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,

Japan over a 12-year period. 17% showed a dystrophinopathy consistent with Becker (5 male patients) or carrier of Duchenne (2 female patients) muscular dystrophy. The misclassification of isolated male patients was 31% while that of isolated female patients was 13%. DNA analysis confirmed a dystrophin gene deletion in all five male Becker dystrophy patients identified. By analysis of this study together with two additional reports in the literature, the authors calculate that approximately 40% of isolated limb-girdle/Becker patients cannot be differentially diagnosed on the basis of clinical and histopathologic criteria. Dystrophin protein and gene studies are required for the accurate diagnosis of these patients and before appropriate genetic counseling can be provided (Arikawa E et al. The frequency of patients with dystrophin abnormalities in a limb-girdle patient population. Neurology Sept 1991; 41:1491-1496).

COMMENT. The study demonstrates the clinical overlap between limb-girdle muscular dystrophy and dystrophinopathies and emphasizes the necessity of dystrophin protein and gene studies for accurate diagnosis of isolated cases of muscular dystrophy.

Hoffman, EP et al, from the University of Pittsburgh School of Medicine, describe a novel, severe case of Duchenne muscular dystrophy with biochemical findings that were consistent with a Becker muscular dystrophy. The muscle contained substantial amounts of abnormal dystrophin and a unique intragenic gene deletion resulting in a dystrophin protein missing the carboxyl-terminal domain. This abnormal protein was more damaging to the myofibers than the absence of dystrophin would have been and supports the hypothesis that an intact carboxyl-terminus is crucial for correct dystrophin function. Previous studies have suggested that the carboxyl-terminus of dystrophin is important for normal dystrophin function. The patient described here had dystrophin that lacked the carboxyl-terminus domain yet it was clearly associated with the plasma membrane (Ann Neurol Oct 1991; 30:605-610).

Matsumura K et al, from the Department of Neurology, Shimoshizu National Hospital, Chiba, Tokyo, Japan, describe a Japanese family with both Fukuyama type congenital muscular dystrophy and Duchenne muscular dystrophy (J Child Neurol July 1991; 6:251-256). DNA analysis and the dystrophin test showed that dystrophin was expressed normally at the sarcoplasmic membrane of the Fukuyama phenotype patient but was completely absent in the Duchenne phenotype patient. Two different childhood muscular dystrophies coexisted in this family. The dystrophin test assisted in the differential diagnosis of the two diseases when DNA analysis by Southern blotting was not informative.