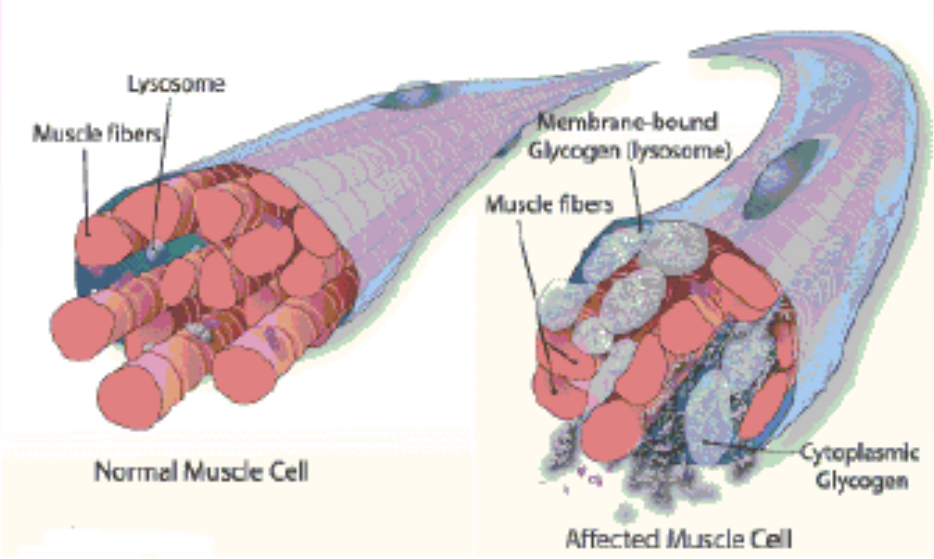
Why is it important to think on Pompe disease?

Assist. Prof Ervina Bilic, MD PhD

Medical School University of Zagreb
Clinical Hospital Centre Zagreb



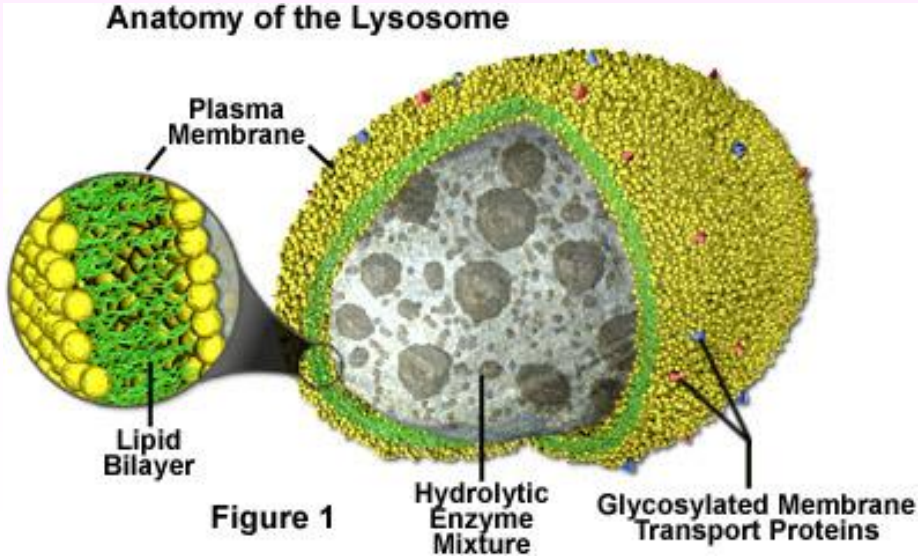
Pompe disease: first cases and the definition of the disease

1932.

- Dutch pathologist, Dr J.C. Pompe, described glycogen vacuolar inclusions in the tissue samples of a young girl died in the age of 7 months.

1952.

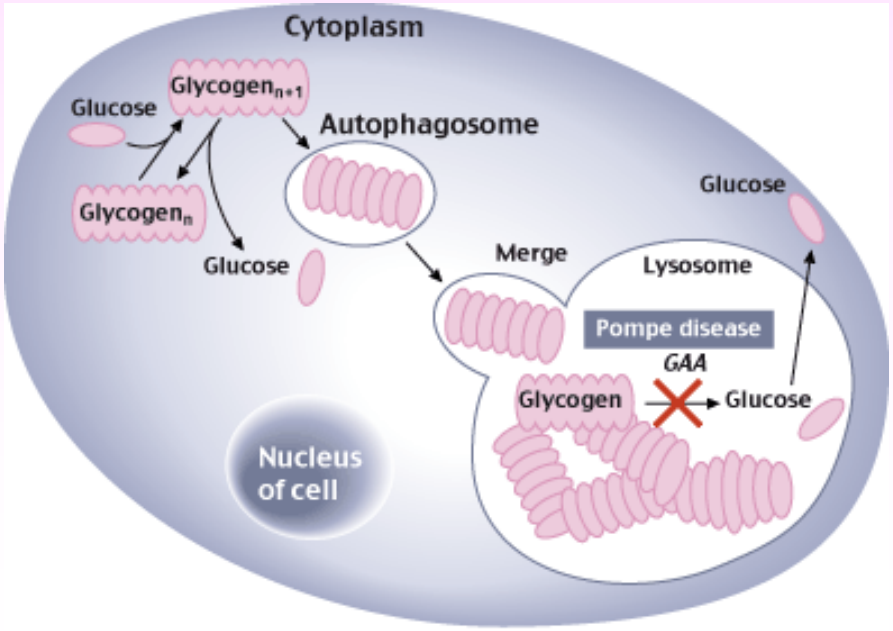
- The glycogen metabolism was described
- The lysosomes were descovered (Cori&Cori)



Hers 1963.

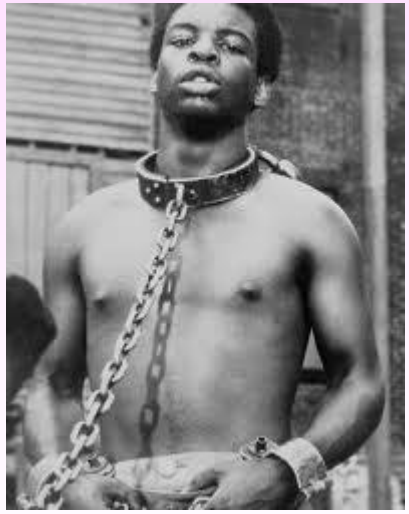
- **Debranching the glucose from the „glycogen tree”**

- **AAG activity decreased in the tissues of PD patients**



AAG
gene mutation

- North and Central Africa
- In America detected after the slaves migrations from Africa

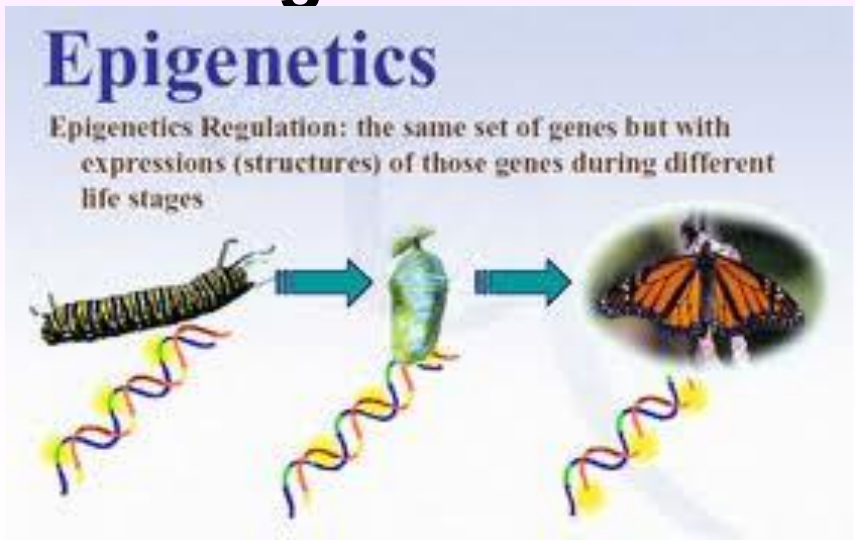


- **In Europe probably present after America**
- **Numerous mutations**
- **Usually patient has two different mutations of the same gene**

AAG activity and clinical presentation

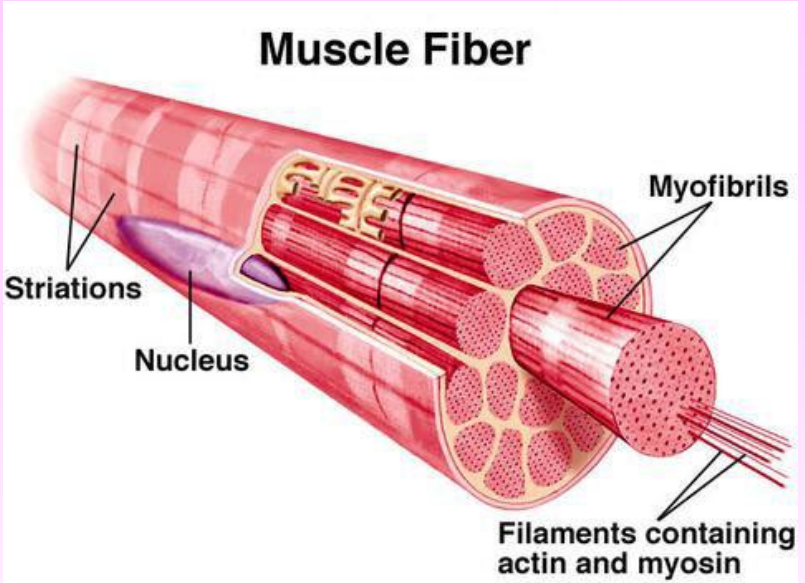
- The same level of AAG activity may give the similar disease presentation
- Epigenetic influences?

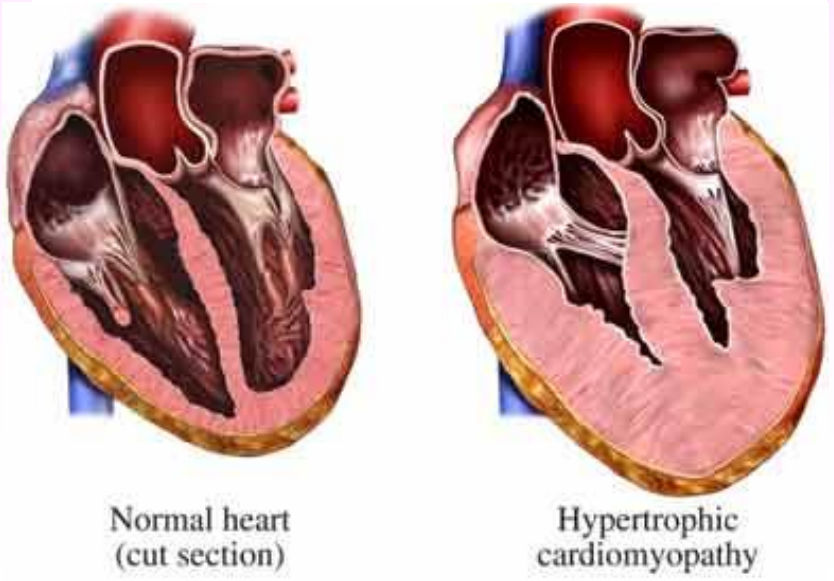
- **25% of normal AAG activity is sufficient for normal lysosomal functioning**



Glycogen accumulation

- The **voluntary and heart muscle** are the most sensitive for any energy metabolism alteration
- The AAG activity is decreased in many other tissues
- **The heart affection: only in patients with early severe PD**

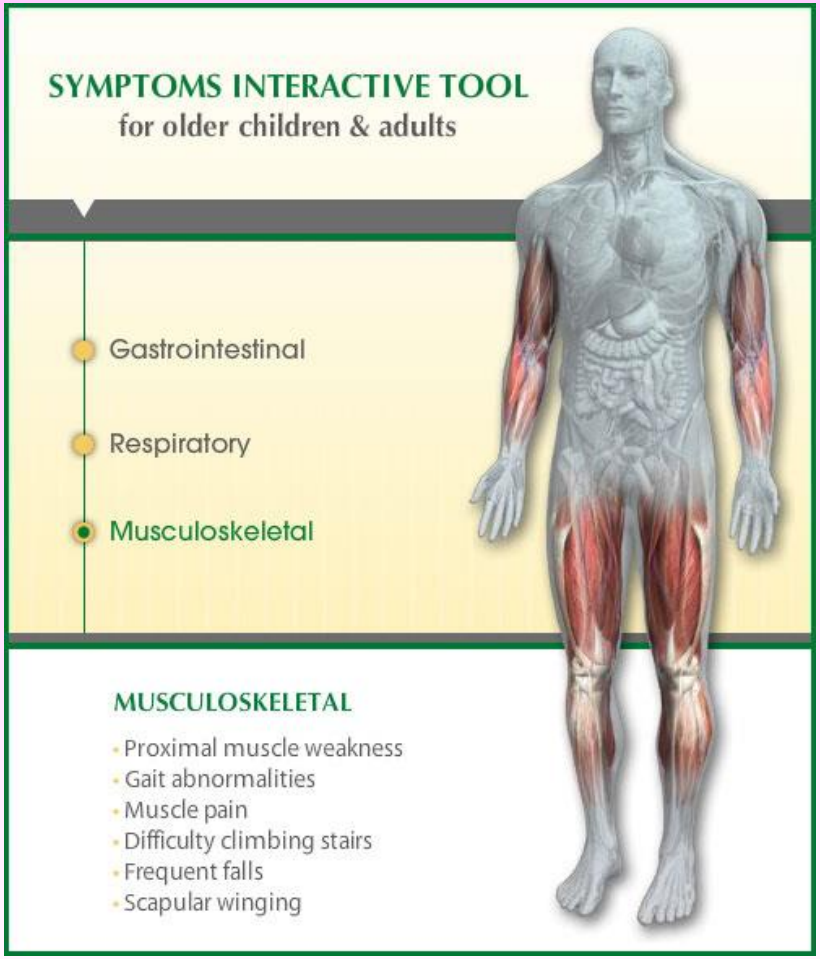


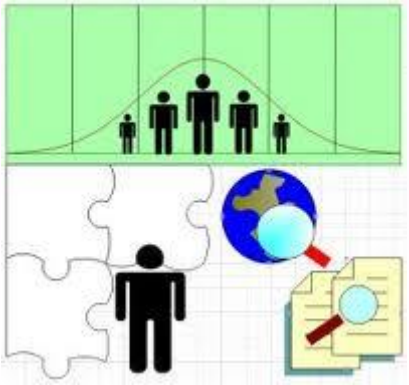


Epidemiology

- Prevalency 1/40 000 do 1/300 000
- **Rare but underdiagnosed disease**

- **The number of adult, late onset, patients is underestimated**





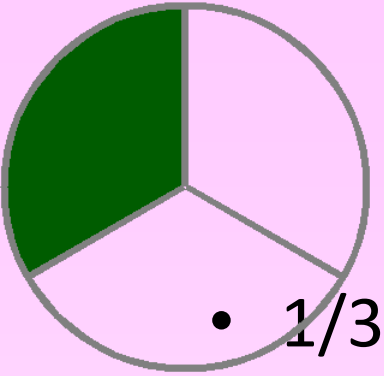
Diagnosis of PD

Classic PD (typical)

- Elevated CK, AST,ALT, LD
- Floppy infant sy
- Chest X ray
- Heart ultrasound

Adult, late form of PD

- CK or AST or ALT or LD may be normal
- EMG may be normal
- Heart: normal
- ECG: arrythmia, WPW



Late onset, adult PD

- 1/3 of PD patients needs respiratory support. Acute respiratory insufficiency may be the first sign of sdult PD
- 1/3 of PD patients has only respiratory symptoms
- **1/3 of PD patients is in wheelchair without diagnose**
- **Who are other undiagnosed adult PD patients?**
- **Patients with elevated liver enzymes of unknown cause, overdiagnosed statine myopathies...**

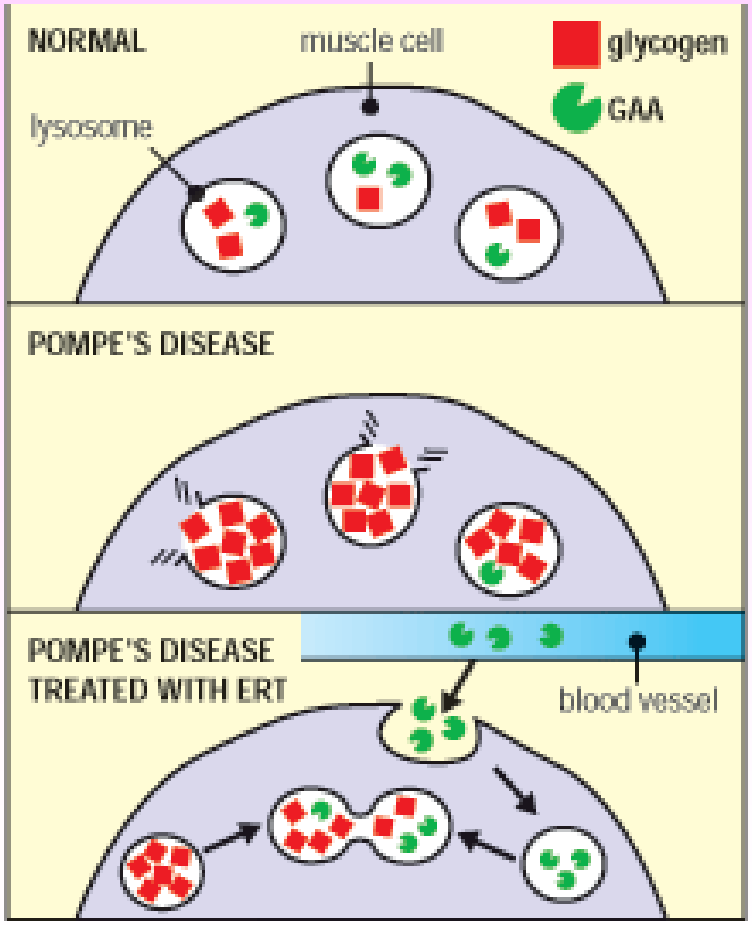
Dietary measurements, exercise

- High proteine intake
- Energy from proteins!
- The exercise regimen: **20-40 sec of exercise followed by rest**

Today we have effective PD treatment with enzyme substitution therapy

- The first investigations: 1974-1980, the enzyme was administred intrathecally and intravenous
- In the begening the source of AAG was human placenta

- **Only the AAG gene cloning made possible wide administration of effective doses of human AAG**



The enzyme ready for PD treatment:

- Spring 2006. in USA and Europe
- ***Myozyme (Genzyme)***
- Safe and effective for long-terme treatment
- It is important to start **early treatment**
- **Good results even in adult form of PD**

The PD patients and Myozyme in real life:

Atypical PD

- The boy, 11 y old in wheelchare
- **After 72 weeks of Myozyme treatment able to stand from sitting position**
- After 96 weeks able to play football

Typical PD

- Baby girl with congenital clinical prestentation, floppy infant sy
- **After 1 y of Myozyme treatment able to sit and craw**

The movie "Extraordinary Measures"

Big love, hard work and happy end

- ...the real story began 20 years ago at Duke University Medical Center when pediatric geneticist Y.T. Chen, MD, PhD, began work on the first and only life-saving treatment for Pompe.

- In 2006, the FDA approved the use of Myozyme, which is manufactured and marketed by Genzyme Corporation, based on Duke's research...

Going back to the title slide …

- Q: **Why is it important to think on Pompe disease?**

- A: Because it is **treatable congenital muscle disease** and early recognition of the disease and early treatment my prevent or delay muscle damage and weakness

Thank you☺

ervina.bilic@mef.hr

Referral Center for Neuromuscular Diseases and Clinical Electromyoneurography Ministry of Health Republic of Croatia