

## P11

Poster

**UK NorthStar Neuromuscular Clinical Network (NSCN): National audit results in Duchenne muscular dystrophy (DMD) corticosteroid practice, vitamin D status and bone health**

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The North Star Clinical Network (NSCN) is a collaboration of seventeen UK centres. The network aim is to develop consensus on best DMD clinical management, with agreed assessment and treatment protocols. Longitudinal data regarding DMD is collected in a web-based database, which enabled these national audits:

**Corticosteroid treatment in DMD in UK:** Data from 240 ambulant boys with DMD (age range 3–18 years) is available. Median age at diagnosis was 4.1 years. 223 were treated with corticosteroids; median age at steroid initiation was 6.3 years (N=203). Starting corticosteroid was prednisolone in 203 and Deflazacort in 10. Starting corticosteroid regime was intermittent (10 days on, 10/20 days off) in 117 and daily in 83 patients.

**Vit D status prior to corticosteroid treatment:** Vitamin D levels in 157 boys. 25 OH Vit D levels were deficient (>37.5 nmol/L) in 91 boys (58%) and insufficient (37.5–50.0 nmol/L) in another 31 boys (20%).

**Vertebral Fractures (VF) in corticosteroid treated DMD:** VF occurred in 30 steroid treated boys at a mean age of 11.5 years (range 7.1–15.5); 78% were symptomatic. Mean latency, from start of steroids to VF, was 4.1 yrs (0.7–7.4). 28/30 were on daily corticosteroid regime at the time of VF. These results informed 2009 ENMC workshop recommendations for bone health in DMD.

The NSCN and its database provide a unique tool to optimise clinical practice on a national level and facilitate translational research.

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## P12

Poster

**An audit of bone density and vertebral fractures during steroid treatment in Duchenne muscular dystrophy**

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Osteoporosis and an increased fracture risk are common in Duchenne muscular dystrophy (DMD). Corticosteroid therapy (CS) given to prolong mobility increases the severity of osteoporosis and risk of vertebral fractures which can have serious functional consequences.

We reviewed case notes of 22 patients with DMD, to examine the effect of CS on BMD (spinal BMD z-scores) and vertebral fractures and oral residronate treatment.

**Results:** 19/22 patients were treated with corticosteroids. Mean age at start of treatment was 7.93 yr (5.03–15.39) and mean steroid duration was 4.1 years (0.5–6). During the steroid treatment eight fractures (two vertebral and six long bones) were reported. Two patients had vertebral fractures (one asymptomatic and one traumatic) reported on routine X-ray screening. A greater number of patients demonstrated minor vertebral changes. Mean time interval between starting steroids and vertebral fractures was 4.47 yr (4.07–4.87).

Mean spine BMD z-score was not low before or within 3 months of start of steroid treatment, mean -1.12 (2.12 to -3.13). At 2 years post steroid treatment BMD z-score was significantly lower, mean -1.6(0.7 to -3.3; binomial test, p<0.01).

On the basis of early X-ray changes and BMD seven patients on steroids were treated with 35 mg oral risedronate, fortnightly. Of the two vertebral fractures reported, one occurred while the patient

was on residronate. All patients tolerated oral residronate without side effects.

**Conclusions:** Boys with DMD, treated with steroids, are at risk of fractures. In steroid-treated boys, BMD z-score was significantly low after 2 yr. The incidence of vertebral fractures in this study group was low (10% vertebral fracture rate for 77.9 patient-years of steroid treatment). This may be due to early intervention with residronate, based on BMD and X-ray screening. Fortnightly oral residronate was well tolerated.

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*Limb Girdle Muscular Dystrophy*

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## P13

Poster

**Identification of a novel group of muscular dystrophies, the Anoctaminopathies, caused by recessive mutations in the putative calcium activated chloride channel, ANO5**

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The Anoctamin (ANO) family consists of 10 proteins several of which have been shown to correspond to the elusive calcium-activated chloride channels (CaCCs). CaCCs are gated by increases in intracellular calcium and they have been linked to several cellular functions including epithelial transport, cell volume regulation, olfactory and photoreceptor transduction, cardiac membrane excitability, and smooth muscle contraction. The only reported human mutations linked with the ANO family are dominant mutations in ANO5, which cause a rare bone fragility disorder gnathodiaphyseal dysplasia (GDD1). Recently we have identified recessive ANO5 mutations in patients with proximal limb girdle muscular dystrophy (LGMD2L) and a distal non-dysferlin Miyoshi myopathy (MMD3). The mutations identified consist of splice site, a single adenine duplication and missense. The duplicated adenine is present in LGMD2L and MMD3. The LGMD2L phenotype is characterized by proximal muscle weakness and prominent asymmetric quadriceps atrophy. The MMD3 phenotype is associated with distal weakness in particular of the calf muscles. The clinical heterogeneity associated with ANO5 mutations is reminiscent of that observed with dysferlin mutations which can cause both a LGMD and distal muscular dystrophy.

ANO5 mutations are associated with loss of muscle membrane integrity and defective membrane repair. Our studies suggest that ANO5 is a putative calcium-activated chloride channel which may function with dysferlin in membrane repair. Our study has identified a novel group of muscular dystrophies "the Anoctaminopathies".