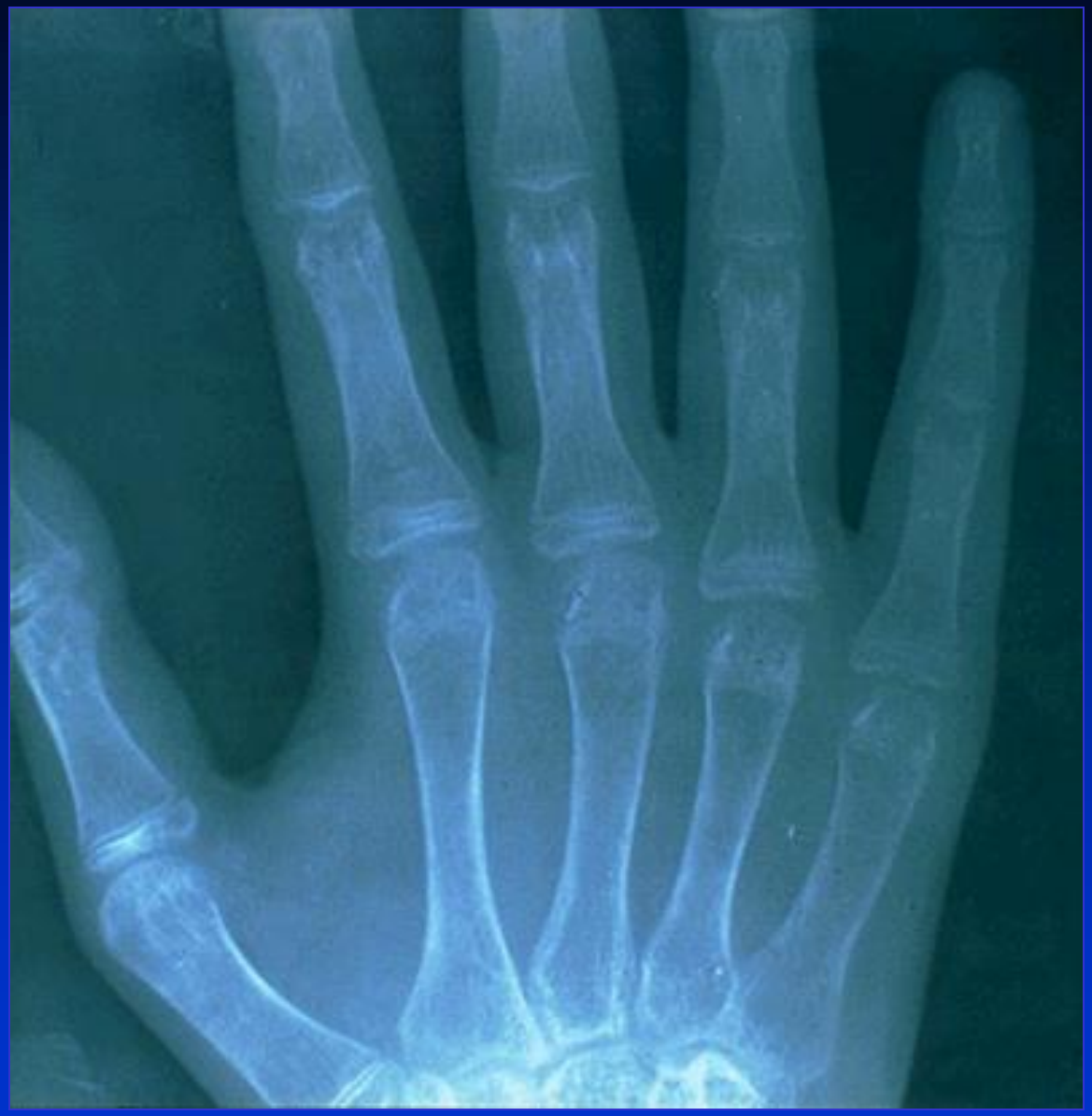


Genetic Diseases – Wilson's Disease



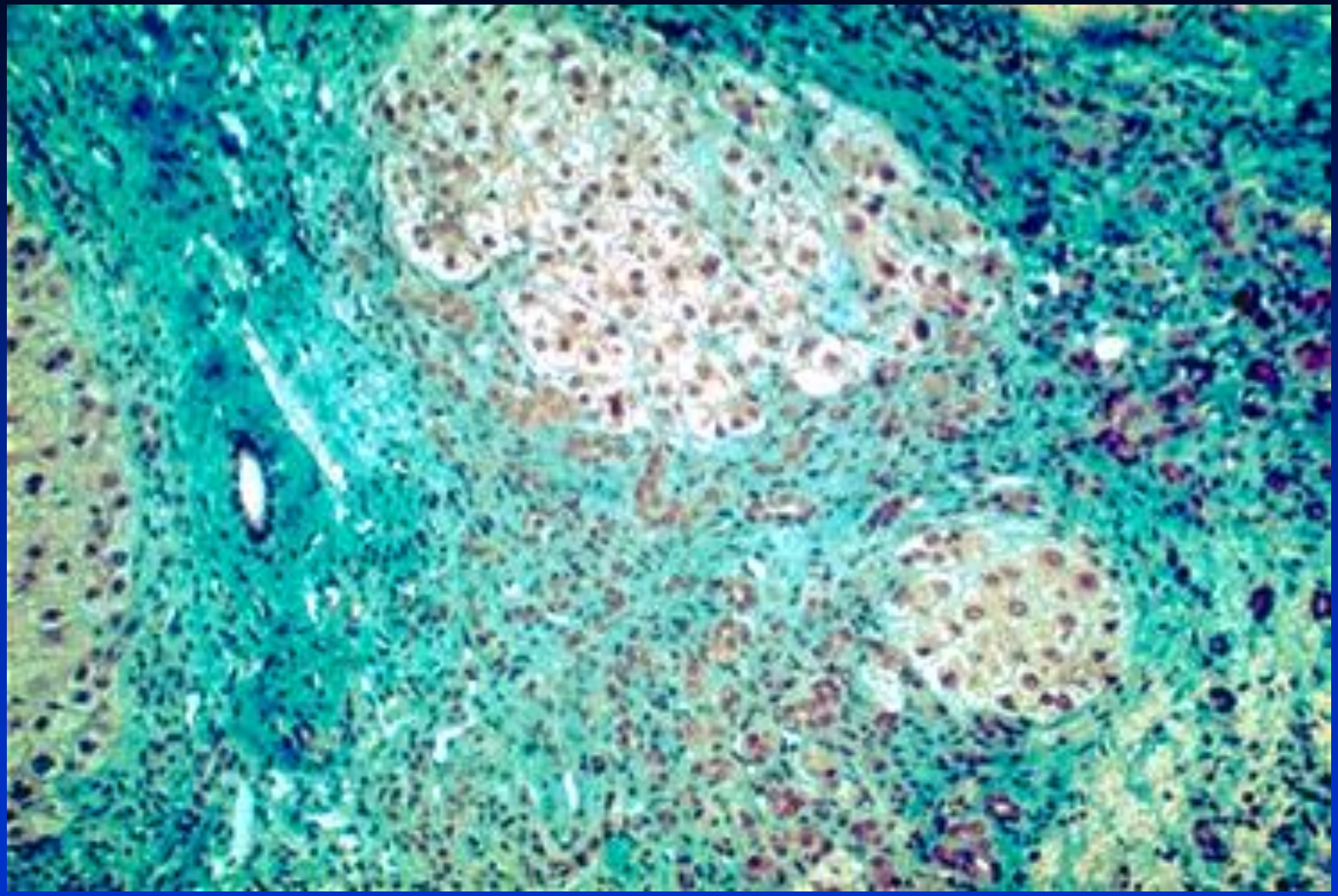
CIK - Hand Radiograph

Genetic Diseases – Wilson's Disease



Resnick, 1998

Genetic Diseases – Wilson's Disease



Genetic Diseases – Wilson's Disease