Electrophysiological Study of Myotonia

THERE has been considerable interest in myotonia, but current theories of its cause are based on evidence obtained in experiments where nerve and muscle responses could not be separated. Microphysiological investigation at a single neuromuscular junction can provide some information about pre- and post-synaptic factors and can also be used to study the common assertion[1,2] that the disorder arises from "electrical instability" in the muscle membrane.

Small bundles of excised intercostal muscle with intact fibres and nerve twigs[3] serve as suitable *in vitro* nerve-muscle preparations. We have investigated the electrical and mechanical responses of such preparations from three myotonic patients and two normal individuals. Details of the preparation and microelectrode technique are given elsewhere[4], and in the present experiments the only change has been the addition of a very sensitive electro-mechanical transducer to record the twitch and tetanus responses of a few muscle fibres.

Action potentials were recorded after indirect stimulation in twenty fibres from myotonic patients and an equal number from normal controls. Action potentials were evoked by direct stimulation in ten myotonic fibres. End plate potentials and miniature end plate potentials have also been recorded in an additional fifteen fibres. Twitch and tetanus characteristics of several small bundles of fibres have also been recorded from each of the three myotonic patients and compared with those of biopsy specimens from normal controls.

In brief, the findings are as follows. First, "insertion myotonia" was not observed in any fibre as it was penetrated by the microelectrode. Second, the membrane potentials of all fibres remained perfectly stable, some for as long as 35 min at a time. Third, with single or repetitive nerve stimulation at frequencies up to 20 c/s there was no iterative muscle firing after any impulse. Moreover, direct stimulation of myotonic fibres caused no after discharges. Finally, comparison of total twitch times in normal and myotonic fibres (normal 250 msec, myotonic 300 msec) revealed a slight prolongation in the myotonic fibres, but there was no evidence of repetitive activity at the surface membrane. The slightly more prolonged action potential in myotonic fibres at 37° C (mean 3·1 msec, control mean 2·7 msec) seems to be evidence in favour of prolongation of the contractile response, but the measurements all suffered some inaccuracy imposed by movement artefact, and the significance of the findings is therefore not clear as yet.

The failure to find repetitive firing in a myotonic muscle fibre *in vitro* could mean that some activating substance is washed away during the preparation of the tissue, that myotonia does not affect the intercostal muscles or that the well known electromyogram pattern of myotonia is a reflexion of a pre-synaptic abnormality. It is not possible to be sure about the first point, but we believe the muscle specimens were truly representative, because there was a clear cut "dive bomber" activity on insertion of the electrode at several intercostal sites in one case and because fibres from two of the *in vitro* preparations showed typical central chains of nuclei. The pre-synaptic disorder which would most readily account for myotonia is back-firing of the motor nerve terminals[5]. Myotonia after percussion or willed movements would thus resemble a "veratrinic" response[6] in the nerve, and its persistence after fractional curarization or proximal nerve block would only require a slight variability in the susceptibility of some motor units. The normal frequency of miniature end plate potentials argues against significant depolarization of the motor nerve terminals.

The prolonged mechanical responses may reflect the dystrophic process in the specimens studied, as we have not examined a case of myotonia congenita, but it seems equally likely that the twitch times of the myotonic muscle could be conditioned by nerve activity. The slowness with which some myotonic fibres appear to contract is clearly not responsible for the characteristic electromyogram signs, and we have found no definite explanation for it.

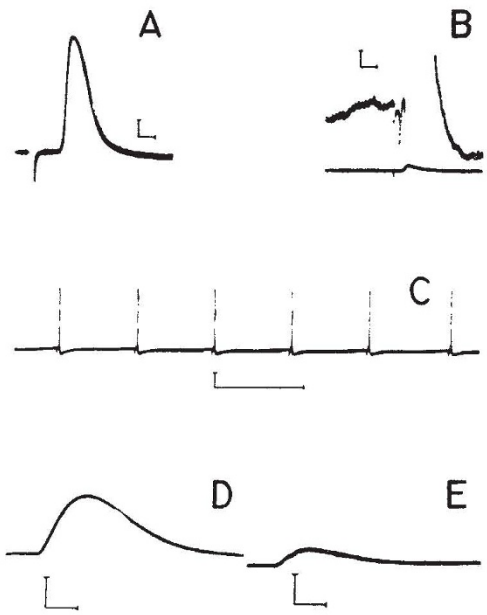

Fig. 1*A*. Ten superimposed sweeps of action potential in myotonic fibre stimulated at 12 c/s. Calibration: time, 1 msec; amplitude, 10 mV; *T*, 36·5° C.

Fig. 1*B*. End plate potential in myotonic fibre at low and high gain, the latter to show pre-synaptic spike. Calibration: top, 500 μV, 2 msec; bottom, 5 mV.

Fig. 1*C*. Myotonic action potentials. Stimulation rate 12 c/s. Calibration: 100 msec; 20 mV; *T*, 37° C.

Fig. 1*D*. Maximal twitch of about sixty myotonic fibres. *T*, 37° C. Calibration: 50 msec, 200 mg.

Fig. 1*E*. Maximal twitch of about forty normal fibres. *T*, 36·5° C. Calibration, 50 msec, 500 mg.

The present experiments do not support the notion that instability of the muscle membrane is the cause of myotonia, and we hope that continuing studies at a unit level with refined microtechniques may throw some light on the fundamental abnormality.

W. W. HOFMANN
GARY ROWE

Department of Neurology,
Veterans Administration Hospital,
Palo Alto, California.

[1] Norris, F. H., *Electroencephal. and Clin. Neurophysiol.*, **14**, 197 (1962).
[2] Creutzfeldt, O., Abbott, B. C., Fowler, W. M., and Pearson, C. M., *Electroencephal. and Clin. Neurophysiol.*, **15**, 505 (1963).
[3] Elmqvist, D., Johns, T. R., and Thesleff, S., *J. Physiol.*, **154**, 602 (1960).
[4] Elmqvist, D., Hofmann, W. W., Kugelberg, J., and Quastel, D. M. J., *J. Physiol.*, **174**, 417 (1964).
[5] Eccles, J. C., *The Physiology of Synapses* (Academic Press, New York, 1964).
[6] Eyzaguirre, C., Folk, B. P., Zierler, K. L., and Lilienthal, J. L., *Amer. J. Physiol.*, **155**, 69 (1948).

HISTOLOGY

Succinic Dehydrogenase in Developing Cat Leg Muscles

HISTOCHEMISTRY has contributed much to the problem of "red" and "white" muscles and the fibre composition of the two types of muscle. Stains for oxidative enzymes have given results which cause opinions to differ with regard to the number of fibre types in normal muscles of the adult vertebrate. Two types of fibres were described