GENERAL DISCUSSIONS
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In the present study, skeletal muscle biopsies from various infantile neuromuscular disorders were studied to compare the morphological features with those of skeletal muscle obtained from foetuses at different stages of development, as these disorders are considered to be due to defect in foetal development.

The development of foetal skeletal muscle could be described in four stages. During 9-10th weeks of gestation, myotubes were predominantly seen. There was no histochemical differentiation into different fibre types. A few fibres with the peripheral nuclei were seen at the 14th week of gestation. Histochemical differentiation was evident at 22nd week, while distinct checker-board pattern was noticed at 28th week of embryonic life. Fibres with morphological features similar to the mature postnatal fibres were noticed at 22-36 weeks of gestation.

The different types of neuromuscular disorders appeared to arise either as defect in neuronal innervation during development or maturation defect of skeletal muscle in the foetus.

Infantile spinal muscular atrophy, constituted the major disease entity. Our observations suggests that denervation in SMA-1 (Werdnig-Hoffmann disease) occurred during the development of foetal muscle in the embryo. In this
condition fibre type distinction was well appreciated. However, both fibre types were involved. A comparison with the foetal skeletal muscle development suggests that the denervation starts after 22nd week gestation. This fact was also corroborated by the observation of neuronal degeneration and loss seen in the spinal cord specimen of a 20-day-old infant with WHD, suggesting that the pathological changes to have started in the foetal stage. Thus denervation atrophy starting during development accounts for the peculiar characteristic morphological appearance of muscle fibres in NADH-TR preparation in Werdnig-Hoffmann disease.

In congenital muscular dystrophy, primary myopathic process starting in the foetal life resulted in the loss of fibres and replacement of a large volume of muscle fibres by connective tissue. In the classical forms, the CPK values were either normal or mildly raised. In the classical form, absence of myonecrosis and phagocytosis explains the normal or slightly raised CPK values. These observations also suggest that the dystrophic pathology must have started early in the foetal life replacing the muscle fibres with connective tissue. A few cases which showed extensive necrosis and increased CPK values are the ones possibly starting late in the foetal life with continued myopathic activity in the postnatal period.

Congenital myopathies comprised a variety of disorders each with different morphological characters. The common
denominator however, was the predominance of type-I fibres.

In the central core and multicore diseases the morphological characteristic feature was the absence of oxidative enzyme reaction in the central region of the fibre or multiple areas. Predominance of type-I fibre was also noticed. These regions revealed lack of mitochondria and disarray of filaments at electron microscopic level. It is presumed that the disorganisation of the mitochondrial distribution occurred approximately at 22nd week of gestation corresponding to the time when the distinction of fibres into different histochemical types begins.

Centronuclear myopathy comprised a large group among congenital myopathies. It appears that the defect occurred during the course of development resulting in arrest of peripheral migration of nuclei, lack of development of the fibres to its normal size and defect in differentiation of type-I and type-II fibres resulting in predominance of type-I fibres.

In the congenital fibre type disproportion, predominance of type-I fibre and type-II fibre hypoplasia also are explained on the basis of dysmaturation of myofibres during development.

In the present series, the morphological study of metabolic myopathies were not adequate to correlate with developmental defect.