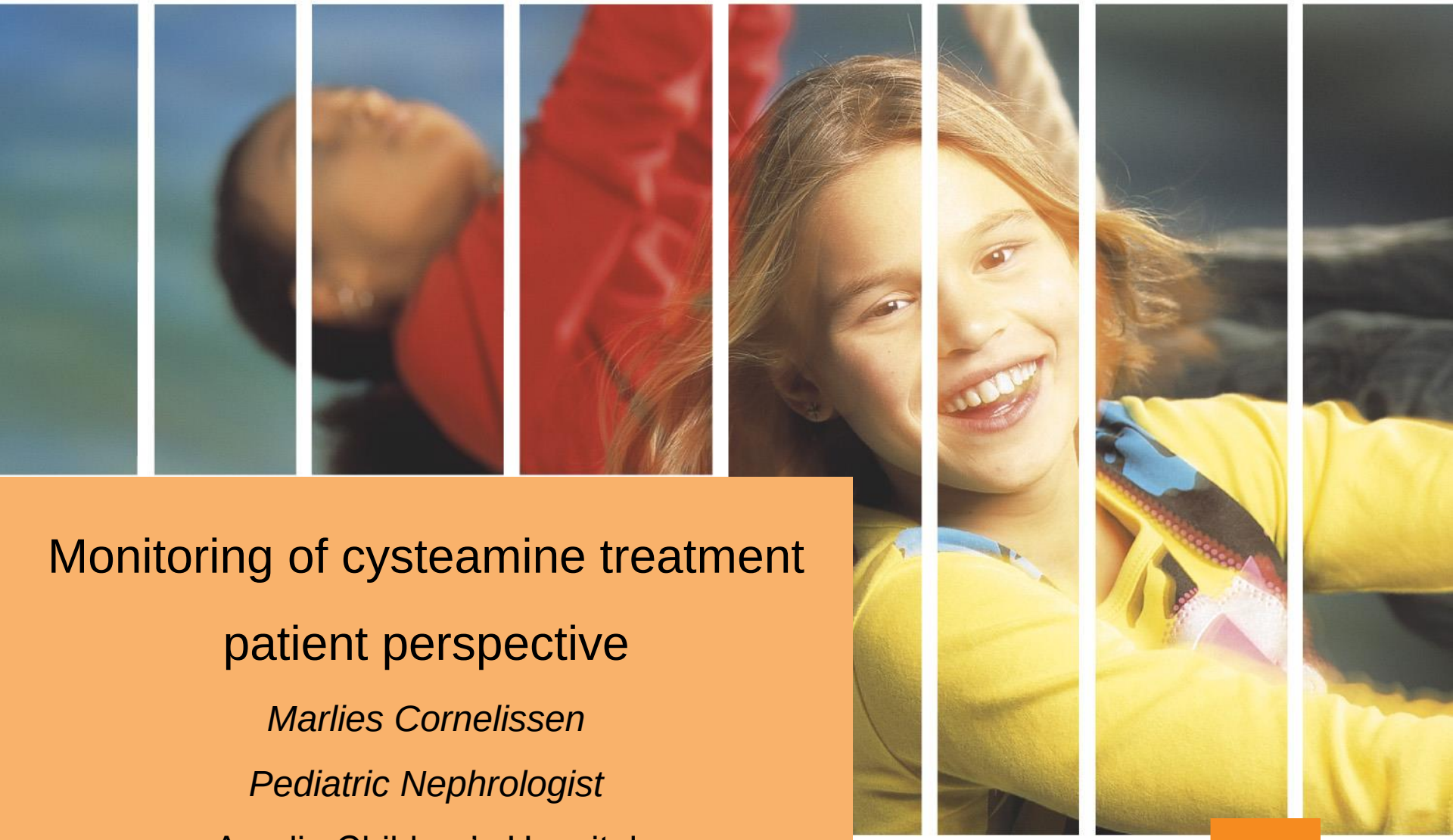

Monitoring of cysteamine treatment patient perspective

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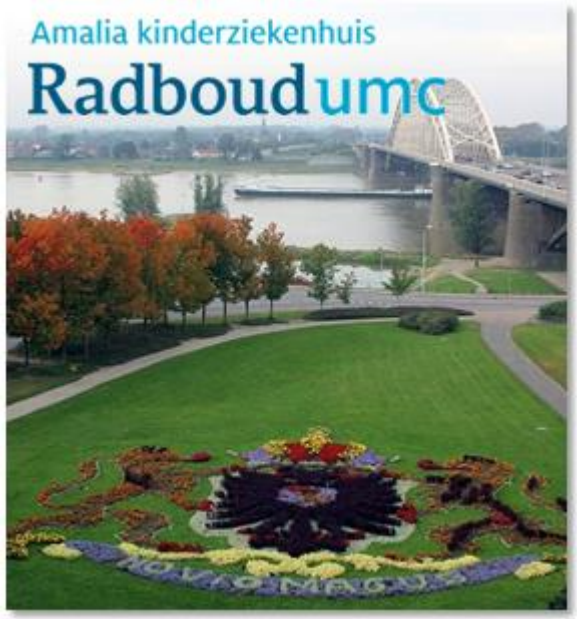
Monitoring of cysteamine treatment

- What is Cysteamine
- How does Cysteamine work
- How to dose Cysteamine
- How to monitor side effects
- Slow release product



Cystinosis

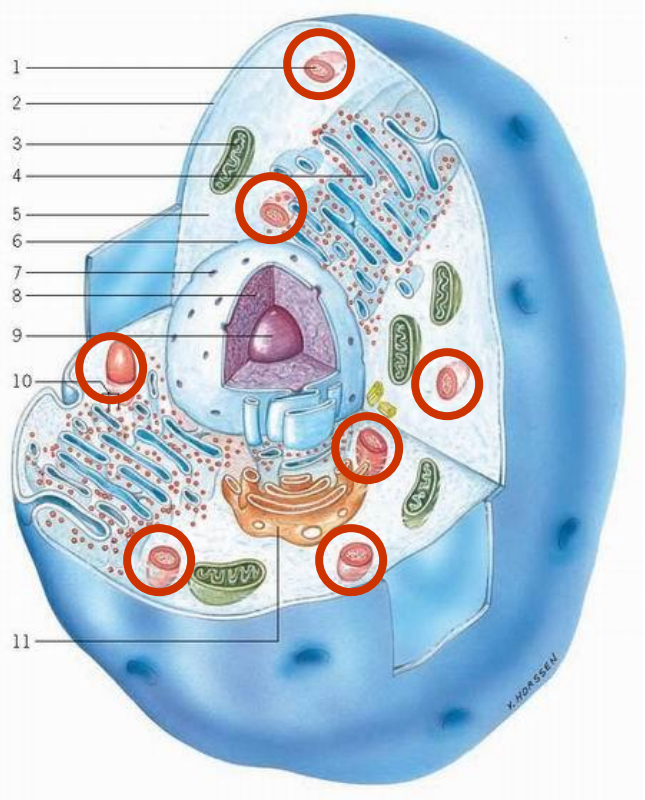
Lysosomal storage disease

Lysosome:

- Vacuüm cleaner
- Waste factory

-> breakdown of cell components
(fats, proteins, sugar, etc)
-> excrete Cystine

In Cystinosis Cystine cannot leave the lysosome

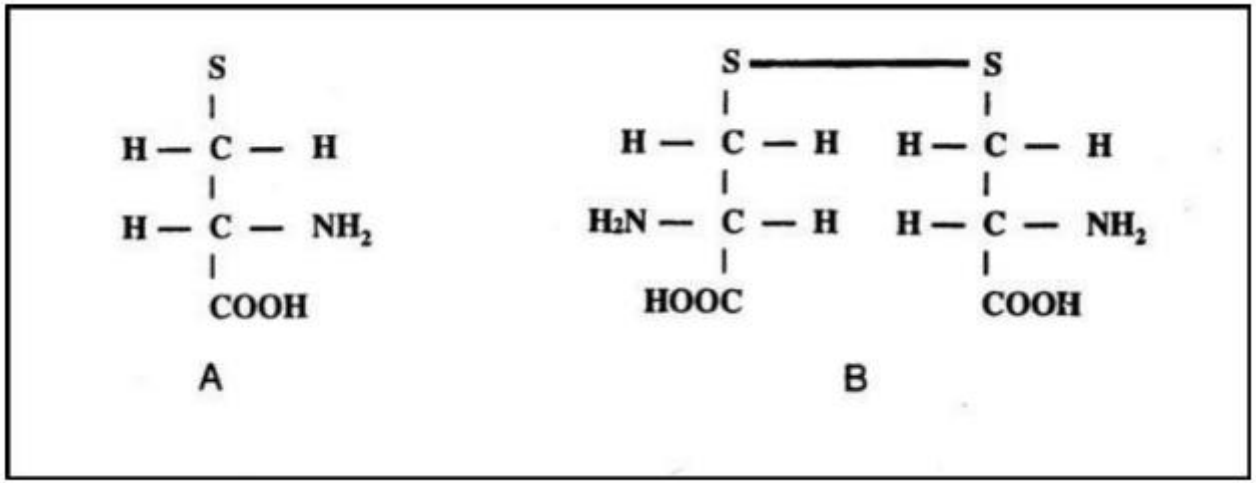


What is Cystine?

Cystine is a normal amino acid

consisting of 2 cysteïnes (bound by Sulfur).

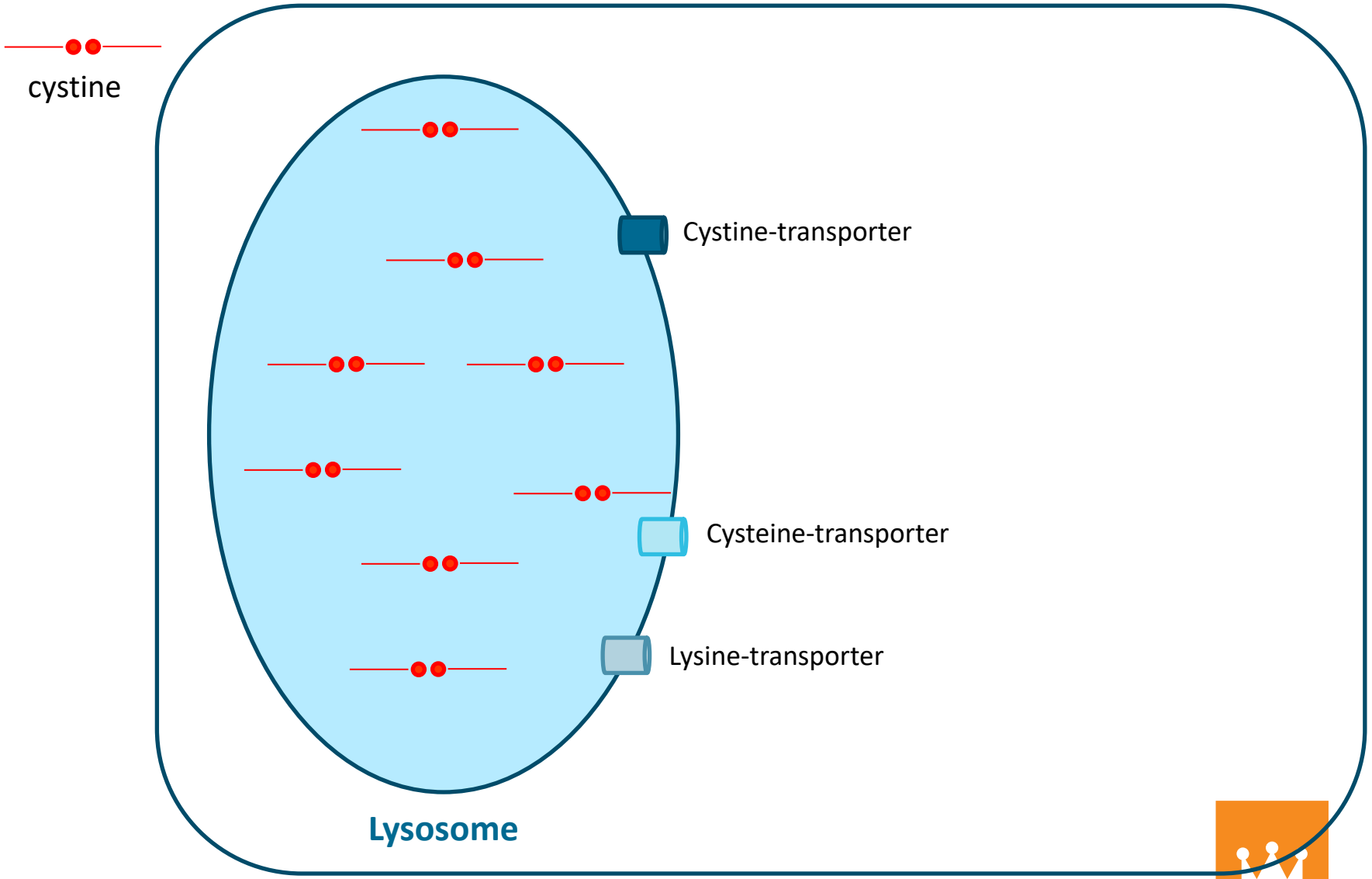
This sulfur binding makes it unsoluble in water.



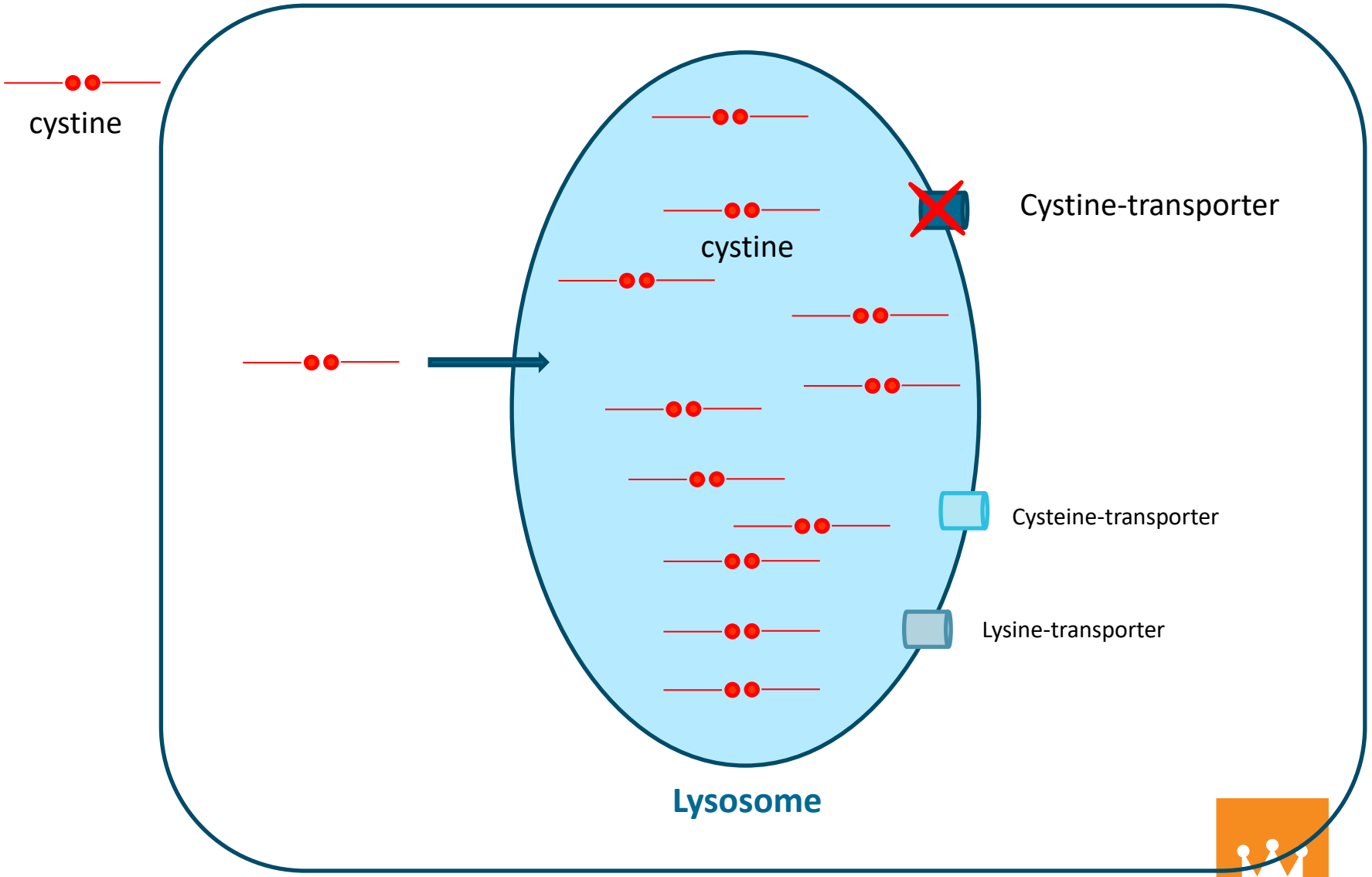
Cysteine

Cystine

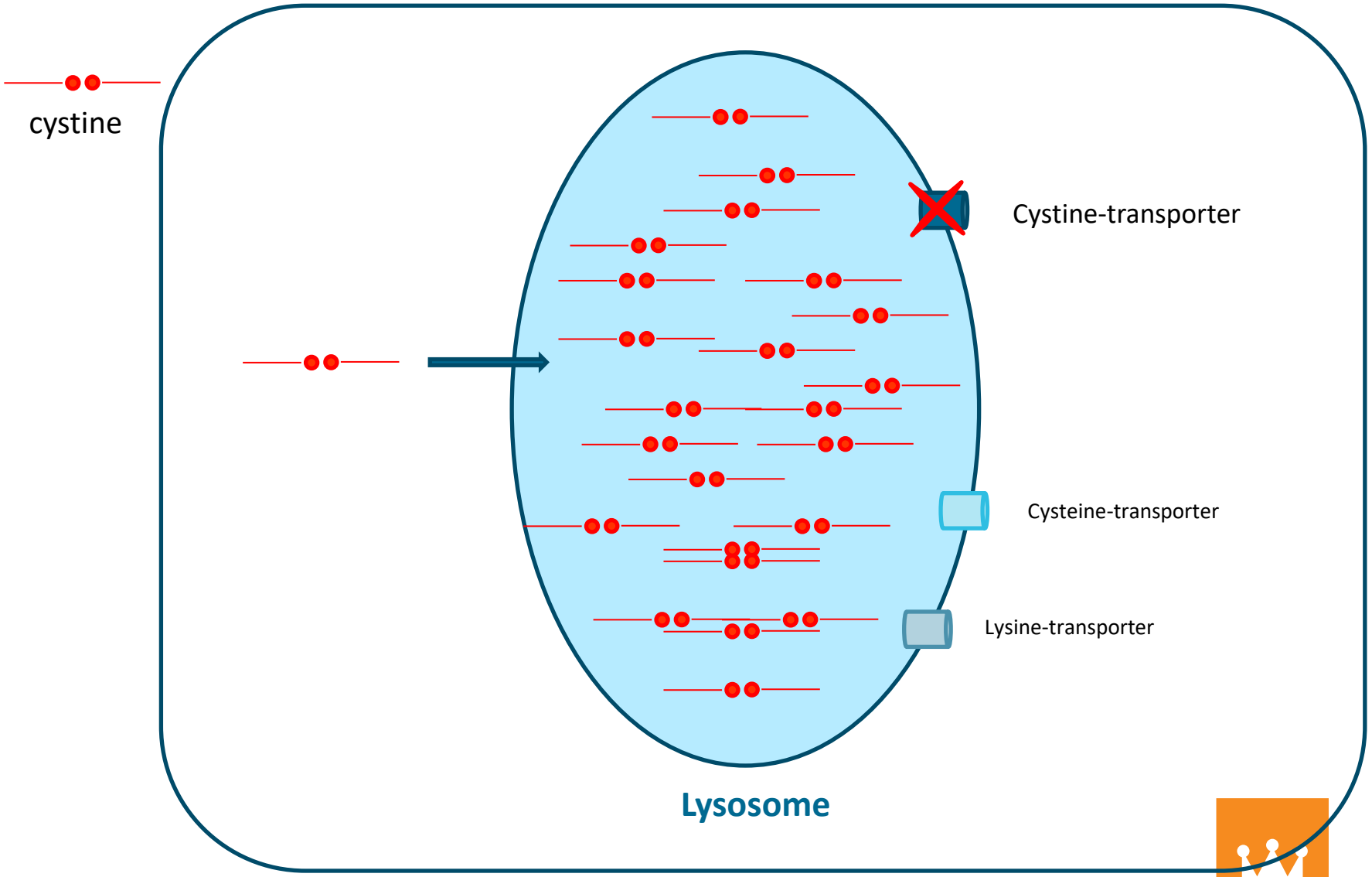
Normal situation



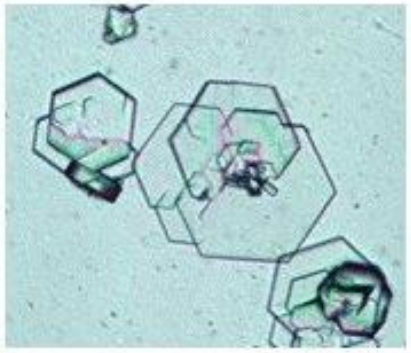
Cystinosis

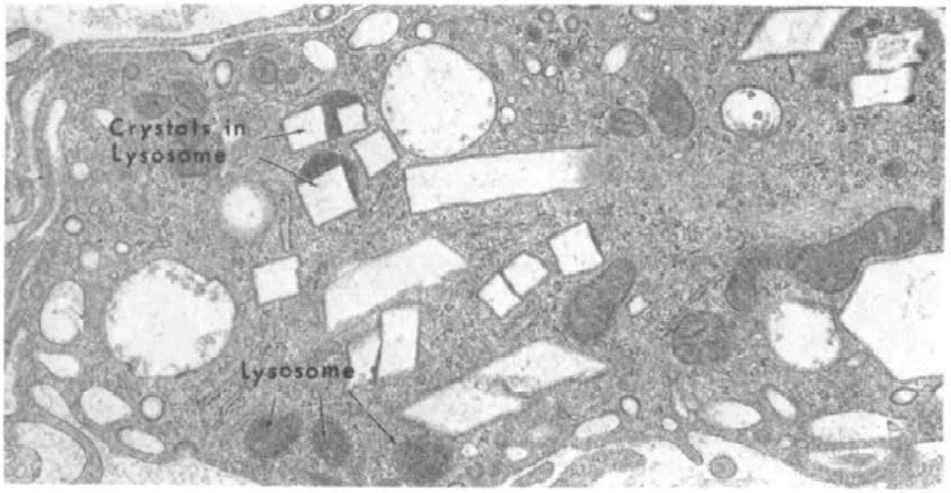

cystine
cystine
Cystine-transporter
Cysteine-transporter
Lysine-transporter
Lysosome

Cystinosis – stacking of Cystine



Cystine stacking in cystinosis





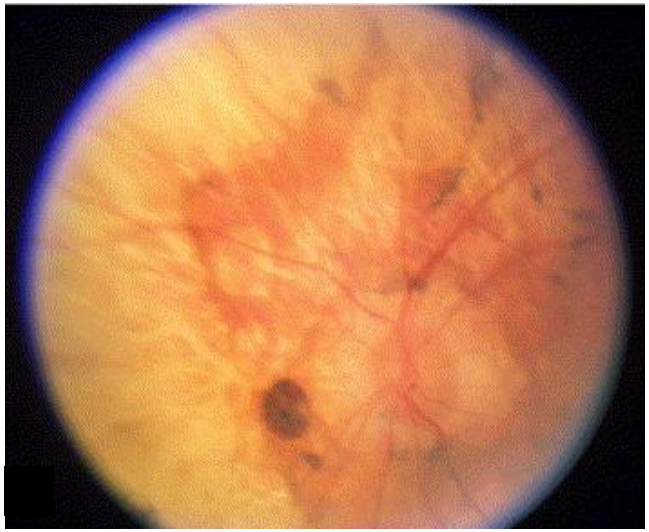
Kidney: 200 - 400 x normal

Liver: 80 - 1000 x normal

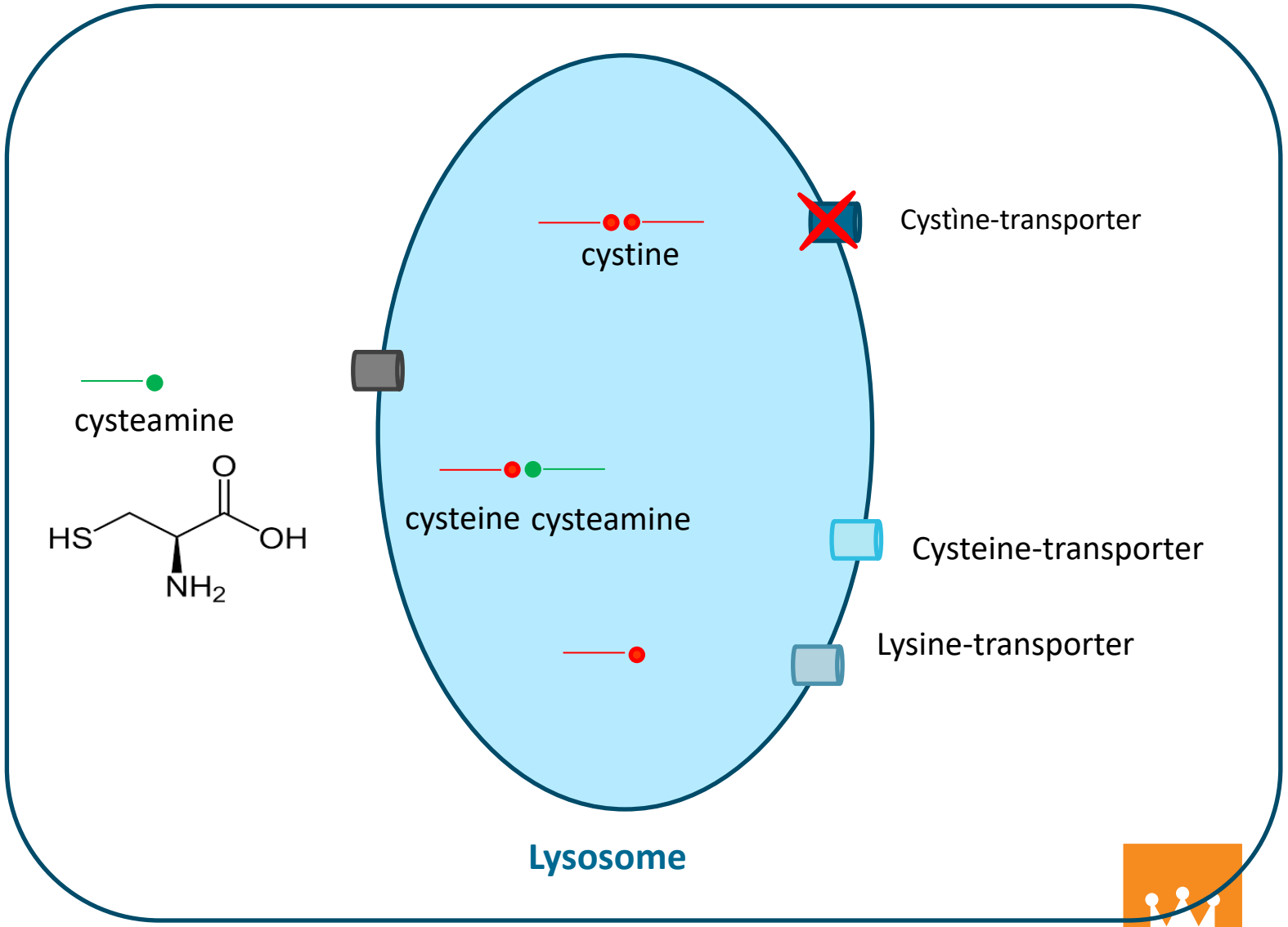
Muscle: 40 - 70 x normal

Brain: 5 - 20 x normal

Gahl et al. 2001



Cysteamine Treatment



Treatment of Cystinosis

2 pillars

- Symptomatic treatment Fanconi syndrome
  - water
  - sodium, potassium, magnesium, phosphate
  - Calcium, vitamin D
  - Carnitin
  - When needed: Thyroxine, growthhormone, insulin, testosteron
- Specific treatment with Cysteamine
  - Cystagon or Procysbi

How to dose Cysteamine capsules

Dose is set by the pharmaceutical company

based on studies and real time experience

- **Cystagon** 1,3 g/m² per day (~ 50 mg/kg), divided over 4 doses
- **Procysbi** 1,0 g/m² per dag (~ 40 mg/kg), divided over 2 doses

Then measure the WBC:

- Goal is to keep WBC < reference value of own lab

  < 1.0 nanomol hemicystine per mg protein (max < 2.0)
- Goal is to keep side effects tolerable
- Discuss how medication is taken; on time, frequency, with food?

Cysteamine absorption may be decreased by 30% when taken with fatty food as compared with fasting state

New option: measure Chitotriosidase (= biomarker of lysosomal disease)

How to dose Cysteamine eye drops

- Dosing in Eye drops (Cystadrops, Cystaran) ?
  - just use as much as possible
  - Monitor eye problems (Eye docter)

How to monitor side effects

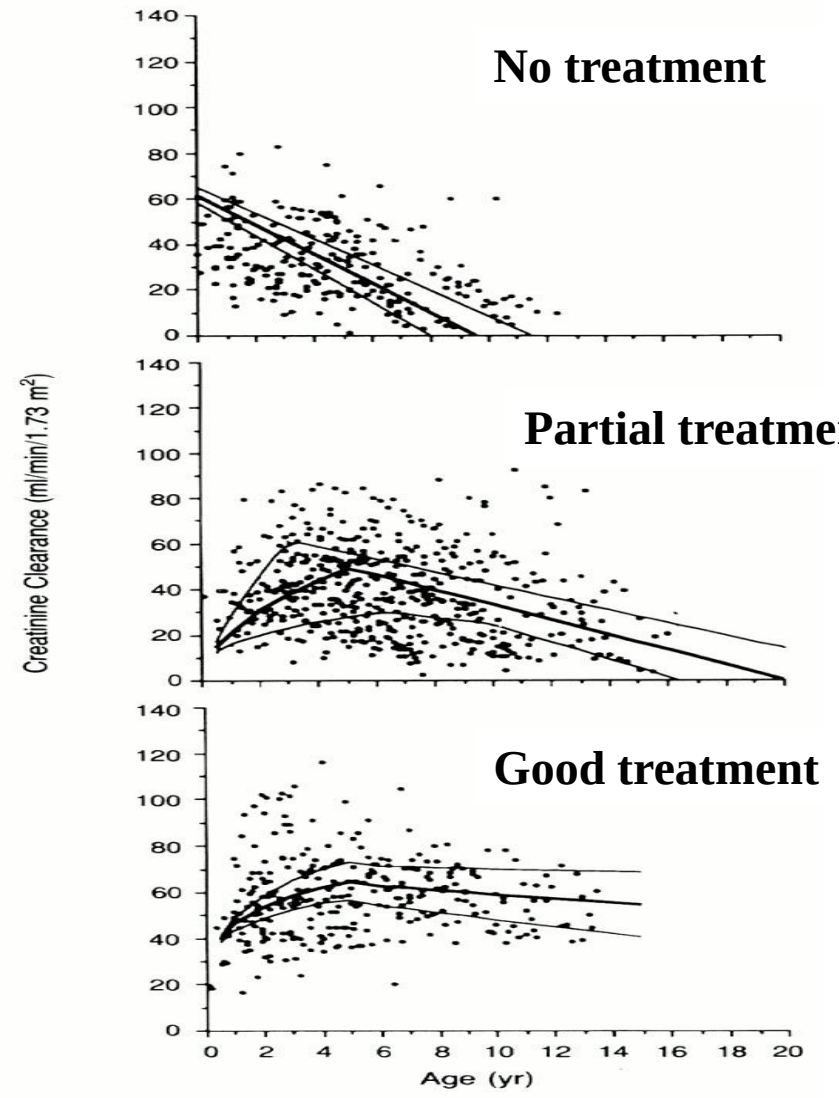
Side effects

- Gastro-intestinal: nausea, throwing up, diarrhea, bad appetite
- Bad smell
- Skin: tags, striae (overdose)

⇒ Monitor in outpatient clinic

⇒ Monitor by lab (liver function, leucocytes, platelets)

Cysteamine is effective in delaying kidney failure



n= 67

n = 32

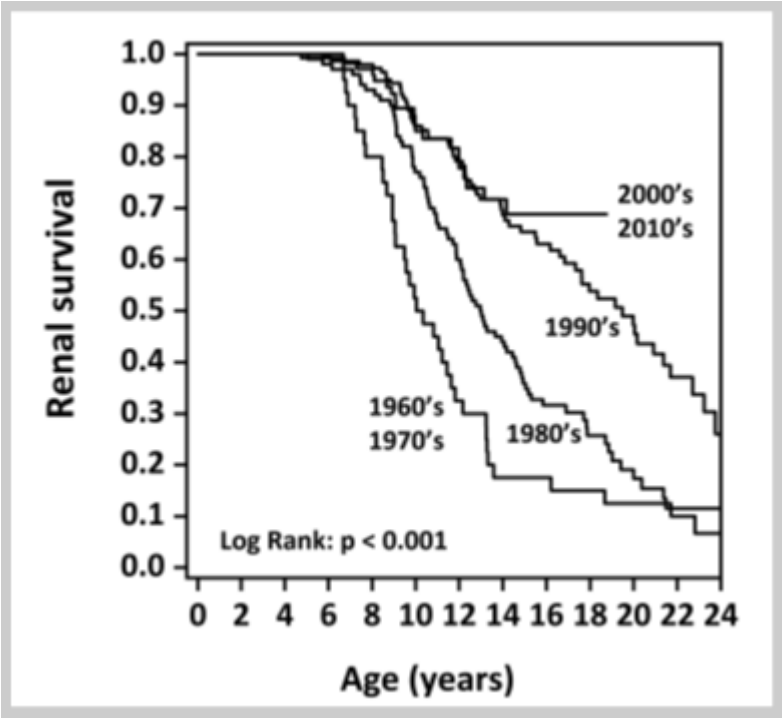
n = 17

Markello et al. NEJM 1993

Cysteamine is effective in delaying kidney failure

Emma et al, june 2021

- **453 patients born between 1964 and 2016**



In 1970 mean 'kidney survival' 10 yrs
in 1990 -> 19 yrs

Treatment with Cysteamine: Effective

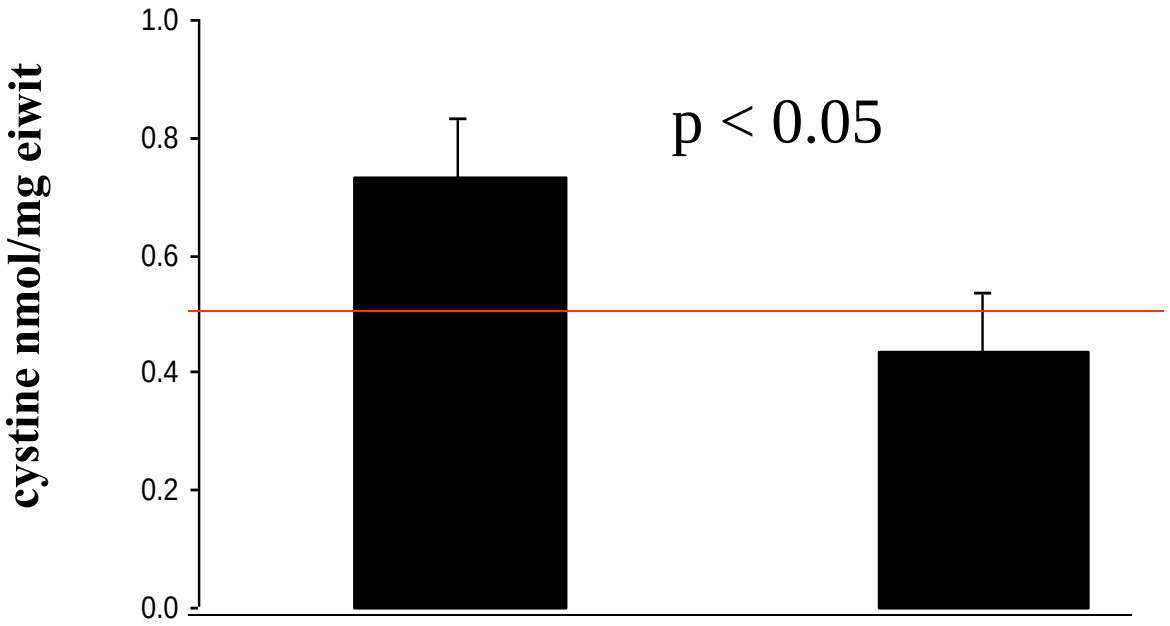
- Delay of kidney failure with several years
- Protection of other organs
- Eye drops can make Cystine cristals disappear

But…

- It does not cure the kidney / organs
- Has to be taken exactly on time
- Difficult to adhere to the prescription,

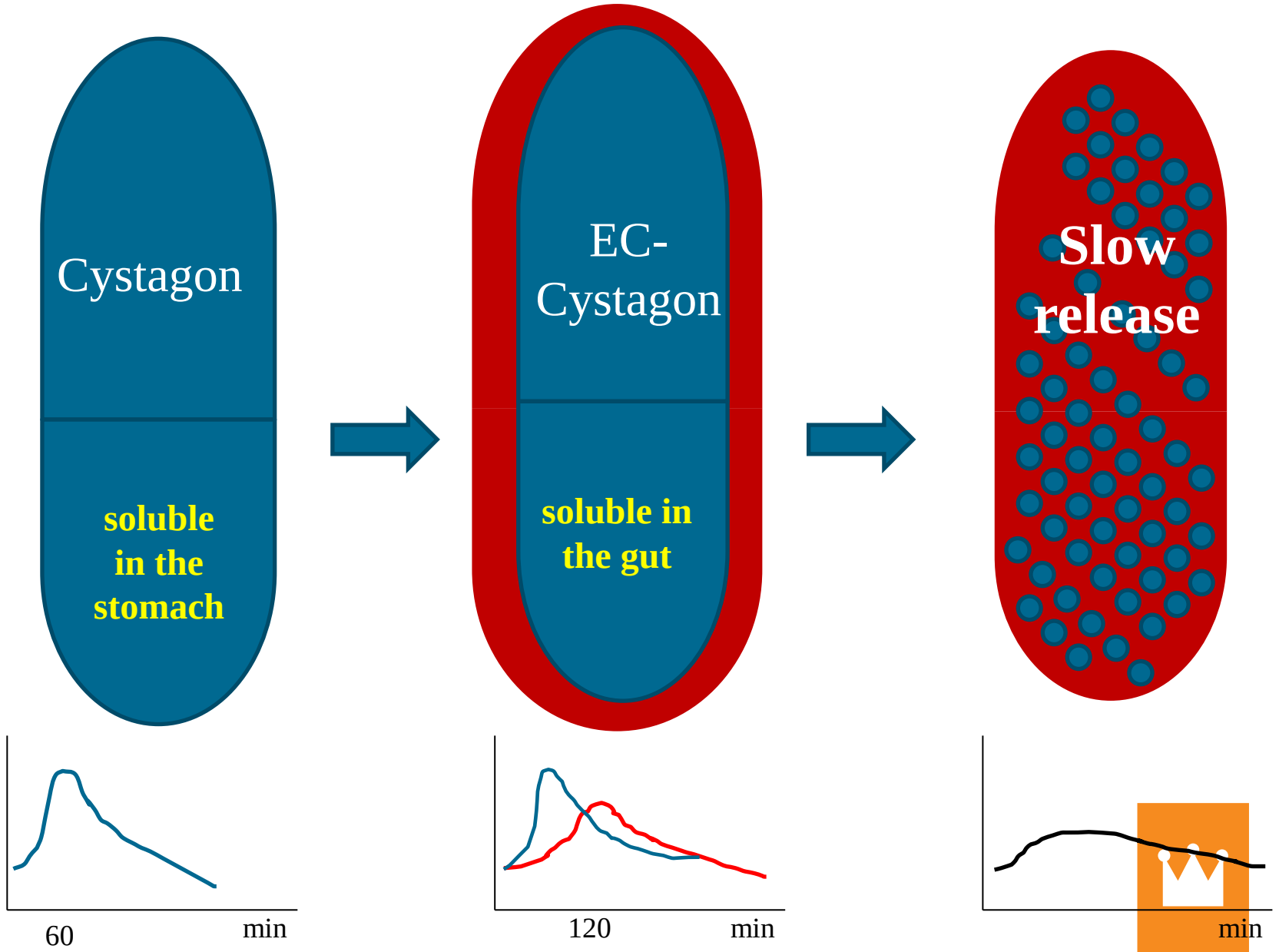
  due to frequency and side effects.

Cystagon- morning cystine level

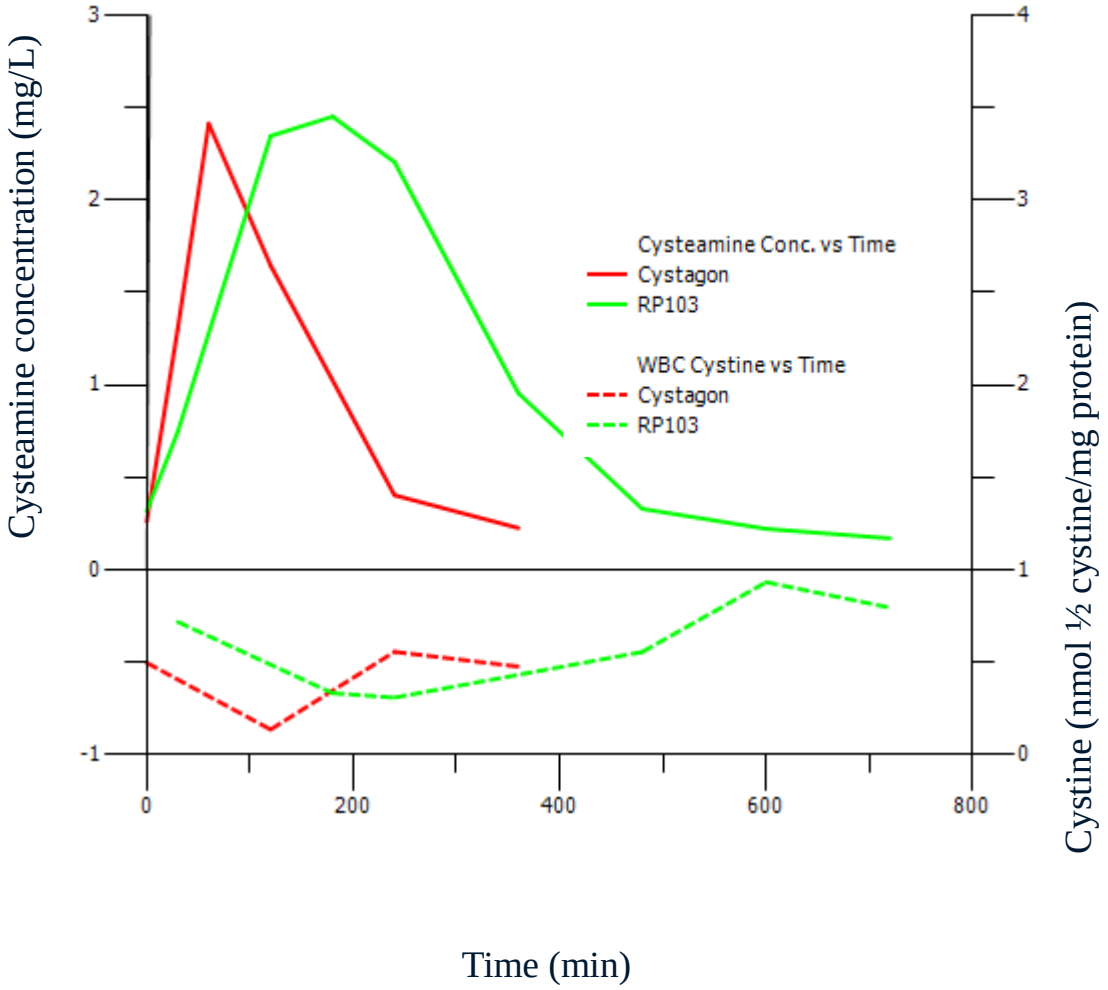


Levtchenko et al. 2006

Delayed Cysteamine: *Procysbi*



Procysbi keeps WBC cystine low for 12 hours



6 hr = ~400 min
12 hr = ~700 min

Studies in Procysbi

- Effectivity and safety of Procysbi is equal to Cystagon
  (not better – not worse)
- Same side effects
- Dosing is ~20% lower
  So Cystagon 4dd 500 mg => Procysbi 2 dd 800 mg
- Monitoring also by WBC

van Stein *et al. Orphanet J Rare Dis* (2021) 16:387
https://doi.org/10.1186/s13023-021-01991-2

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Check for updates

A comparison of immediate release and delayed release cysteamine in 17 patients with nephropathic cystinosis

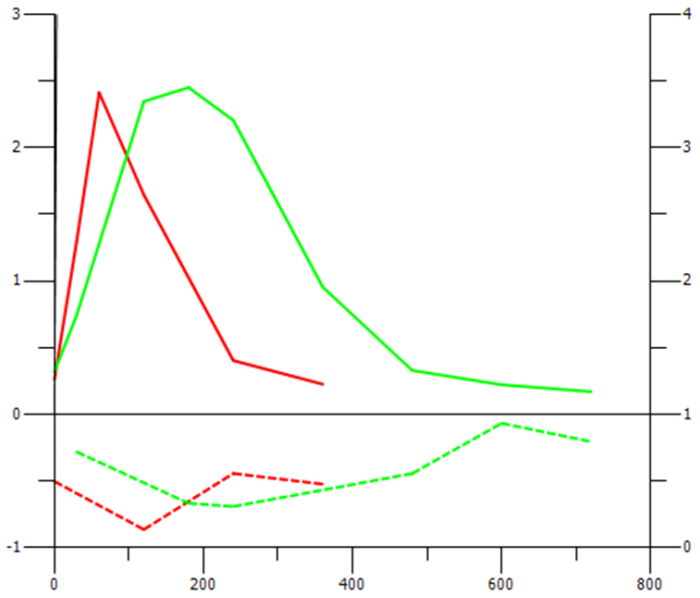
Christina van Stein[1*], Sabrina Klank[1], Marianne Grüneberg[1], Chris Ottolenghi[2,3], Jürgen Grebe[1], Janine Reunert[1], Erik Harms[1] and Thorsten Marquardt[1*]

Blood sampling in Procysbi

Bloodsampling advice – in my view- is problematic

- Sample exactly 30 min after ingestion of the next dose
  because in the first 30 min there is no effect from the new ingestion
  but
  if timing is 35 min you will have effect of the new ingestion
  => not a reliable WBC (too good result).

  I myself prefer to measure after 12-12,5 hrs
  without taking the next dose
  - no chance of too favorable WBC
  - next dose max 30 min too late



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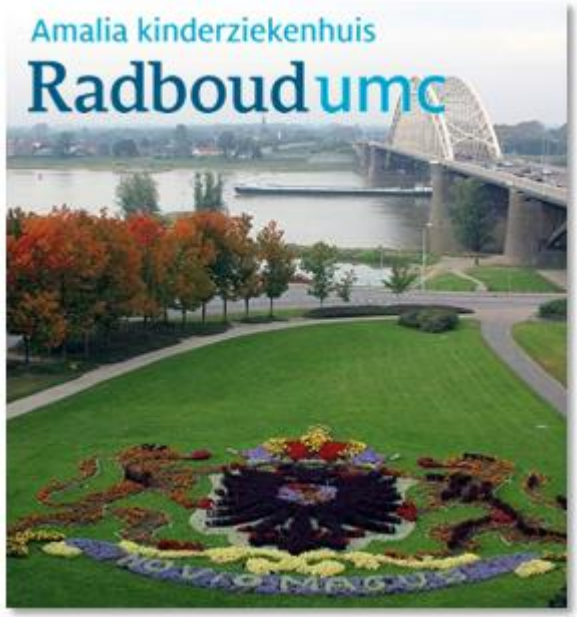

Thank you