

## **Special Report: National Foundation - March of Dimes Clinical Genetics Conference on Muscle and Its Disorders—June 8-11, 1986, Philadelphia**

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The National Foundation-March of Dimes has reinstated the clinical genetics conferences that were so successful in the 1960s and 1970s. The earlier conferences focused on the delineation of birth defects. However, because of advances in molecular genetics, developmental genetics, and clinical genetics, a new format became desirable. The new March of Dimes clinical genetics conferences are aimed at providing a better understanding of a particular organ system. At this year's conference, the subject was muscle. Clinical and basic research dealing with normal and abnormal muscle differentiation, muscle biochemistry, and muscle function was presented, allowing clinicians and researchers to learn from each other's work.

Sir Andrew Huxley convened the conference with a historical overview of muscle disorders. Several presentations on molecular research related to the actin and myosin genes followed. Not only have these genes been mapped and their differences described, but the progressive switching on and off during development and in different tissues is becoming well defined. The mapping of specific genes that are tightly regulated during embryologic and fetal development was clearly outlined at the meeting. Much of this work has been done in culture of muscle cells, but there seemed to be correlations in different animal model systems and in muscle from various sites of the body.

The clinical aspects of well-

defined muscle disease, both dystrophies and metabolic disorders, were reviewed. However, a whole new set of specific disorders, many of which can now be understood on a molecular level, were reported by various investigators. Various aspects of myogenesis—both in normal and abnormal cells, and during development and in regeneration—were discussed, as were the interaction of nerve and muscle and the biochemistry related to those interactions.

Experiments of nature—in which individuals with muscular dystrophy have also been growth-hormone-deficient or have had denervation, as by polio, but have not developed the usual muscle deterioration—indicate that many environmental factors can affect genetically determined muscle

function and deterioration. It appears that the size of muscle cells in Duchenne's muscular dystrophy may be critical in the dystrophic process. Growth hormone deficiency can slow the rate of progression of muscular dystrophy, possibly by limiting the size of the muscle cell. This and other observations give hope that new approaches to symptomatic therapy can be found. Fortunately, new techniques for studying muscle size, composition, and function, such as nuclear magnetic resonance, are beginning to yield clues about normal muscle physiology at the molecular level and about the distribution of abnormalities within the muscle cells.

Many well-known syndromes in which the etiology has not been defined—such as Marfan,

Schwartz-Jampel, and Marinesco-Sjögren syndromes—were examined as possible muscular dystrophies.

Perhaps the most exciting recent advance has been the molecular analysis of the Duchenne's muscular dystrophy gene locus. Two approaches have been used: that of "walking" along the X chromosome and the use of DNA from girls with Duchenne's muscular dystrophy who have X-autosome translocations that can be studied on a molecular level. The area of the Duchenne gene is now starting to be "peppered" with probes that allow prenatal diagnosis and carrier detection. It is now considered likely that the gene locus for Becker's muscular dystrophy is either within or very close to that for Duchenne's muscular dystrophy.

Linkage analysis of other myopathies and muscle problems is improving as well. For example, the linkage of myotonic dystrophy, by using more closely linked genes, now enables much more accurate prenatal diagnosis and premorbid recognition.

In general, the conference was exciting and stimulating, because it encouraged interaction between basic research scientists and clinicians. It is exciting to see how much progress has been made in an area in which new findings and techniques can be rapidly applied to clinical conditions. We look forward to seeing this same approach being used in future March of Dimes conferences to elucidate other organ systems. In this way, birth defects and genetic diseases will be further delineated.