Meetings

Myopathies

The primary myopathies comprise a large group of presumably metabolic disorders affecting striated muscle in man and animals. Familial and sporadic forms of muscular dystrophies are probably the most important among the primary myopathies from a clinical point of view; the etiology of these diseases is unknown, and no effective therapeutic measures are available. The exploration of these as-yet obscure muscle conditions was the purpose of a symposium held in New York City, under the auspices of the New York Academy of Sciences. Meeting on 18 and 19 November 1965, a group of scientists from Australia, Europe, and America, including pathologists, electron microscopists, biochemists, geneticists, and clinicians, discussed the complex and many-faceted problems of experimental primary myopathies and their relationships to human muscle diseases.

In his opening address, A. T. Milhorat (Institute for Muscle Disease, New York) emphasized that a direct approach to the study of primary muscle diseases in man often presents technical difficulties, but the occurrence of myopathies as either inherited or experimentally induced conditions in a number of animal species now permits hitherto unfeasible investigations and is contributing to our knowledge of the biochemistry, genetics, and morphogenesis of muscular dystrophies and related disorders. The relatively recent discovery of the genetically determined type of muscular dystrophy in laboratory animals has created a great opportunity for research on naturally occurring primary myopathies, as contrasted with the nutritionally induced types. Detailed descriptions of such hereditary myopathies in three animals for which breeding data indicate an autosomal recessive mode of inheritance were presented: the mouse (W. T. West, State University of New York, Brooklyn, and H. Meier, The Jackson Laboratory, Bar Harbor, Maine); the Syrian hamster (F. Homburger, C. W. Nixon, and J. R. Baker, Bio-Research Institute, Cambridge, Massachusetts); the chicken (V. S. Asmundson, F. H. Kratzer, and L. M. Julian, University of California, Davis). Expression of the genes in the carrier state has been detected in all these three animal models, just as in the human dystrophies. On the other hand, the hereditary nature of the myopathy that has been observed in the white Pekin duck (R. H. Rigdon, University of Texas, Galveston) is not yet clearly established.

One of the basic questions which remains unanswered is how closely the mutations in other mammalian species approach the primary errors of the various hereditary human myopathies. But even if it is assumed that the genetic aberrations in human dystrophies are not identical with those responsible for the development of myopathies in other species, the mutant models have already proven valuable in delineating and defining primary and secondary changes of muscle-wasting at the chemical, structural, and functional levels.

For example, at the earliest stage in which there is evidence of a loss of muscle constituents in the dystrophic chicken muscle, there is also evidence for an associated increased anabolism. Decreased protein content of such dystrophic muscle becomes evident by the second week after hatching, whereas cathepsin activity is not significantly increased until 2 weeks later. It was suggested that initially there may be a failure in protein synthesis, and that only in later stages is there an attempt at regeneration which involves increased protein synthesis and an associated marked elevation in cathepsin activity (I. M. Weinstock, Institute for Muscle Disease, New York).

Studies on human dystrophic muscle pointed to a similar defective protein metabolism (T. Nihei and G. Monckton, University of Alberta Hospital, Edmonton). These authors have further investigated the ribonucleic acid (RNA) system and have obtained data which suggest that the messenger RNA is abnormal in the dystrophic muscle. However, a connection between this change and the defective protein synthesis has not yet been established and, in fact, the question of whether this type of protein synthesis is genetically controlled is far from settled. In any event, it has been convincingly demonstrated that, contrary to earlier reports, the enzymatic activities, actin-binding abilities, and amino acid composition of myosins are the same in both normal and dystrophic muscles, at least in chickens and mice (M. Bárány, E. Gaetjens, and K. Bárány, Institute for Muscle Disease, New York).

Progress has been made with regard to differential diagnosis of myopathies by morphologic (G. Milton Shy, University of Pennsylvania, Philadelphia) and histochemical (W. K. Engel, National Institutes of Health, Bethesda, Maryland, and G. Jasmin, University of Montreal, Montreal) techniques. However, there is still much confusion concerning the interpretation of findings, mainly because of the complications due to secondary changes. Similarities between the ultrastructural changes occurring in muscle fibers of dystrophic patients (G. W. Pearce, Newcastle General Hospital, Newcastle-upon-Tyne), dystrophic hamsters (J. B. Caulfield, Massachusetts General Hospital, Boston), and dystrophic mice (W. Wechsler, Max Planck Institut für Hirnforschung, Münich) were stressed. The significance of such similarities is, however, questionable because the reaction of muscle to injury is not only limited, but the different forms of muscle fiber degeneration are largely nonspecific. In addition, it is as yet impossible to interpret in functional terms the observed ultrastructural changes. In fact, a reciprocal relationship between the increase in concentrations of serum creatinephosphokinase (CPK) and the severity of structural changes in the muscle was found in patients and carriers of Duschenne muscular dystrophy (A. T. Milhorat, S. A. Shafiq, and L. Goldstone, Institute for Muscle Disease, New York). Early in the disease, the concentration of serum CPK is grossly increased, and the muscle consists largely of nor-

mal fibers intermingled with occasional fibers in various stages of degeneration. As muscle degeneration advances, the concentration of CPK gradually decreases. This same pattern holds true for the dystrophic hamster (F. Homburger, C. W. Nixon, and J. R. Baker, Bio-Research Institute, Cambridge).

Many data are now available to indicate that serum enzyme determinations are valuable in detecting human dystrophic carriers (F. Schapira, J. Demos, G. Schapira, and J. D. Dreyfus, Hôpital des Enfants Malades, Paris), while the value of isoenzymes in the diagnosis of myopathies is still questionable (C. M. Pearson, University of California, Los Angeles). Studies of the sex-linked recessive sub-variety of the Duschenne type of dystrophy have indicated that a single routine estimation of serum CPK will identify about 70 percent of the female carriers of this disease. Serial estimates of serum enzyme before and after complete bed rest and strenuous exercise, as well as electromyographic recordings and muscle biopsies, are all helpful in identifying the remaining 30 percent (J. N. Walton and R. J. T. Pennington, Newcastle General Hospital, Newcastle-upon-Tyne).

The involvement of the heart muscle is a frequent complication in human progressive muscular dystrophy, and the cardiac disorder often advances to congestive failure. While myocardial degeneration in classic types of dystrophies usually develops during the late stages, a new type of muscular dystrophy has now been recognized which originates in the heart muscle (F. H. Norris, A. J. Moss, and P. N. Yu, University of Rochester). Myocardial lesions characterized by focal myolysis occur regularly also in the strain of dystrophic hamsters; in a large percentage of these animals (more than 90 percent), the cardiac involvement progresses to congestive heart failure (E. Bajusz, F. Homburger, and J. R. Baker, Bio-Research Institute, Cambridge, Massachusetts, and L. H. Opie, University of Oxford). Thus, this inbred line of Syrian hamsters provides not only the first opportunity for studies on the involvement of the cardiovascular system in a genetically determined myopathy, but it also presents a useful disease model for analysis of the mechanisms of congestive heart failure.

Two papers dealt with nutritional myopathies. It was suggested that one biological role of selenium lies in a selenium-containing compound which may be a carrier of vitamin E, and that selenium and vitamin E are somehow involved in sulfur metabolism (M. L. Scott, Cornell University, Ithaca). Finally, a myopathy responsive to vitamin E was reported to occur in the Rottnest Quokka; this reversible disease model proved to be valuable for the study of certain aspects of regeneration in muscle disease (B. A. Kakulas, University of Western Australia, Perth, and R. D. Adams, Massachusetts General Hospital, Boston).

In his concluding remarks F. Homburger stated that a good insight into the progress of studies of primary myopathies has been obtained. None of the basic problems has been completely solved, but there is now much wider recognition of the necessity to relate biochemical findings to functional observations, and to correlate morphologic and chemical abnormalities. This changed approach alone indeed constitutes great progress.

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Chemistry at High Temperatures

Several reasons exist for continuing and expanding high-temperature research. There are serious gaps in our knowledge of chemical and physical phenomena in the energy range of 0.1 to 10 electron volts (corresponding to thermal energies in the range of 1000 to 100,000°K). Syntheses of many unfamiliar and interesting compounds are now feasible through the use of high-temperature and high-pressure techniques. Definitive theories of chemical bonding and of molecular interactions require knowledge of thermodynamic properties, molecular parameters, and transport properties extended to conditions attainable only at extremes of temperature. Thus, John L. Margrave (Rice University) introduced a conference on the present and future problems in chemistry at high temperatures, held at Rice University, Houston, Texas (26–27 January 1966). The conference, attended by 46 invited participants, was sponsored by the Committee on High Temperature Chemical Phenomena of the Division of Chemistry and Chemical Technology, National Academy of Sciences–National Research Council, with financial support from the Director of Chemical Sciences, Air Force Office of Scientific Research.

Margrave, the chairman of the sponsoring committee, went on to describe work in progress at his laboratory, including particularly the synthesis and properties of uncommon fluorides for a variety of elements (CF, SiF_2, perfluorosilanes, monofluorides of the transition and rare-earth elements, and others).

Experimental atomic energy data obtainable at high temperatures by spectroscopic techniques can account for the crystal structures of the metallic elements (Leo Brewer, University of California, Berkeley). However, experimental spectroscopic data are lacking for many important diatomic molecules even in their ground states. Myron Kaufman (Harvard University) outlined new techniques for determining molecular properties of high-temperature species. Kaufman and William Klemperer have detected both electric and magnetic deflection from molecular beams, and thus have gained information about the polar character and paramagnetic properties of such materials as BaO, SiO, and LaO. William Weltner, Jr. (Union Carbide Corporation) discussed matrix-isolation of high-temperature molecules, such as the monoxides of the transition metals, and mentioned techniques for obtaining absorption spectra and electron-spin resonance spectra of the molecules trapped in solid argon, neon, and other media. Promising results were obtained by W. A. Chupka (Argonne National Laboratory) with the mass spectrometer for ions produced by photoionization. Thresholds for the photon-induced processes can be determined with a precision of 0.01 electron volt.

S. S. Penner (University of California, San Diego) discussed problems related to the interface between gas dynamics and chemical kinetics. Such problems are encountered in combustion and propulsion engines, planetary entry phenomena, gas-dynamic techniques adapted to the chemical process industries, and the design and manufacture of chemical propellants. For example, in the exhaust from a rocket, chemical reactions may be taking place with the temperature changing at the rate of 10^4 degrees per second. The feasibility was noted of a "comprex" engine for producing chemicals with the aid of repeated shocks, a case in point being the production of acetylene from methane and air raised to transient high temperature by this means. The principles involved and