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MUSCLE DISORDERS

GENETICS OF FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

More than 500 subjects from 41 families with dominantly inherited facioscapulohumeral muscular dystrophy (FSHD) were studied at the Royal Hospital for Sick Children, St. Michael's Hill, Bristol and the University of Wales College of Medicine, Heath Park, Cardiff, Wales. 168 subjects were affected and 330 were unaffected. Dominant inheritance was proven in 28 families and no evidence for recessive inheritance was found in the remainder. New mutation accounted for six isolated cases. The prevalence of FSHD in Wales was estimated at 2/100,000. Estimates of penetrance values were less than 5% at 0-4 years, 21% at 5-9 years, 58% at 10-14 years, 86% at 15-19 years and 95% at 20 years and over. Early onset is associated with the greatest chance of disability in later life. Proximal lower limb weakness was present in 39% aged less than 20 years, 46% aged 20-40 years, and 68% aged more than 40 years. Asymmetry of scapular and upper limb involvement was evident in 65% of 113 affected subjects. Creatine kinase is elevated in 80% of affected males under 40 year and 48% of affected women, but use of CK as a presymptomatic test for FSHD is limited. There was no clinical evidence of significant genetic heterogeneity between the 11 largest families studied. (Lunt PW, Harper PS. Genetic counselling in facioscapulohumeral muscular dystrophy. J MED Genet Oct 1991; 28:655-664).

COMMENT. The genetic homogeneity for FSHD demonstrated in this study facilitates genetic counseling and answers to questions raised by family members. Different modes of presentation, particularly with respect to pelvic and peroneal involvement may be observed in various members of large kindreds. The recent assignment of the gene for

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FSHD to chromosome 4 will help to clarify some of the counseling issues, including families diagnosed as FSH type spinal muscular atrophy where the same genetic locus is involved. The risk of disability and wheelchair requirement in later life can be assessed by the reported age of onset and the occurrence of proximal lower limb weakness by age 20 years. The authors estimate that 19% of FSHD heteroxygotes will require a wheelchair by 40 years or over and 30% remain only mildly affected throughout life. Since asymmetry of weakness correlates with handedness, the overuse of limbs and particularly body building exercises should be discouraged.

HEAD CIRCUMFERENCE AND IQ IN DUCHENNE MD

The head circumferences of 64 patients with Duchenne muscular dystrophy were greater than normal and the intellectual performance tested by the Wechsler was significantly impaired in a study performed at The Royal Liverpool Children's Hospital, Alder Hey, Liverpool and The University of Newcastle upon Tyne. There was no correlation between head circumference and intellectual performance. Subsequent studies in 19 patients monitored with CT suggested that the large head was related to increased brain size (Appleton RE et al. Head circumference and intellectual performance of patients with Duchenne muscular dystrophy. Dev Med Child Neurol Oct 1991; 33:884-890).

COMMENT. These patients with DMD appear to have relative and, less frequently, absolute macrocephaly which was unrelated to height and showed some familial tendency, the fathers having larger heads. The cause of the macrocephaly and increased brain size was not determined. Macrocephaly was defined as relative if the head circumference was disproportionately large for height or absolute, if greater than the 97th centile. There was no correlation between the head circumference and intellectual performance of either the entire group of 47 patients or of the 12 patients with absolute macrocephaly.

The predictive value of a reduction in the size of the brain in the first year for mental retardation at 7 years has been investigated in 41 term infants with microcephaly. Half the microcephalic children were mentally retarded at the age of 7. Head size 2 standard deviations below the mean had a very low predictive value for mental retardation (11%). Disproportionate head-to-height ratio did not significantly affect outcome (Dolk H. Dev Med Child Neurol Nov 1991; 33:974-983). The study was based on the US National Collaborative Perinatal Project Data of over 50,000 pregnancies and was performed at the Department of Epidemiology, Catholic University of Louvain, Brussels, Belgium.

DYSTROPHIN IN LIMB-GIRDLE DYSTROPHY

Dystrophin content in muscle was analyzed by both immunofluorescence and immunoblot in 41 patients with a clinical diagnosis of limb-girdle muscular dystrophy seen at the National Institute of Neuroscience, Tokyo,