Screening Programme and Information Campaign for Adult Pompe disease in Czech Republic: Results and Edification

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Pompe disease

- **Joannes Cassianus Pompe** (1901-1945) was a Dutch pathologist
- In 1932 he reported a girl of 7 months, who suffered and died to extreme hypertrophy of the heart
- He was executed by the German army in April 1945 for espionage

- **Glycogen storage disease type II** (GSD II or **acid maltase deficiency**

Over idiopatische hypertrophy van het hart. Nederlandsch Tijdschrift vor Geneeskunde, Amsterdam, 1932; 76: 304.
Cardiomegalia glycogenica (glycogenic cardiomegaly). Doctoral thesis. Amsterdam : Dekker & Van de vegt NV. Nijmegen-Utrecht, 1936.

Pompe disease- facts

- PD is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid α-glucosidase (GAA)
- Lysosomal glycogen accumulates in many tissues with prominent involvement of skeletal, cardiac, and smooth muscles
- Classic infantile PD
- Adult-onset form
  - slowly progressive myopathy predominantly involving skeletal muscles that can present as late as the second to sixth decade of life

Pompe disease- facts

- **Adult- onset**
  - No cardiac involvement
  - Limb girdle muscle weakness
    - UE 73%, LE 89%
  - Trunk weakness
    - 65%
  - Respiratory problems
    - 66%
    - Exercise intolerance
    - Respiratory failure
      - Involvement of diaphragm
  - CK elevation

No specific signs or symptoms

Age distribution

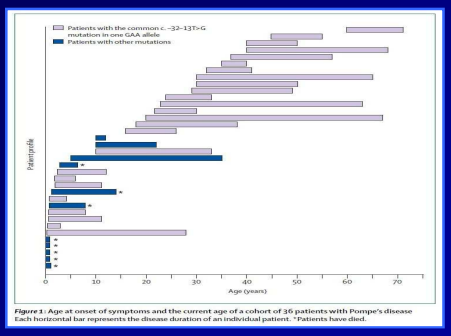


Figure 1: Age at onset of symptoms and the current age of a cohort of 36 patients with Pompe's disease
Each horizontal bar represents the disease duration of an individual patient. *Patients have died.

Van der Ploeg AT, Reuser.A.J.J. Pompe Disease. Lancet 2008; 372: 1342-53

Pompe disease – Europe 2008

	Population (mil)	No of patients
The Netherlands	16	106
Austria	10	13
Belgium	10	30
Portugal	10	13
Hungary	10	6
Czech Republic	**10**	**4***
Switzerland	7	9

Aim of the study

- To the present time no patient with adult form was discovered in Czech population, despite of the fact that the incidence of all forms of PD is estimated to be 1:40,000.
- Therefore we suppose that these patients are living covered by other false diagnoses, esp. limb girdle muscular dystrophy.
- With regard to the new enzyme replacement therapy and simple and reliable diagnostic screening tool (dried blood spots on filter paper) we aimed to uncover previously undiagnosed adult PD patients among persons with muscle weakness of uncertain or unknown etiology.

Situation in CR / 2008

- 4 established patients
  - Children
- Theoretical prevalence >35

Candidates for screening using DBS

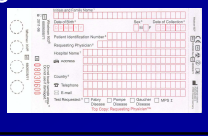
- Patients with muscle weakness of unknown etiology
- Patient with abnormal CK level*

*Fernandez C et al. Diagnostic evaluation of clinically normal subjects with chronic hyperCKemia NEUROLOGY 2006;66:1585–1587

- 2008- distributed more than **300** diagnostic sets
  - To the members of Czech Neuromuscular Society (CNS)
  - To departments of neurology in hospitals
  - To other neurologists who are asked for diagnostic set via web pages of CNS
- **Two hundred** information and diagnostic sets were delivered directly to the patients
  - Members of Czech Muscular Dystrophy Association
  - Two other organization of disabled people in Czech Republic

Diagnostic set

- Informed consent
- Information for professionals
- Test strip for DBS
- Envelope and small plastic bags for test strips
- Information about patients



Information part

- Informed consent
- Information letter and short project summary
- Project flow-chart
- Instructions for DBS
- Information about patient




How to ask for the diagnostic set?

- **Phone hot-line**
- **Web pages of Czech Neuromuscular Society**

Information campaign

- Medical staff
  - Lectures and articles for neurologists
- Patients
  - Lectures on meetings and articles in patient's magazines

Results

- To the end of December 2010 **219** specimens were returned and examined
  - Return rate 44%
- Five positive cases were discovered
  - Confirmation
    - GAA activity in peripheral blood leucocytes
    - DNA testing

Results

	2008	2009	2010	Posit.
Patients UH Brno	29	32	21	2
Other neurologists CR	5	44	16	3
AMD meetings	2	8	0	0
AMD- packages	0	62	0	0
All	36	146	37	5

Results

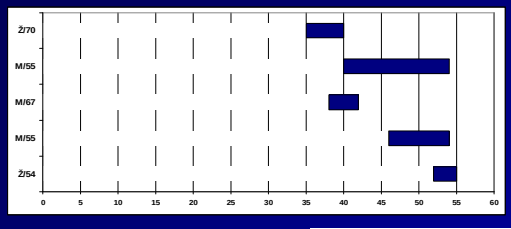
	n	positive
Weakness	209	5
Apnea	8	0
Hyper CK	2	0
All	219	5

Signs and symptoms

Sex/YoB	Signs	Walk	FVC	AV	CK	DNA
F/55	UE, LE	100 m Crutches		no	8,8	c. -32-13T>G / c.307T>G
M/55	Trunk	100 m	4,3	no	4,4	c. -32-13T>G / c. -32-13T>G
M/67	UE, LE, R*	unable, wheelchair, AV	1,5 *	Yes	12,8	c. -32-13T>G / c. 295_314del20
M/55	UE, LE, R	20-30 m Crutches	2,9/ 1,6	no	3,7	c.1655T>C (p.L552P) / p.P493L*
F/70	UE, LE, Trunk	without restriction	3,0	no	18,0	c.-32-13T>G / c.307T>G

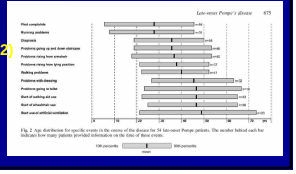
*new mutation

Diagnostic gap



Mean age of manifestation 42 years (35-52)

Mean 7 years (Pompe registry 2011- 8 y)



Questions and edification

- Geographic distribution
- The resignation of the majority of patients on final diagnosis
- Diagnosis focused registries and databases
- Dispersal of patients
  - Many doctors, different specialists

Geography

Thank you for your attention