

P4.09**Electrocardiographic abnormalities in Duchenne muscular dystrophy prior to the onset of cardiac dysfunction**J. James, K. Kinnett, Y. Wang, R. Ittenbach, L. Cripe*Cincinnati Children's Hospital Medical Center, The Heart Institute, Cincinnati, United States*

Background: Duchenne muscular dystrophy (DMD) presents with skeletal muscle weakness; cardiac involvement occurs later in the disease. The primary purpose was to estimate the proportion of young (<6 years) DMD patients with manifestations of cardiomyopathy using electrocardiography (ECG) and echocardiography. A secondary purpose was to estimate the relationship between dystrophin mutation site and an abnormal ECG. **Methods:** Database review identified 78 steroid-naïve DMD patients <6 years old. The initial ECG was analyzed, the site of dystrophin mutation identified and echocardiograms reviewed for abnormalities. Statistical analysis included estimating simple binomial proportions of ECG abnormalities. Chi-square tests were used to evaluate the relationship between genotype and ECG abnormalities. **Results:** In total, 61/78 ECGs (78%, CI95% = 69–87%) demonstrated at least one abnormality. The most common finding was left ventricular hypertrophy in 52/77 (68%, CI95% = 57–8%), followed by right ventricular hypertrophy in 17/77 (22% CI95% = 13–31%), biventricular hypertrophy (13/77, 17% CI95% = 9–25%), and prominent mid-precordial voltages (12/77, 16%, CI95% = 7–24%). Abnormal Q waves in lead III or V6 were present in 44/77 (57%, CI95% = 46–68%). None had left precordial ST segment depression. In the 58 of 78 patients with concurrent echocardiography, there was only one abnormal study (left ventricular dilation and depressed systolic function). There was no statistically significant relationship identified between ECG abnormalities and dystrophin genotype. **Conclusions:** ECG abnormalities are common in young DMD patients. While the exact mechanisms resulting in ECG changes are unknown, these data suggest that cardiac stress due to dystrophin deficiency is experienced well before the onset of detectable cardiac compromise. This data supports the concept that cardiac issues should be assessed early and remain an integral component of care.

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P4.10**Duchenne/Becker in the family: are women aware of the potential risks?**A.T.J. Helderma-van den Enden¹, J.C. van den Bergen², M.H. Breuning¹, J.J.G. Verschuuren², A. Tibben¹, E. Bakker¹, H.B. Ginjaar¹¹*Leiden University Medical Center, Center for Human and Clinical Genetics, Leiden, The Netherlands,* ²*Leiden University Medical Center, Department of Neurology, Leiden, The Netherlands*

Background: Duchenne muscular dystrophy (DMD) is the most common inherited neuromuscular disease. After identification of the mutation in the index patient, family members can be reliably investigated. Carriers should be informed about their risk of having offspring with the disease and about their own risk for cardiomyopathy for which regular cardiac surveillance is recommended. In a small country like the Netherlands with well organized genetic services, one would expect that most DMD families are adequately informed about the above mentioned risks for carriers. We have investigated whether women at risk had been tested at a molecular level. **Method:** In the national Duchenne/Becker database 311 DMD

and 99 BMD patients/families had been registered up to July 1, 2009. These families were asked to list the number of sisters and maternal aunts of the DMD/BMD patient and anything that was known about their genetic status and that of the mother. This information was compared with the information known at the genetic laboratory. **Findings:** Thirty-five out of 104 adult sisters/maternal aunts of DMD patients with a 50% risk of being a carrier and 45 out of 148 adult women with a 4.3% risk due to germ line mosaicism for DMD had not been tested by DNA analysis. **Conclusion:** Our study indicates that about one third of the potential carriers have not been tested. Given the possible far-reaching clinical consequences of being a carrier, further studies are needed to investigate the reasons why potential female carriers have not been tested.

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P4.11**Bone strength in boys with Duchenne muscular dystrophy (DMD): a longitudinal study**N. Crabtree¹, K. Ward², N. Shaw¹, H. Roper³, J. Adams², Z. Mughal²¹*Birmingham Children's Hospital, Birmingham, United Kingdom,* ²*St Mary's Hospital, Manchester, United Kingdom,* ³*Birmingham Heartlands Hospital, Birmingham, United Kingdom*

DMD is the most common childhood neuromuscular disorder causing loss of ambulation in early life. Steroids are currently used to improve muscle strength and prolong ambulation. The aim of this study was to compare longitudinal changes in bone strength in healthy children with longitudinal changes in bone strength in children with DMD, who either remained ambulant or lost independent ambulation during the period of follow-up.

Forty children were studied, 17 healthy boys (age 9.1 ± 1.5 years) and 23 boys with DMD (age 8.6 ± 2.1 years), taking intermittent steroids. PQCT was used to measure bone geometry, density and strength of the non-dominant tibia. Measurements were made at the distal metaphysis and mid diaphysis sites. Data were adjusted for age, height and duration of steroids.

After 15.0 ± 3.1 months, seven DMD boys lost independent ambulation. Longitudinal growth between the groups remained constant. In DMD boys who remained ambulant there was a slowing down in periosteal bone growth at the mid diaphysis (0.8 vs. 2.6 mm²/month; *p* < 0.05). Whereas for DMD boys who lost ambulation, there was a significant reduction in the rate of bone growth at the mid diaphysis (0.4 mm²/month; *p* < 0.05) and at the distal metaphysis (2.8 vs. 6.2 mm²/month). In contrast, the rate of change in bone density at the distal metaphysis (−2.8 vs. 0.3 mg/cm³/month; *p* < 0.001) and cortical bone mass (−0.2 vs. 1.3 mg/mm³/month; *p* < 0.001) & stress-strain index (2.0 vs. 9.9 mm³/month; *p* < 0.05) at the mid diaphysis was only significantly different from healthy boys in the seven boys who lost ambulation.

This data suggests that ambulation and hence muscle function & gravitational load has the greatest effect on bone strength and density in boys with DMD. Whilst they remain ambulant the effect of the relatively high dose steroids appears to be negligible. However, when they eventually lose independent ambulation significant losses in bone strength occurs as a direct result of both diminished periosteal bone growth and mineral accrual.

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