to generalized muscle weakness and cardiorespiratory failure within the first year of life, more slowly progressive phenotypes exist, with symptom onset varying from early childhood to late adulthood. In these 'milder' phenotypes, respiratory muscle weakness is a common feature, leading to ventilator dependency in a substantial number of patients. However, the proportion of patients with pulmonary involvement, the extent of diaphragmatic weakness and the relation with the severity of skeletal muscle weakness are not well studied in a large population. *Methods:* Pulmonary function was evaluated through spirometry in sitting and supine position, measurement of maximum inspiratory and expiratory pressures and capnography in a cohort of 20 children and 70 adults with Pompe disease. *Results:* Vital capacity (VC) was reduced in 55% of patients in sitting and in 75% of patients in supine position. Twenty-six patients (29%) used artificial ventilation either non-invasive ($n = 20$) or invasive ($n = 6$). Time between symptom onset and start of ventilatory support was on average 15 years. Forty-two patients (47%) had signs of diaphragmatic weakness, manifested by a difference between VC in sitting and supine position of more than 20% or a substantial decrease in maximum inspiratory pressures. Capnography showed signs of hypoventilation in ten patients, of which five used artificial ventilation. These patients had also clinical signs of increased ventilatory need, indicating inadequately adjusted respiratory support. In general, the degree of respiratory muscle weakness related to the extent of skeletal muscle weakness. *Conclusion:* Detailed evaluation of pulmonary function in children and adults with Pompe disease showed a decreased pulmonary function in over 50% of patients. This highlights the need for pulmonary function testing in all patients during follow-up to discover and treat respiratory problems in an early stage, preventing acute respiratory failure.

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G.P.11.11

Phenotypes of Pompe disease siblings

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Background: Late onset Pompe disease (glycogen storage disease type II, acid maltase deficiency) is an autosomal recessive myopathy with progressive weakness of proximal skeletal musculature and diaphragm. Most patients are compound heterozygotes, with a T>G mutation of Intron 1 in one allele and one of many other sequence abnormalities in the α-glucosidase gene. However published genotype/phenotype correlations do not yet provide prognostic guidance. *Objective:* To study intra-familial variability of disease history in Pompe siblings. *Methods:* Related patients were extracted from the French Pompe Registry ($N = 62$) and interviewed. We found 12 sib-ships; 7 of two, 4 of three and 1 of four siblings. *Results:* Mean age was 56 years (range 35–72), 43% females and 57% males. Where genetic data were available, the same mutations were present in each affected sibling. The common intron 1 'IVS1' mutation was present in 83%. Onset of troublesome symptoms occurred at 38 ± 14 years. These were lower limb muscle weakness in 88%. None had initial respiratory symptoms. The difference in age at symptom onset between adjacent siblings was 8 ± 8 years. Use of mobility aids (handrails or walking stick) occurred in 87%, at 41 ± 14 years, with a mean age difference between sibs of 8 ± 7 years at first use. Diagnosis occurred at 47 ± 17 years. Eleven patients required ventilatory support, usually nocturnal CPAP, from 51 ± 18 years. At least half the sib-ships presented variability (more than 8 years difference between siblings) in age of use of wheelchair or ventilator. *Conclusion:* Siblings with late-onset Pompe disease did not all follow the same clinical course, with substantial variability between siblings in half the sib-ships. This information may be useful in advising adult Pompe patients with previously diagnosed siblings.

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G.P.11.12

Tongue weakness in Pompe disease

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Glycogenosis type II or Pompe disease (PD), is an autosomal recessive lysosomal storage disease caused by a deficiency of acid alpha-glucosidase. Diagnosis in adult onset forms (AOPD) can be confirmed by biochemical tests avoiding a muscle biopsy. Early respiratory muscle weakness has been recognized as a common finding. Nevertheless suspicion and clinical diagnosis is difficult due to its similarity with many other neuromuscular diseases like LGMD's, FSH, adult SMA, Duchenne or Becker dystrophies among others. 11 AOPD from minimally affected to severely disabled forms, with ages ranging from 13 to 46 were fully clinically evaluated with manual muscle and quantitative muscle testing using the CINRG QMS. Besides skeletal and respiratory weakness all patients, even the so called presymptomatic, were found to have some degree of tongue weakness under careful examination. Weakness was manually assessed through the cheek and with the tongue sticking out and pushing laterally. Two patients complained of having difficulties handling food in the mouth and both had slurred speech. One presymptomatic case with completely normal MMT showed tongue weakness as well. Conclusion Tongue weakness is an early feature in AOPD and may help in its clinical recognition.

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DYSTROPHINOPATHY - CLINICAL OBSERVATIONS; POSTER PRESENTATIONS

G.P.12.01

Epidemiology of the dystrophinopathies in the Netherlands

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Introduction: The development of clinical trials for Duchenne muscular dystrophy (DMD) patients requires solid data on the epidemiology and natural history of both Duchenne and Becker muscular dystrophy (BMD). The densely populated Netherlands with 16 million inhabitants forms a good candidate for epidemiological and natural history studies. *Material and methods:* Care for DMD patients in the Netherlands is concentrated in university neuromuscular centers and rehabilitation hospitals, while diagnostic genetic testing for DMD has been centralized in the LUMC since 1983. Most Dutch patients are members of one or both patient organisations (Vereniging Spierziekten Nederland (VSN) and Duchenne Parent Project (DPP)). These centers and patient organisations are united in the ALADIN consortium (All Against Duchenne in the Netherlands). Since 2003 a national neuromuscular database CRAMP (Computer Register for All Myopathies and Polyneuropathies) is available. Through all these organisations a large part of the patients with a dystrophinopathy can be reached. *Results:* The LUMC genetic database