variability among affected individuals; those severely affected displayed foot drop and hypotonia from the first year of life and became wheelchair bound in the sixth decade of life, whereas less affected family members did not notice weakness until early adulthood. Nerve conduction studies showed mixed results. One family member had a slightly elevated compound muscle action potential (CMAP; 7 mV), and a low motor unit number estimation (MUNE; 59), compatible with a neurogenic etiology.

Another affected family member had a mixed myopathic/neuromyopathic EMG with both large and small amplitude polyphasic motor units, possible early recruitment in one muscle, and no spontaneous activity. Linkage analysis revealed forty-eight genes located in a 4.8 Mb region on chromosome 1, with a LOD score >3. Exon sequencing showed only one non-synonymous variant located in this region that passed SIFT testing and is not a known variant in dbSNP, a c.591C>A p.Glu197Asp change in exon 4 of ACTA1. Mutations or polymorphisms in this highly conserved residue of ACTA1 have not been seen previously. ACTA1 is a highly conserved alpha actin expressed in skeletal muscle. Mutations in this gene have been implicated in nemaline myopathy, actin aggregate myopathy, fiber-type disproportion, and core myopathy. This family may represent a new milder but progressive phenotype associated with a novel ACTA1 mutation.

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P3.49
Myopathy associated with mutations in CHKB in three UK patients
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A new entity of congenital myopathy in Japanese and Turkish children caused by autosomal recessive mutations in the gene encoding for choline kinase beta (CHKB) was recently described by Nishino et al. We describe the clinical features of three caucasian British patients with the condition, confirmed by genetic analysis. We found a spectrum of severity from severe: presenting with learning difficulty, autism, ichthyosis and early death from cardiomyopathy to a milder phenotype in a female patient who is now in her early twenties. She presented with progressive limb girdle weakness from early childhood, calf hypertrophy, myalgia, learning difficulties and a mildly elevated serum CK activity (600 U/l), The third patient had intermediate features with a small discrete area of linear ichthyosis on the upper trunk. Brain imaging was normal, brain magnetic resonance imaging showed mixed results. One family member had a slightly elevated CMAP and a low MUNE with both large and small amplitude polyphasic motor units, possible early recruitment in one muscle, and no spontaneous activity. Linkage analysis revealed forty-eight genes located in a 4.8 Mb region on chromosome 1, with a LOD score >3. Exon sequencing showed only one non-synonymous variant located in this region that passed SIFT testing and is not a known variant in dbSNP, a c.591C>A p.Glu197Asp change in exon 4 of ACTA1. Mutations or polymorphisms in this highly conserved residue of ACTA1 have not been seen previously. ACTA1 is a highly conserved alpha actin expressed in skeletal muscle. Mutations in this gene have been implicated in nemaline myopathy, actin aggregate myopathy, fiber-type disproportion, and core myopathy. This family may represent a new milder but progressive phenotype associated with a novel ACTA1 mutation.

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P3.50
Autophagic vacuolar myopathy in a girl
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Autophagic vacuolar myopathies (AVM) are defined as a group of diseases sharing an important morphological hallmark which is the occurrence of autophagic vacuoles. A subgroup of AVM is characterized by the sarcolemmal features of its autophagic vacuoles (AVSF). Based on this classification, several diseases with different etiologies, phenotypes and morphologies are related including acid maltase deficiency, Danon disease, infantile autophagic vacuolar myopathy and X-linked myopathy with excessive autophagy (XMEA). XMEA is a hereditary AVM that affects preferentially proximal muscles of male children, with slow progression of muscle weakness, without cardiac, respiratory or central nervous system involvement. EMG shows myotonic features without clinical signs of myotonia. XMEA is morphologically characterized by the occurrence of numerous AVSF with complement membrane attack complex (MAC) immunoreactivity, intense exocytosis and redundant muscle fiber basal lamina. Calcium deposits are also observed near the sarcolemma. We present a 12 year old girl displaying proximal muscle weakness in lower limbs, elevated creatine kinase and aldolase, normal nerve conduction velocity, and myotonic features in EMG, without evidence of myotonia. Molecular investigation for Steinert Myotonic Dystrophy had normal result. Karyotype is normal (46, XX), excluding the possibility of a translocation X-autosome. Lysosomal and alpha-glycosidase tests were normal. Histological analysis of the muscle demonstrated vacuoles with immunoreexpression of dystrophin, spectrin, dystroglycan, merosin, sarcoglycan and MAC. Ultrastructural examination revealed autophagic vacuoles lined by luminal basal lamina displaying exocytosis associated with redundant basal lamina and macrophages. This is the second report of female cases of AVM with sarcolemmal features in the literature. Further investigation may reveal if the patient is a carrier of XMEA or a new form of AVM with a similar phenotype.

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P3.51
A new form of autosomal recessive myopathy associated with male hypogonadism links to chromosome 11q
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We describe a new form of myopathy that fits best within the congenital myopathy spectrum of disorders. Three adult siblings (two males, one female) have congenital-onset mild generalised static muscle weakness. Their parents have normal muscle strength and are second cousins, making autosomal recessive inheritance most likely. The affected children walked between ages 16 and 20 months, have always required the handrail to climb stairs and have waddling gait. Muscle strength is MRC scale 4+ in most muscle groups with sparing of facial and ocular muscles. Both affected male siblings have hypogonadism associated with oligospermia and require testosterone replacement therapy. The female sibling had normal fertility. All siblings report intermittent paraesthesias and muscle aches. There is also a family history of ocular abnormalities (severe myopia, retinal detachment, glaucoma and cataracts) that likely follows an autosomal dominant inheritance pattern, affecting the two male siblings.
POMPE DISEASE: POSTER PRESENTATIONS

P3.52
Risk of dysrhythmic cardiomyopathy may be considered in patients with adult onset Pompe disease
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Pompe disease is an autosomal recessive disorder caused by deficiency of the lysosomal enzyme acid alpha-glucosidase. Adult onset subtype presents with progressive proximal weakness and respiratory insufficiency. Using quantitative MRI, we report here muscle changes resulting from a 24-month enzyme replacement therapy (ERT) in 3 adult-onset Pompe disease patients. ERT was administered every two weeks in three men. Patients were assessed by a standardized protocol including manual muscle testing, quantitative muscle testing, six-minute walking test (6MWT), respiratory evaluation. Quantitative MRI of thigh muscles including T1-weighted and T2 maps was performed at 1.5T (Siemens Vision Plus and Avanto) at baseline and after the 24-month treatment period. A previously-described segmentation method (Mattei et al, MAGMA 2006) was used in order to quantify relative fat and muscle volumes. Mean age at onset was 34.4 years while therapy was started at 43 years. Clinical assessment showed improvement in 2 patients for the 6MWT. Qualitative MRI assessment showed a marked progression of fatty degeneration in 2 patients. Quantitatively, MRI measurements illustrated a 25% loss of the thigh muscle mass (from 63% of the total thigh volume at T0 to 45% at T24). This muscle loss was associated to an increased fat volume (subcutaneous and intra-muscular) from 36% at T0 to 52% at T24. A large between-subjects variability of muscle alterations was observed in our small group before and after the 24-month treatment period. At this stage, an overall clinical stability was observed whereas a significant progression of fatty degeneration and a decrease of the thigh muscle volume were measured. These interesting findings question the irreversibility of muscle alterations in Pompe disease and raise the potential interest of an earlier treatment. This issue would have to be further investigated in a larger group of patients.

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P3.53
Quantitative muscle MRI findings in three patients with adult-onset Pompe disease after a 24-month enzyme replacement therapy
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Pompe disease is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase. Adult onset subtype presents with progressive proximal weakness and respiratory insufficiency. Using quantitative MRI, we report here muscle changes resulting from a 24-month enzyme replacement therapy (ERT) in 3 adult-onset Pompe disease patients. ERT was administered every two weeks in three men. Patients were assessed by a standardized protocol including manual muscle testing, quantitative muscle testing, six-minute walking test (6MWT), respiratory evaluation. Quantitative MRI of thigh muscles including T1-weighted and T2 maps was performed at 1.5T (Siemens Vision Plus and Avanto) at baseline and after the 24-month treatment period. A previously-described segmentation method (Mattei et al, MAGMA 2006) was used in order to quantify relative fat and muscle volumes. Mean age at onset was 34.4 years while therapy was started at 43 years. Clinical assessment showed improvement in 2 patients for the 6MWT. Qualitative MRI assessment showed a marked progression of fatty degeneration in 2 patients. Quantitatively, MRI measurements illustrated a 25% loss of the thigh muscle mass (from 63% of the total thigh volume at T0 to 45% at T24). This muscle loss was associated to an increased fat volume (subcutaneous and intra-muscular) from 36% at T0 to 52% at T24. A large between-subjects variability of muscle alterations was observed in our small group before and after the 24-month treatment period. At this stage, an overall clinical stability was observed whereas a significant progression of fatty degeneration and a decrease of the thigh muscle volume were measured. These interesting findings question the irreversibility of muscle alterations in Pompe disease and raise the potential interest of an earlier treatment. This issue would have to be further investigated in a larger group of patients.

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P3.54
Auditory system involvement study in 20 patients with late onset Pompe disease
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 Glycogen storage disease type II (GSD II), also known as Pompe disease, is an autosomal recessive inherited disorder, caused by a reduced activity of the alpha-glucosidase. Two different clinical forms have been described: a rapidly fatal infantile form and a late onset form. Hearing loss has been described in classic infantile Pompe patients (Van Capelle C. et al., 2010) but, so far, no extensive studies have been performed in the late onset form. The main purpose of this study was to investigate the possible involvement of the auditory system in a cohort of patients with the late onset GSD II. We have enrolled 20 patients with late onset GSD II, 12 males and 8 females. The age range was from 8 to 74 years.