LETTERS TO THE EDITOR

British neurology: a national focus

British neurology is held in especial high esteem by national and international medical community. For over 100 years the natural focus for British neurological practice has been the National Hospital, Queen Square. It has played a leading part in the development of neurology as a descriptive science and has also served as a place of training in neurology for physicians and neurologists from both the United Kingdom and abroad. Most of the United Kingdom university chairs in neurology are currently held by neurologists trained at Queen Square.

In 1950, the Institute of Neurology was created to help develop academic neurology and encourage the evolution of the subject from a descriptive to a mechanistic science. In this task, the Institute has been singularly successful and has obtained consistently high ratings in the University Funding Council’s research exercises. The Hospital and Institute now have several internationally renowned groups with research focused on movement disorders, multiple sclerosis, neuropsychology, neurogenetics, peripheral nerve and muscle disease, dementia, neuropsychiatry, neuropsychology, and epilepsy. The recent award of £22 million by Wellcome Trust and The Leopold Muller Trust to the Institute to create both the Department of Cognitive Neurology and its PET unit with functional MRI, shows tremendous confidence in the Institute’s academic credentials. The application to common neurological disorders of the emerging technologies of molecular cell biology and molecular genetics has already provided valuable insights into our understanding of the causes of multiple sclerosis and the major neurodegenerative diseases. The benefits of this programme are already being reaped in the creation of new strategies to treat, for instance, Duchenne muscular dystrophy. We believe that the National Hospital and the Institute of Neurology have a pivotal part to play in developing, elaborating, and promoting these advances as well as in training neurologists in their application.

The recent denial of Trust status to the National Hospital has brought into sharp focus the complexities of providing a clinical neuroscience service in the 1990s. Neurological practice is continuing to evolve and the National Hospital is at the leading edge of this process. Neuroimaging by CT and MRI provide but one example of the extent to which new methods have revolutionised inpatient and outpatient neurological care. The increase in neurological units within the United Kingdom has established additional centres of excellence. The advent of the new health care market has added a further dimension of uncertainty that will impinge on the service provided at Queen Square.

There is a growing appreciation, however, that neurology and neuroscience are entering a new and exciting phase of development. We believe in the principle that the nature of the neurological specialties require that they have a national focus for clinical practice, research, and training. This will maintain the cohesiveness of the specialties and will serve to provide a centre for clinical neuroscience research. An adequate flow of patients is required to serve both of these commitments. Today’s market forces demand that this flow be secure and provide a sound financial foundation for clinical services. These changes have a physiologically informed clinical and basic neuroscience research faculty of appropriate size, and be in close association with multidisciplinary clinical and academic services.

We suggest that regardless of any political or financial considerations, there is a unique opportunity to create a major neurological institution of national and international stature to assimilate the various facets of clinical and academic practice in neurology and the neurosciences. The principal purpose and function of this initiative are clearly identified. The Hospital and Institute of Neurology look forward to contributing to the new era of British clinical neuroscience. The heritage of “Queen Square” must be valued and its future secured through a clarity of purpose, not to protect, but to develop, expand, and enrich its role and authority.

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A unique case of dystrophinopathy

Becker and Duchenne dystrophies are allelic X-linked diseases—the first mild, the second severe—characterised by a gene deletion in the long arm of chromosome X. Dystrophin, the gene product, is absent in Duchenne and present although abnormal in Becker dystrophy. Other signs of Becker muscular dystrophy are progressive symmetric muscular weakness, a more than five-fold increase in serum creatine kinase, myopathic electromyography (EMG), and muscle biopsy characterised by variability of fibre diameter, focci of regenerating fibres, presence of necrotic fibres, and variable increase in connective and fat tissue. Blood creatine kinase is high from birth, whereas other signs of the disease appear in late childhood or adolescence; patients remain ambulant beyond the age of 16.

We report abnormal expression of dystrophin with gene deletion in a male child, who at birth presented bilateral diaphragm paralysis, generalised muscle weakness, and ptosis of the eyelids. Other features were a prominent forehead, broad and flat nasal root, hypertelorism, low-set ears, high arched palate, and bilateral cryptorchidism.

After correction of the respiratory acidosis, exhaustive plasma and urine tests, including lactate and pyruvate, amino acids, organic acids, carnitines, lysosomal enzymes, and creatine kinase were normal, and repeatedly so; as were the chromosomal map, abdominal ultrasound, brain NMR, acoustic evoked potentials, electrocardiogram and echocardiogram, and the results of the new biochemical tests. F and G. Muscle biopsy at three months led to diagnosis of congenital myopathy with type II hypertrophy. Muscle immunostaining with a panel of antibodies to different portions of the dystrophin molecule showed patchy dystrophin distribution on the surfaces of muscle fibres with five antibodies, whereas dystrophin localisation seemed greatly reduced using the anti-D8 antibody. Western blotting showed a dystrophin band of reduced molecular weight and intensity. Analysis of peripheral blood genomic DNA by a multiplex polymerase chain reaction protocol to detect exons in the deletion prone “hot spot” regions of the dystrophin gene, showed deletion of exons 49–52. Exon 53 was found deleted by Southern blot analysis.

Molecular biopsies (with immunocytochemical and immunoblot analyses) and blood DNA analysis were repeated at 13 months with identical results: in particular the muscle did not present dystrophic signs.

The clinical condition of the child improved gradually although he needed a respirator for 20 months. At the most recent check up, at 33 months, he was able to walk and climb actively (although he has mild hypotonia), but could not talk. He is mentally retarded and of short stature. The child is the second of non-consanguineous parents, the sister has mild Becker’s disease but normal strength. Plasma creatine kinase and EMG were normal in both parents and muscle biopsy was normal in the father. In the mother fibre size varied considerably but immunostaining showed dystrophin located normally. From analysis of DNA polymorphisms the probability of the mother being heterozygous for the gene defect was estimated at 80%.

This is a puzzling case presenting Becker-like dystrophinopathy from the molecular and immunochromosomal point of view but with normal blood creatine kinase and no clinical signs of muscular dystrophy, although there is congenital myopathy with mental retardation.

The financial support of Telethon, Italy to M Mora and F Cornello is gratefully acknowledged.

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