

Cystinosis

Paul Goodyer, MD

McGill University

Montreal Children's Hospital



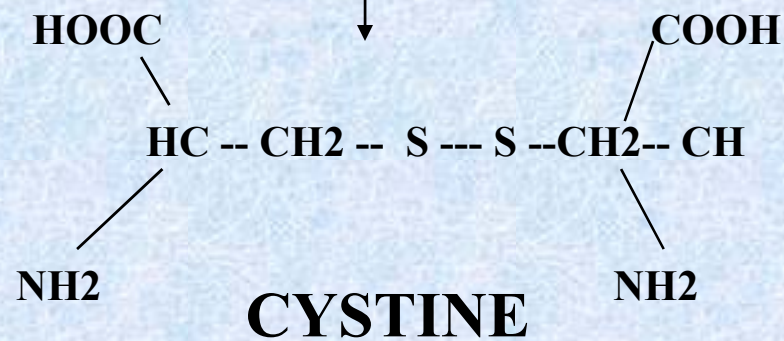
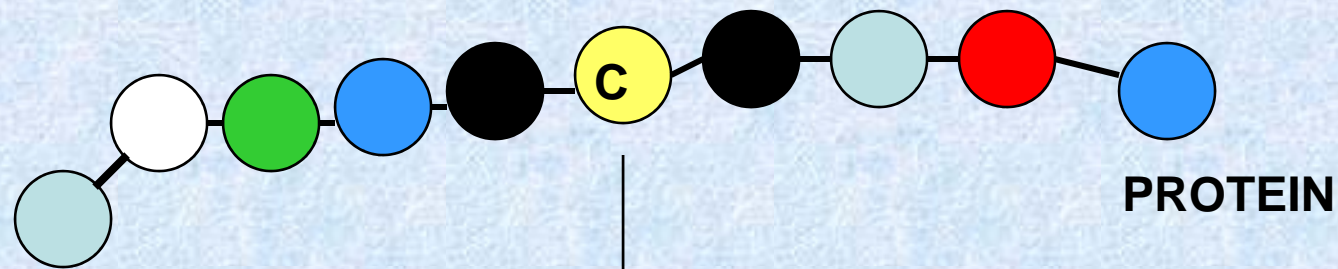
Cystinosis: Some History

- 1903 (**Aberhalden**) – several kids with failure to thrive and cystine accumulation in their tissues.
- 1931 (**Fanconi**) -- urinary loss of substances normally reclaimed during passage of fluid through the renal tubules.
 - Sugar, salt, phosphate, potassium, bicarbonate, amino acids and protein
- 1952 (**Bickel**) -- progressive damage to the kidney (and other tissues).
- 1998 (**Antignac**) -- cystinosis gene identified

Cystinosis: Some History

- 1903 (**Aberhalden**) – reported several children with failure to thrive and ***cystine*** accumulation in their tissues.
- ***What's Cystine***

What's Cystine?

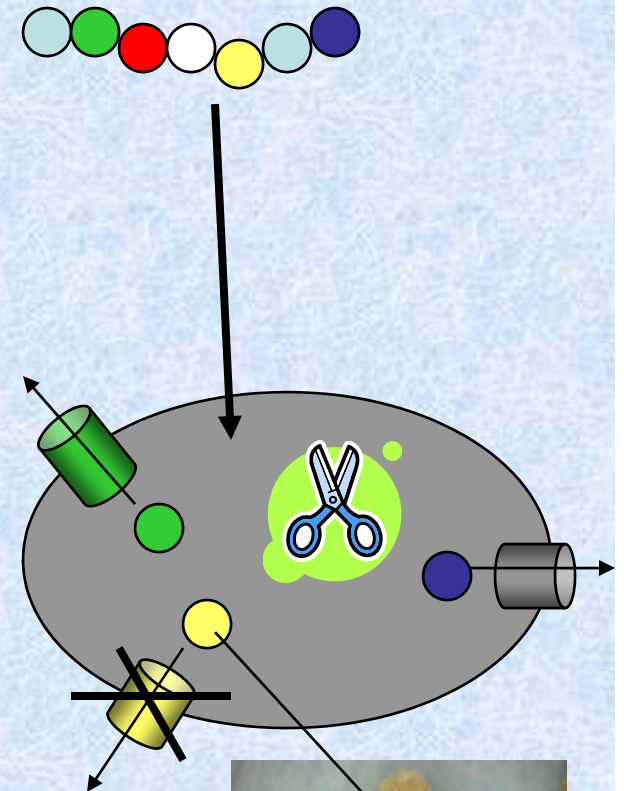


Why does cystine build up in tissues of kids with cystinosis?

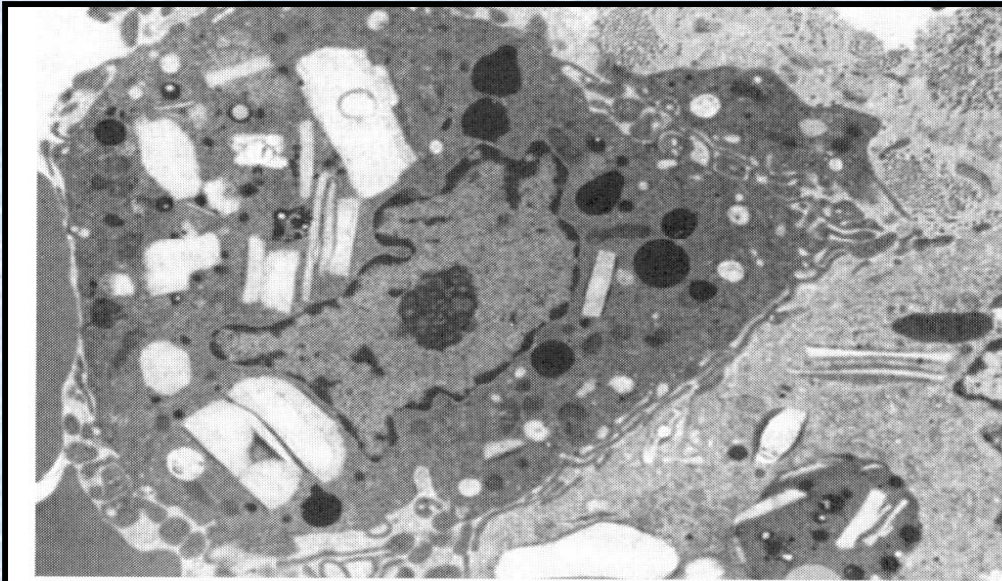


1967

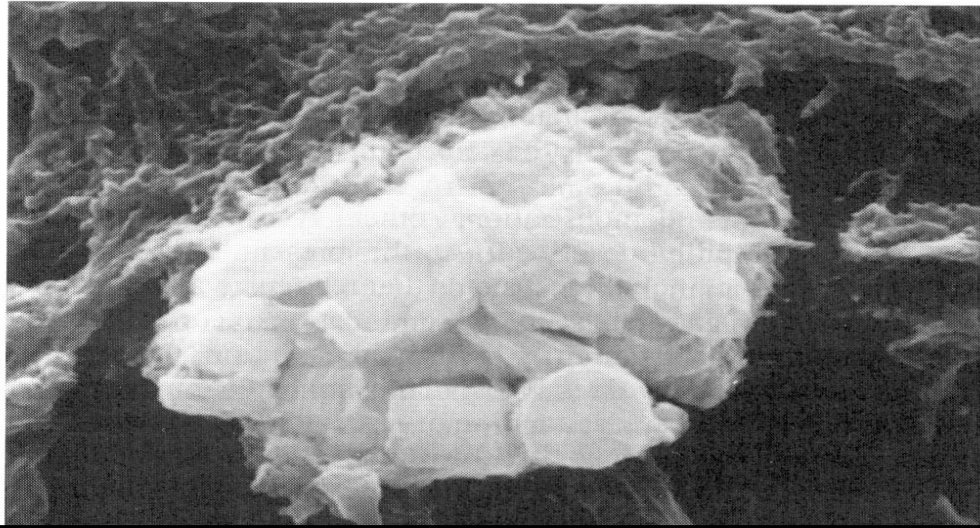
Protein



Cystine crystals inside lysosomes



B



Without treatment,
cystine is trapped in
lysosomes

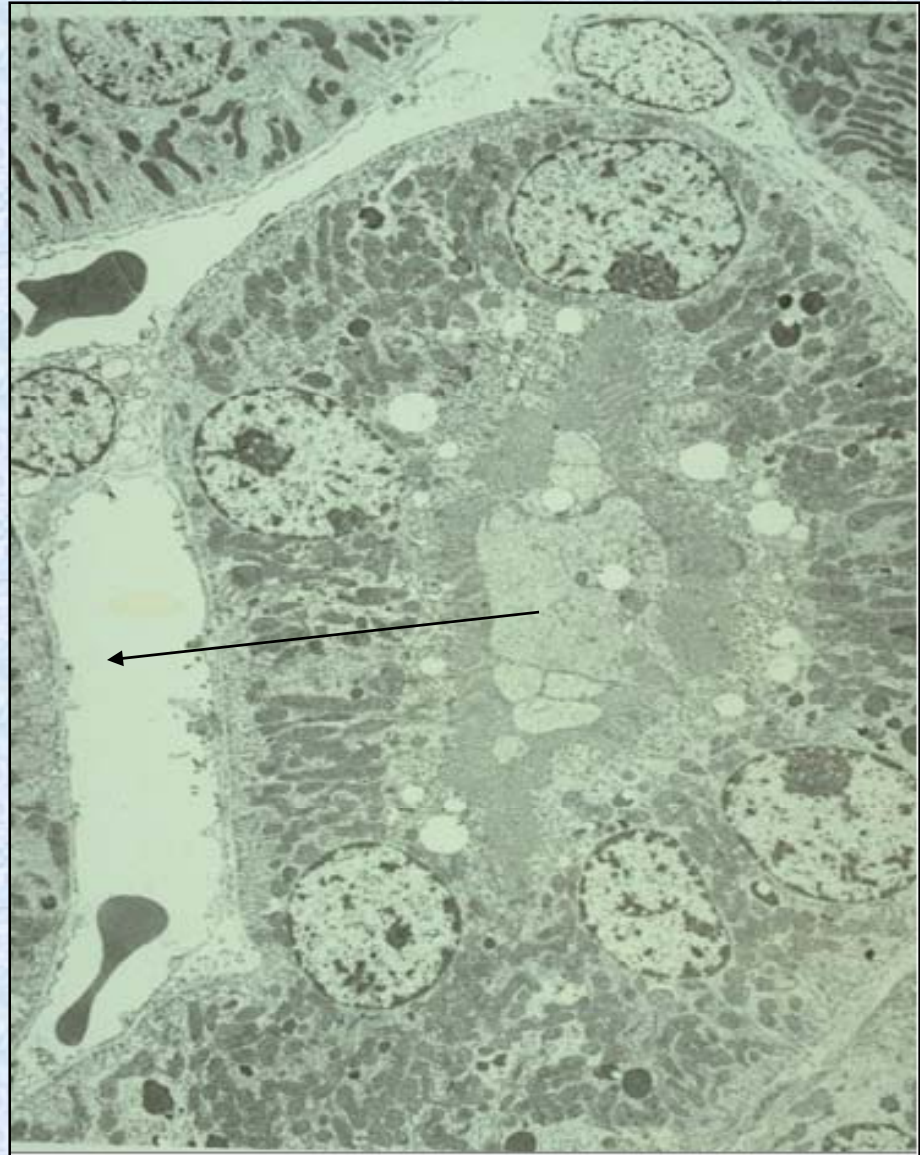
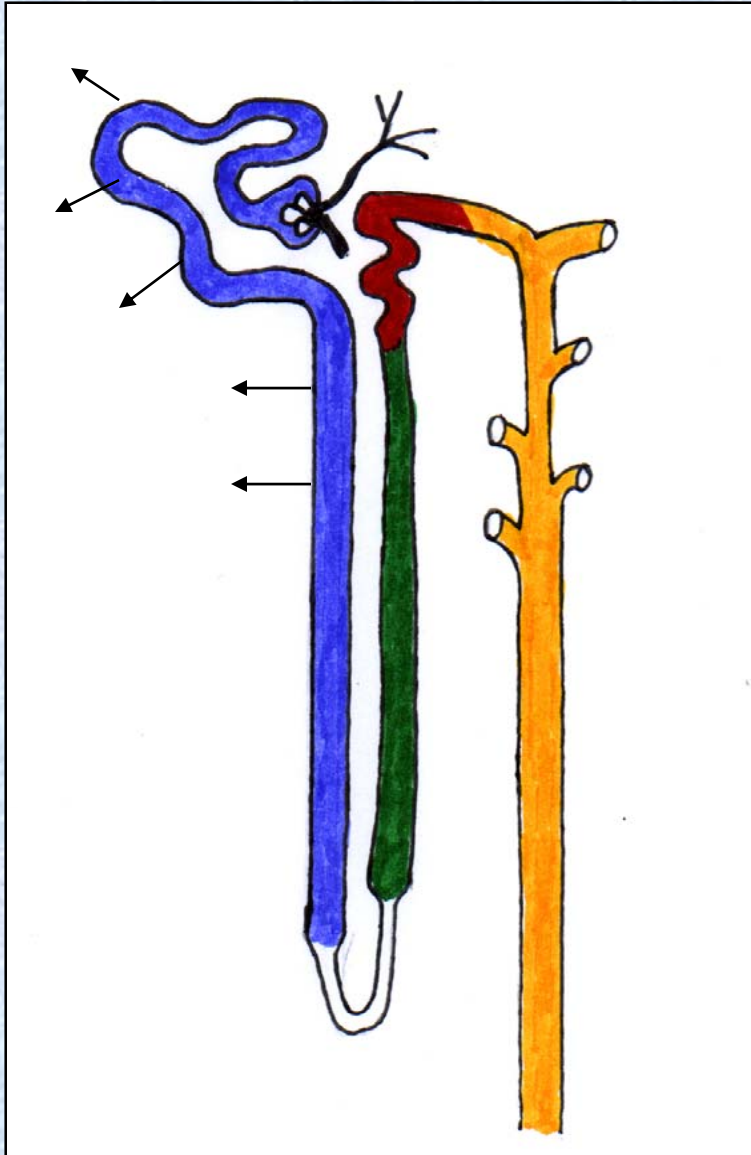
10-100 times as much
cystine as normal

**Cystine
crystalizes and
damages the cell**

Cystinosis History

- 1903 (Aberhalden) – several kids with failure to thrive and cystine accumulation in their tissues.
- **1931 (Fanconi) -- urinary loss of substances normally reclaimed during passage of fluid through the renal tubules.**
 - Sugar, salt, phosphate, potassium, bicarbonate, amino acids and protein
- 1952 (Bickel) -- progressive damage to the kidney (and other tissues).

What's Fanconi Syndrome?





UNTREATED Cystinosis

A 10-year old girl from India

Salt and Water

Potassium

Bicarbonate

Phosphate

Glucose

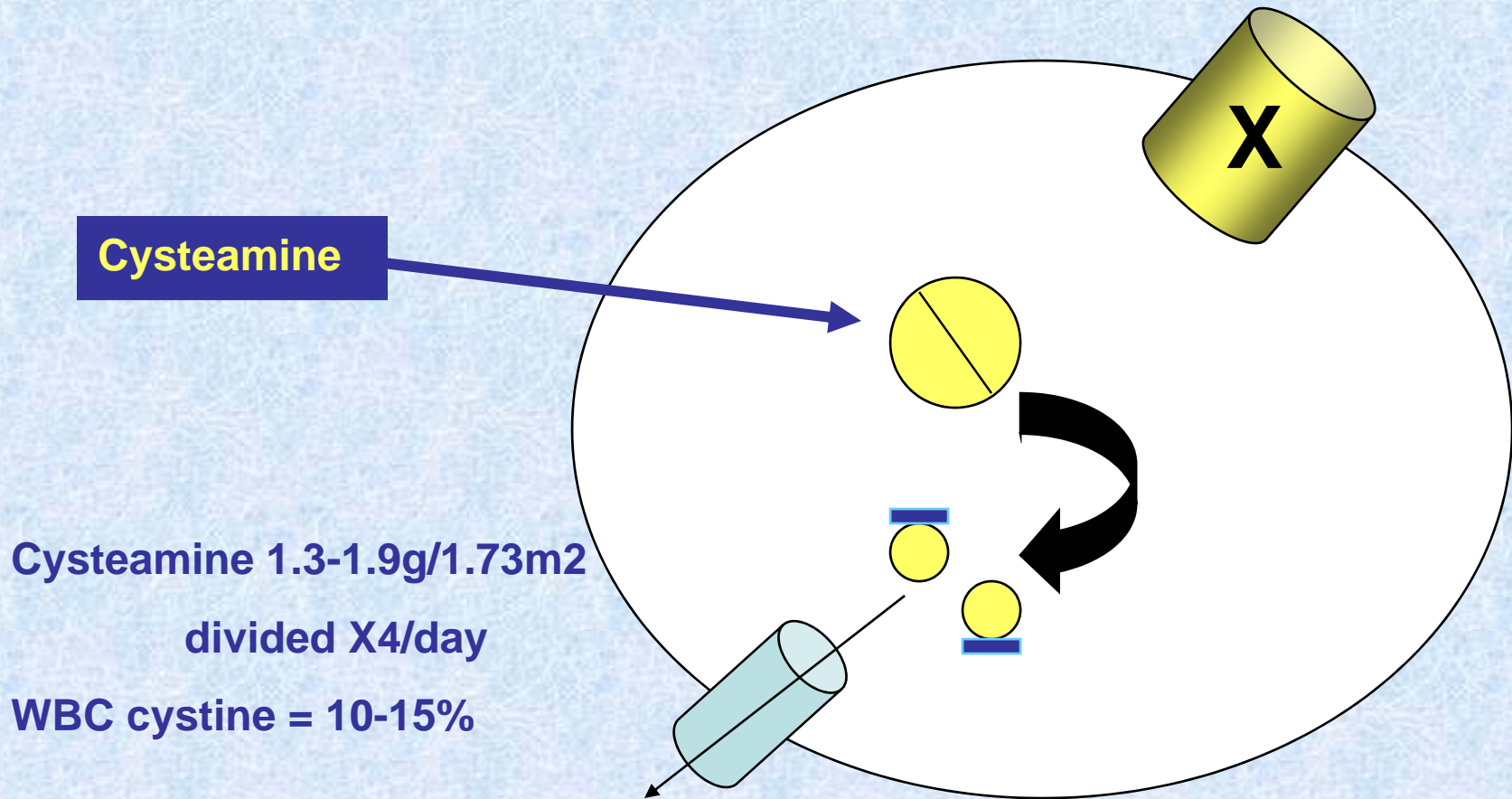
Amino Acids

Protein

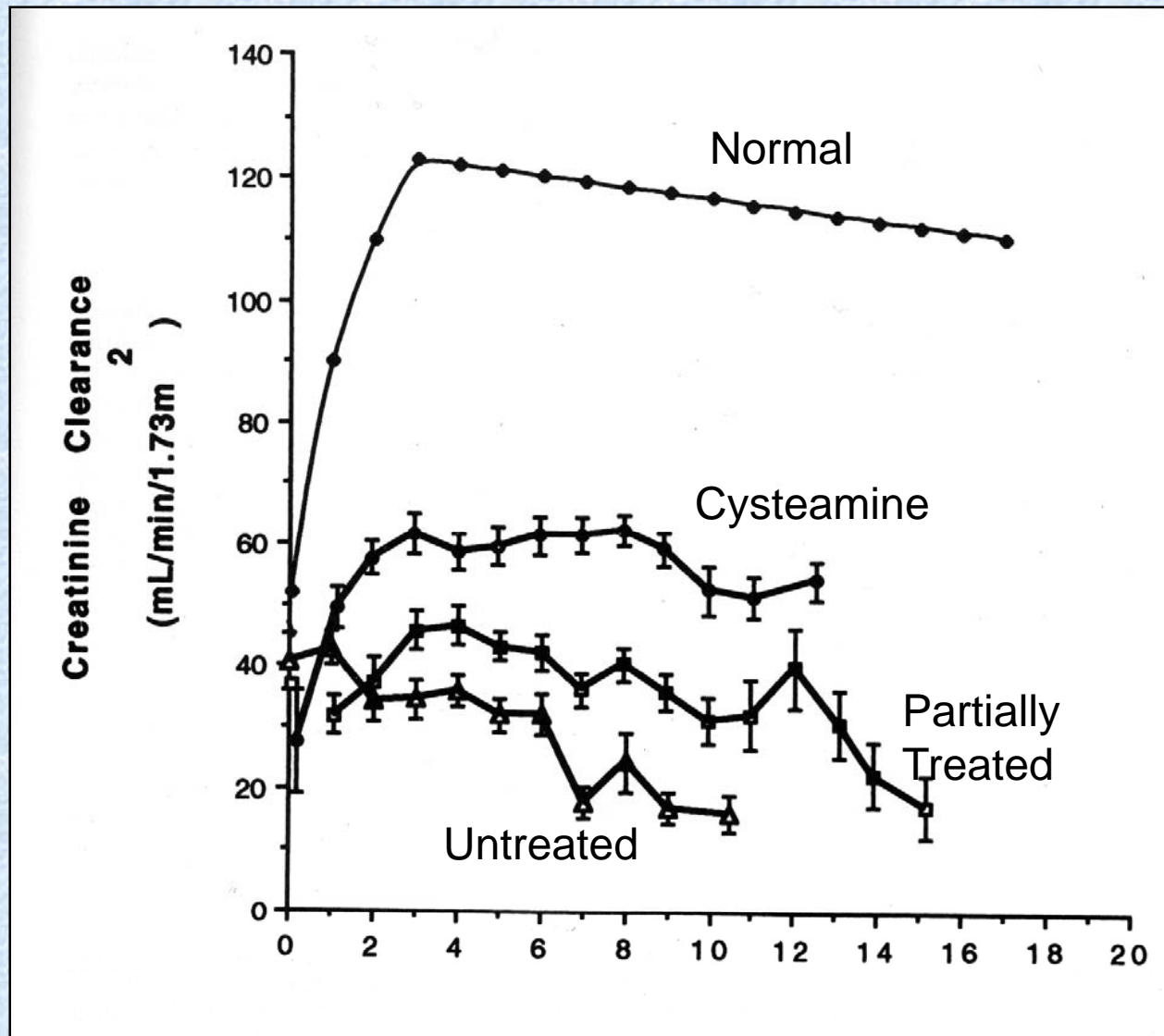
Cystinosis History

- 1903 (Aberhalden) – several kids with failure to thrive and cystine accumulation in their tissues.
- **1931 (Fanconi) -- urinary loss of substances normally reclaimed during passage of fluid through the renal tubules.**
 - Sugar, salt, phosphate, potassium, bicarbonate, amino acids and protein
- **1952 (Bickel) -- progressive damage to the kidney (and other tissues).**

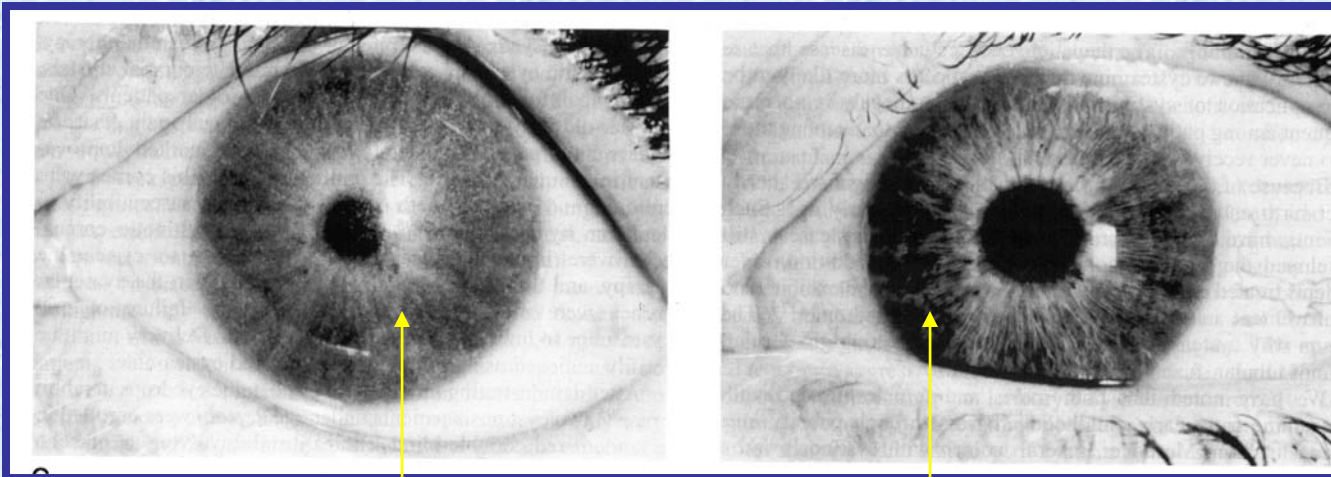
Cysteamine cleaves cystine into smaller pieces



Cysteamine treatment of Cystinosis



Effect of cysteamine eyedrops

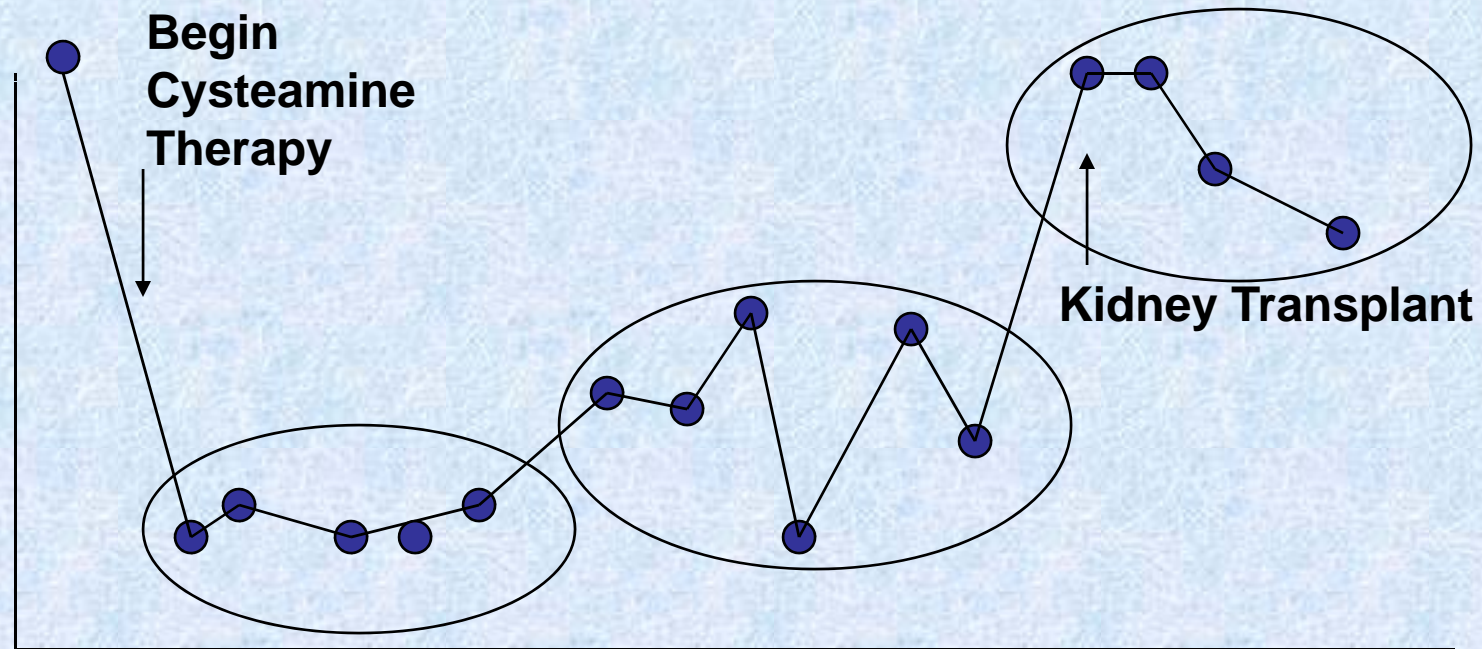


**Diffuse corneal
cystine crystals**

**Partial clearing
with cysteamine
eyedrops**

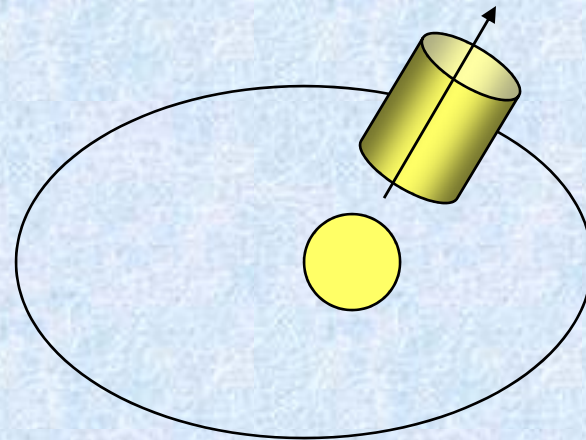
Monitoring Cysteamine therapy

White blood cells isolated from blood 4-6 hours after a dose of cysteamine – analyzed for cystine content.



Where does cystinosis come from?

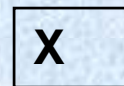
- 1998 (Antignac) – found the cystinosis gene on chromosome 17 --“Cystinosin”
- Blueprint for the cystine exit channel from lysosomes



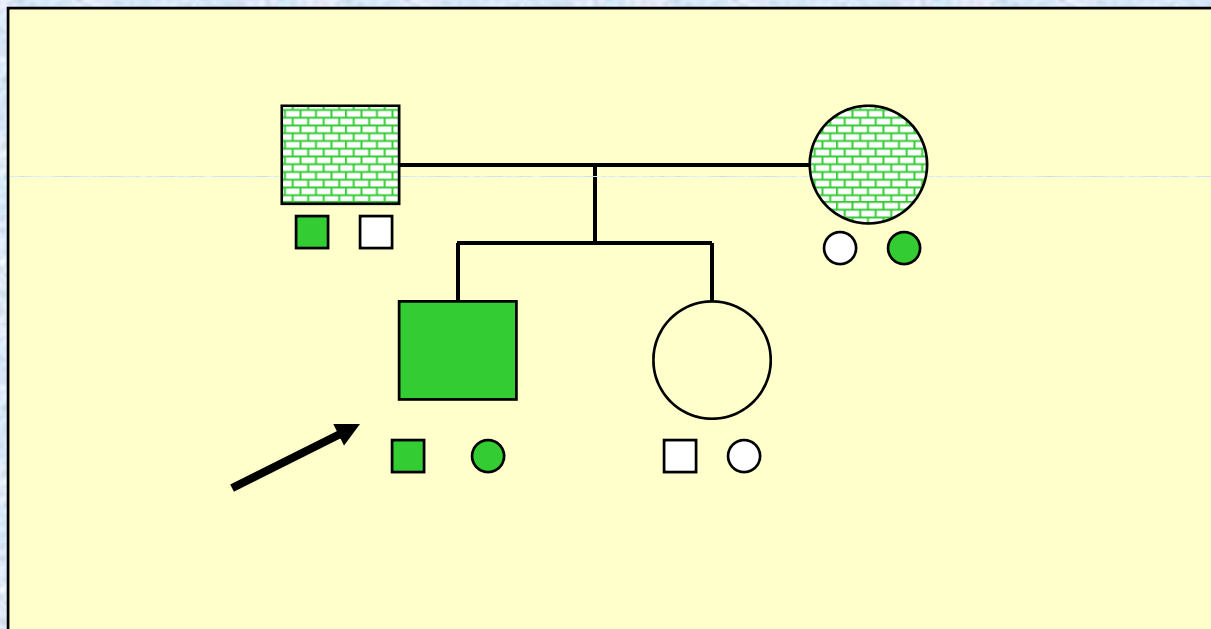
...GAT TTG AAC CTA GGG TAT CCA AGA CGT...



...GAT TTG AAC CTA **GGC** TAT CCA AGA CGT...

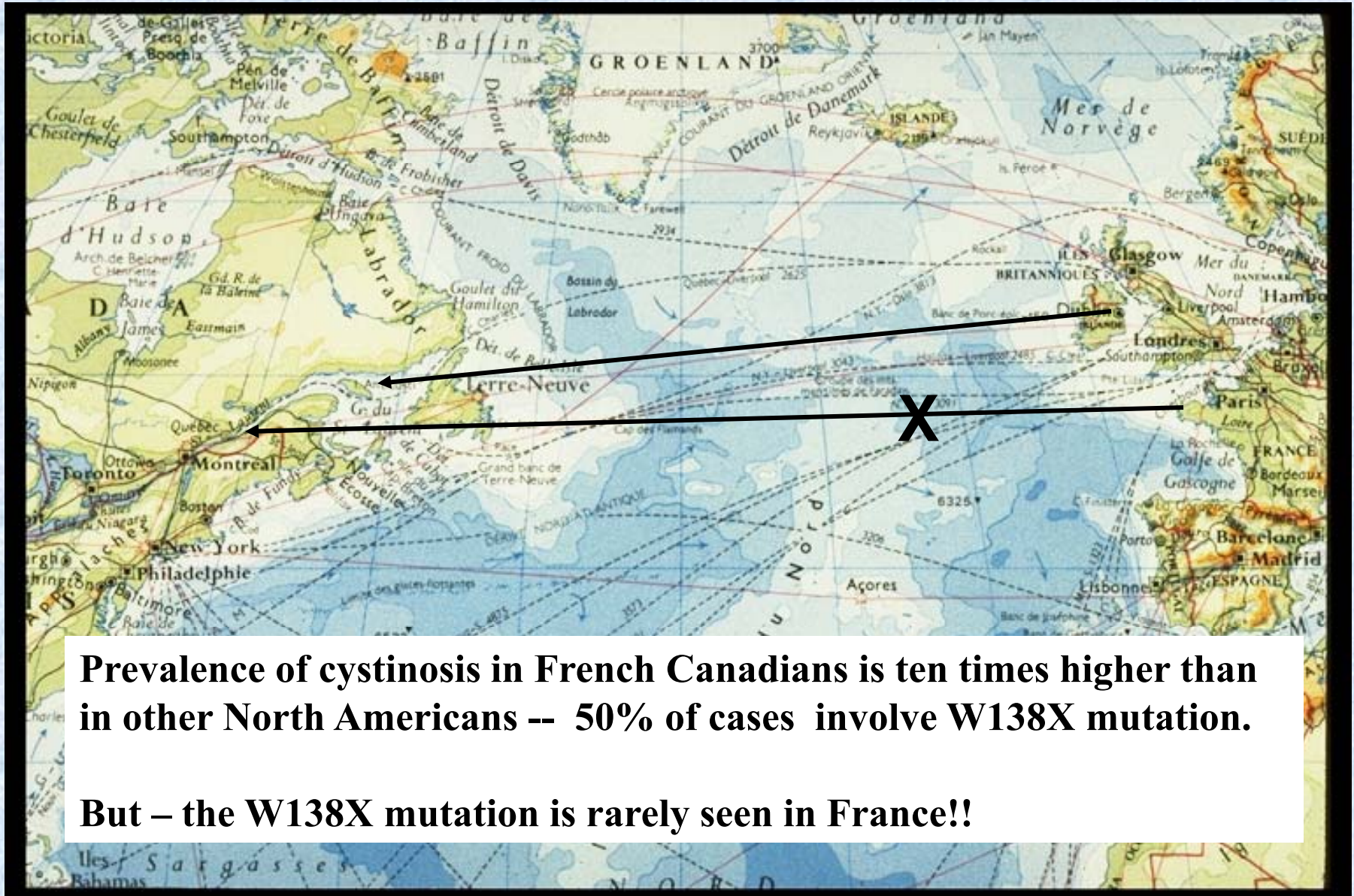


Cystinosis is “RECESSIVE”



5-10 per million births

Cystinosis in Quebec



Prevalence of cystinosis in French Canadians is ten times higher than in other North Americans -- 50% of cases involve W138X mutation.

But – the W138X mutation is rarely seen in France!!

Genetic Renal Disease

