CONCLUSIONS

Muscular dystrophies are a clinically and genetically heterogeneous group of disorders unified by the presence of ‘dystrophic’ changes on muscle biopsy defined as increased fibre size variability, increased connective tissue and the presence of degenerating and regenerating fibres. These are broadly divided on the basis of age of onset and pattern of weakness into those with onset of weakness at birth (congenital muscular dystrophy) and those with later onset limb-girdle weakness, the X-linked dystrophinopathies (Duchenne, Becker, and female carriers of a mutated dystrophin gene), and the limb-girdle muscular dystrophies (LGMD). Before the era of clinical molecular genetics, neuromuscular diagnosis was imprecise and dependent upon the combination of the family history, the clinical features and laboratory investigations, especially muscle biopsy, serum enzymes and electromyography. Prognostic information, genetic counselling and family planning rested upon informed opinions rather than fact. It is now recognised that diagnosis on clinical criteria were sometimes incorrect because of the lack of correspondence between phenotype and genotype.

The aim of the study was to characterise differential diagnosis of dystrophinopathies, sarcoglycanopathies and congenital muscular dystrophy for correlation between phenotype, genotype with protein abnormalities in 29 muscular dystrophy patients. Of these, 19 were diagnosed as suffering from DMD, 2 BMD, 4 female carriers, 3 LGMD and 1 CMD. In summary, the effect that deletion breakpoints have on open reading frame was found to exert the most influence on the clinical phenotype in DMD/BMD patients. However, clinical and molecular correlation based on alteration of the reading frame were not valid in ~29% of the cases which is higher than that observed in Western countries (5-8%). Relative levels of muscle dystrophin not only
correlated with immunocytochemical patterns of subsarcolemma staining but also with the clinical severity exhibited by the DMD/BMD patients. Increasing dystrophin abundance does seem to correlate with the milder clinical course.

In 3 young girls, the extent of dystrophin-negative fibres can be considered prognostic to some degree. The patient with large number of dystrophin negative fibres showed a more severe course than a patient with less number of dystrophin negative fibres. However, even these limited correlations perhaps did not hold up in the older symptomatic patient due to the biochemical and genetic normalisation occurring along with failed regeneration and muscle wasting.

Secondary dystrophin abnormalities were observed in two patients with primary sarcoglycanopathy and in one patient with congenital muscular dystrophy. The pattern of dystrophin abnormalities found in these patients is similar to that seen in milder primary dystrophinopathies (BMD). Thus, abnormalities of dystrophin should not be used to exclude patients from sarcoglycan analysis without confirmation of primary dystrophinopathy, as dystrophin abnormalities may be secondary.

A slightly different standard pattern of restriction fragments was detected in the present study when human DNA, normal or disease-risk was cleaved with HindIII and hybridised with probe 11-14. Since a few deletions have been mapped to this region with probe 11-14 in DMD patients a complete restriction map is important when screening for deletions is undertaken for dystrophin gene.