

Diagnosis of Pompe Disease: Timing and Methods Used as Reported to the Pompe Registry

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Introduction

Pompe Disease

Pompe disease (acid maltase deficiency) is a rare, genetic, metabolic myopathy characterized by deficiency of the enzyme acid α -glucosidase (GAA). GAA deficiency leads to the abnormal accumulation of lysosomal glycogen and eventually causes progressive, debilitating myopathy with weakness of the skeletal, respiratory, and cardiac muscle. Clinical manifestations of the disease vary significantly with respect to age at onset, rate of disease progression, and extent of organ involvement.

The Pompe Registry

- The Pompe Registry was developed to enhance the understanding of Pompe disease by collecting data on disease identification, progression, variability, and natural history. The Registry captures clinically relevant data such as the time from symptom onset to disease diagnosis.
- In the short term, physicians may use the Registry data to compare individual patient parameters with those of a larger patient cohort worldwide in real time.
- In the long term, collected data should better characterize the Pompe disease population and provide insight into the effectiveness and safety of various treatment options.
- This information may be used by the medical community to develop disease-specific recommendations for the monitoring and treatment of patients.

Methods

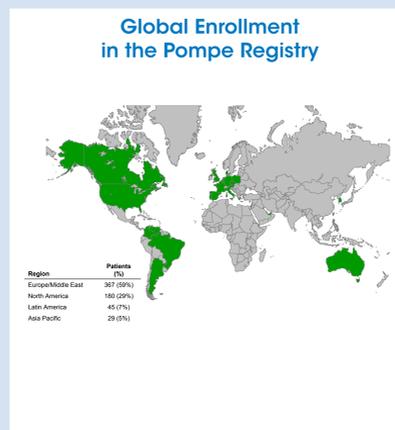
- The Pompe Registry is a voluntary, global, observational program collecting data on all patients with Pompe disease regardless of age, clinical presentation, or treatment status.
- All patient data are confidential and de-identified (referenced by number only). Analyses are based on the number of patients with available data for a given parameter.
- Parameters assessed for this work included country of residence, age at symptom onset and diagnosis, genotype, and predominant symptoms.
- Patients are categorized according to age at onset of Pompe symptoms, based on the earliest symptom onset date reported to the Registry.

Patients were divided into two groups: those with symptom onset at age 12 months or younger and those with symptom onset at any age greater than 12 months.

Patients with no symptom onset information are excluded from analyses stratified by age at symptom onset.

Data Overview

- As of January 2009, 621 patients, predominantly from the US and Europe (86%), were enrolled in the Pompe Registry. In all, 26 countries are represented.

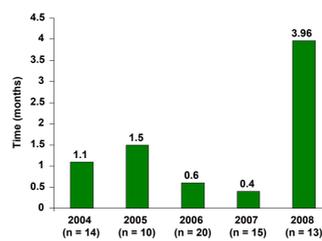


- The majority of patients are Caucasian (72%); 7% are Asian, 3% are Hispanic, 3% are black, and 12% have unknown race or ethnicity.

Pompe Disease in Patients ≤ 12 Months of Age at Symptom Onset

- 143 patients were reported to have onset of symptoms at ≤ 12 months of age
 - Median age at symptom onset 3 months
 - Median age at diagnosis was 4.7 months
- Median time from symptom onset to diagnosis was 1.8 months.

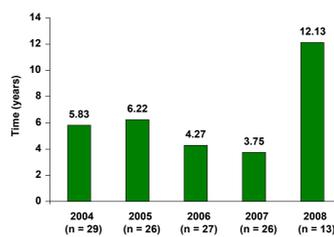
Time from Symptom Onset to Diagnosis in Patients ≤ 12 Months of Age at Symptom Onset



Pompe Disease in Patients > 12 Months of Age at Symptom Onset

- 424 patients were reported to have onset of symptoms at > 12 months of age
 - Median age at symptom onset was 27.6 years
 - Median age at diagnosis was 35.8 years
- Median time from symptom onset to diagnosis was 4.25 years.

Time from Symptom Onset to Diagnosis in Patients with Symptom Onset > 12 Months of Age



Diagnostic Methods

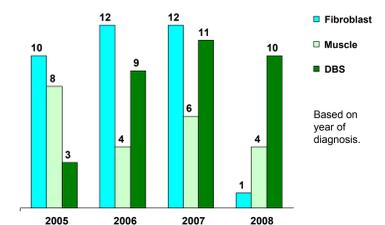
- Pompe disease is usually suspected based on clinical presentation or family history.
- Diagnosis can be confirmed by the identification of absent or deficient GAA enzyme activity or the presence of two disease causing GAA gene mutations.
- GAA enzyme activity can be measured in skin fibroblasts, muscle tissue, lymphocytes, or leukocytes.
- Reported method of diagnosis (n=567) reveals 429 (76%) used GAA enzyme assay
 - Cultured skin fibroblasts (150/429 or 35%)
 - Muscle tissue (131/429 or 31%)
 - Leukocytes (123/429 or 29%)
 - Lymphocytes (115/429 or 27%)
 - Dried blood spot (42/429 or 10%)
 - More than one assay method (125/429 or 29%)
- 174/567 (31%) used DNA analysis (more than one sample source of diagnostic method can be reported)
- Diagnosis confirmed with more than one method (235/567 or 41%)

Enzyme Assay	Patients with diagnostic information reported	
	Infantile-Onset (n=143)	Late-Onset (n=424)
Fibroblast	120 (87%)	309 (75%)
Lymphocyte	57 (48%)	93 (30%)
Muscle	19 (16%)	112 (36%)
Leukocyte	33 (28%)	90 (29%)
DBS	19 (16%)	23 (7%)
Other	7 (6%)	18 (6%)
>1 assay method	43 (36%)	82 (27%)
DNA analysis	55 (40%)	119 (29%)
Other*	51 (37%)	172 (42%)
Diagnosis confirmed with more than one method	74 (54%)	161 (39%)

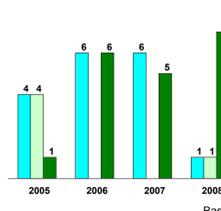
* Other includes primarily muscle or skin biopsy or presence of vacuolated lymphocytes

Change in Enzyme Assay Methods

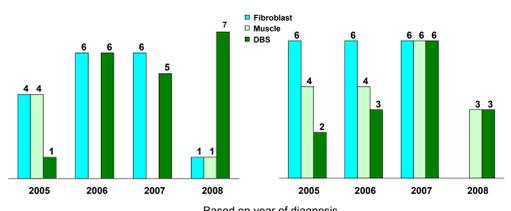
All Patients



Patients with symptom onset ≤ 12 months of age



Patients with symptom onset > 12 months of age



Discussion and Conclusions

- Pompe disease is a progressive metabolic myopathy with variable age of onset, severity, and rate of progression.
- As of January 2009, there were 621 patients with Pompe disease from around the world enrolled in the Pompe Registry.
- Preliminary data in these patients highlight a delay in diagnosis. Progress in diagnostic delay is likely the result of increased disease awareness and blood-based diagnostic procedures.
- Earlier diagnosis is critical and will be made possible by improved awareness of the disease and diagnostic testing.
- Diagnosis of patients in the Registry was done primarily through GAA enzyme assay of skin fibroblasts, lymphocytes, leukocytes, or muscle tissue. DNA analysis was also used although less frequently.
- As the Pompe Registry matures, data on symptom prevalence and age at symptom onset in various patient subgroups may allow physicians to identify patients at an earlier stage in the disease.