Recent studies have demonstrated acquired muscle inexcitability in critical illness myopathy (CIM) and have used direct muscle stimulation (DMS) techniques to distinguish neuropathy from myopathy as a cause of weakness in the critically ill. The mechanisms underlying weakness in CIM are incompletely understood and DMS is only semiquantitative. We report results from a series of 32 patients with CIM and demonstrate significant slowing of muscle-fiber conduction velocity (MFCV) and muscle-fiber conduction block during the acute phase of CIM, which correlates with prolonged compound muscle action potential (CMAP) duration, clinical severity, and course. We also used a paired stimulation technique to explore the excitability of individual muscle fibers in vivo. We demonstrate altered muscle-fiber excitability in CIM patients. Serial studies help define the course of these pathophysiological changes. Parallels are made between CIM and hypokalemic periodic paralysis. Our findings provide further evidence for muscle membrane dysfunction being the principal underlying abnormality in CIM.
CIM, suggesting primary dysfunction of the muscle-fiber membrane. Although not the main emphasis of the investigation, one previous study has reported evidence of slow muscle-fiber conduction velocity (MFCV) in CIM. The investigators did not draw particular attention to this finding, considering it secondary to fiber diameter reduction; however, they did demonstrate concurrent muscle inexcitability, by means of reduced DMS CMAP amplitudes. The interrelationships between CMAP parameters, particularly duration, MFCV, and individual muscle-fiber excitability in vivo, have not been studied previously.

The prime objective of this study was to determine whether there is dysfunction at the level of the muscle membrane in human CIM. We aimed to study the excitability characteristics of single muscle fibers in vivo as well as to correlate these with CMAP parameters and clinical findings.

**PATIENTS AND METHODS**

We studied 32 patients with CIM, with an average age of 49 years. Patients were assessed clinically and underwent neurophysiological examination including nerve conduction studies, routine EMG, and repetitive nerve stimulation at ICU bedside.

Patients diagnosed with CIM fulfilled the following criteria: acute severe illness; acute quadriplegia or quadriparesis; and no evidence of alternative diagnosis. Electrophysiologically, patients had normal SNAPs and motor conduction velocities, small CMAP amplitudes, and EMG findings consistent with a myopathy or electrically inactive muscle. Patients with electrophysiological findings consistent with other disorders were excluded.

We had no histological data, so accordingly, where the clinical and electrophysiological findings were consistent with a probable diagnosis of CIM in line with the proposed criteria, we extended the examination, when possible, to study MFCV and muscle-fiber excitability. Lacomis et al. suggested that evidence of muscle inexcitability might replace histological evidence. Patients were classified broadly into two categories according to their overall muscle power, taken as an average. Patients who were able to move limbs against gravity at grade 3 or better on the Medical Research Council (MRC) scale were classified as having mild–moderate weakness. Those who had no movement of limbs or who could only move with gravity eliminated (MRC grade 2) were classified as having severe–very severe weakness.

We used the technique for calculation of muscle-fiber conduction velocity as described by Troni et al. DMS of tibialis anterior (TA) muscle fibers with a monopolar needle was performed in 7 patients (age 14–71 years) and in 5 control subjects (age 25–35 years) who had no known neuromuscular disease. This muscle was chosen specifically because of its size, accessibility, longitudinally orientated muscle fibers, and the eccentric location of the endplate in relation to the muscle belly. Other muscles were therefore not studied with this technique for these reasons.

The endplate zone of the muscle was identified using liminal surface stimulation, so this region was avoided. A monopolar stimulating needle electrode (26G, surface area 0.34 mm²; Teca, Oxford Instruments, Old Woking, UK) was placed approximately at the junction of the proximal two thirds with the distal one third of the TA muscle belly. A concentric recording needle electrode (26G; Teca, Oxford Instruments, Old Woking, UK) was then inserted 50 mm proximally. Both needles were inserted to a depth of about 20 mm perpendicular to the skin surface and maintained in a perpendicular position by taping the looped electrode leads to the skin surface. A surface ground electrode was placed between the needles and a surface anode electrode was placed 30 mm distal to the monopolar needle (Fig. 1). Fine needle manipulation and variation of the stimulus strength resulted in recording a complex of multiple single muscle-fiber action potentials (MFAPs) (Fig. 2). Responses earlier than 8 ms were likely to be conducted via intramuscular nerve twigs and were not included. Sequential sweeps were recorded to demonstrate that the responses were stimulus-induced, all-or-none, stable, and reproducible. The technique took approximately 20–60 minutes to perform. Responses were frequently acquired.
with stimulation at low intensity, typically between 1 and 3 mA (with stimulus duration of 0.1 ms). Muscle-fiber action potentials were recorded using filter settings between 500 Hz and 10 kHz. The needle was repositioned along the 50-mm arc to exclude variable muscle-fiber alignment in case of lack of response. If still no response was seen at an interelectrode distance of 50 mm, the recording electrode was moved toward the stimulating electrode (to a measured distance between 20 and 30 mm). If after repositioning no responses were obtained, the muscle was assumed to be inexcitable. The latency to each muscle-fiber action potential was measured and MFCV calculated. The ratio of the fastest to the slowest MFCV was also determined. The ambient temperature in the ICU and the use of thermal blankets ensured that the limbs tested were warm. Hence, temperature was not measured routinely.

We assessed muscle-fiber excitability in 7 patients and 5 normal controls using a paired stimulus protocol to measure muscle-fiber absolute refractory period. We used the same electrode arrangement and further manipulated needle tip positions (by rotational and depth movements) and reduced stimulus intensity in order to obtain a single, stable, and well-defined muscle-fiber action potential. Paired stimuli were applied and the interstimulus interval (ISI) was then reduced in a stepwise fashion, to predetermined intervals of 20, 10, 8, 6, 5, 4, 3, and 2 ms. The effect on the second response was observed (Fig. 3). By a bracketing procedure, the refractory period was measured where possible to the nearest 0.1 ms.

**CMAP Measurements.** CMAP duration in the abductor pollicis brevis (APB) and abductor hallucis (AH) muscles from supramaximal stimulation of the median and posterior tibial nerves, respectively, was measured as the interval between CMAP onset and the first zero crossing. CMAP parameters were measured in 26 patients and in 27 age-matched controls. Although care was taken to obtain data from these...
two chosen muscles, in 6 patients the CMAP data were not available for the aforementioned muscles. This was due either to inexcitability (2 patients) or inaccessibility (4 patients) due to dressings, vascular access, and other obstacles. Although it might have seemed prudent to measure CMAP parameters from TA, the considerable variability in normal responses and the often-present initial positive component would make such measurements unreliable. Furthermore, stimulation near the fibular head might inadvertently result in direct muscle stimulation, and more proximal stimulation of the peroneal nerve is unreliable.

We used unpaired \( t \)-tests to compare nerve conduction data and MFCVs. Non-parametric Mann–Whitney \( U \)-tests were used for comparing results of excitability studies.

RESULTS

Of the 32 patients included, 20 were still alive at the time of writing. Twelve patients died secondary to the underlying critical illness, although sometimes weeks or even months after the onset of quadriplegia. The patients were in the ICU for variable periods of time, with most being referred for neurophysiological evaluation after difficult ventilatory weaning. The precise duration of illness was not available for most patients because of the difficulty in dating the onset of the weakness, which had several reasons. None of the patients had pre-existing or other confounding neuromuscular disorders. Although several patients had received some steroid therapy, often early on during ICU admission, none received them on a long-term or regular basis. None of the patients had an elevated serum creatine kinase (CK) to suggest a necrotic myopathy; the serum CK ranged from 23 to 620 IU/L, at an average of 233 IU/L (normal: \( <110 \) IU/L). Clinical and electrophysiological findings suggested no alternative diagnosis.

CMAP Duration. CMAP durations were frequently prolonged in CIM patients and possessed smooth contours (Fig. 4). The mean CMAP duration recording over APB in 25 patients was 9.0 ms (range 5.3–30.3, SD 4.9 ms) compared with 5.0 ms in 26 controls (SD 0.6, mean + 2 SD = 6.2 ms, range 3.9–6.3 ms) \((P < 0.0005)\). The mean CMAP duration over APB was greater than the mean + 2 SD of the control group in 18 of 25 (72%) patients. The mean CMAP duration over AH in 16 patients was 9.4 ms (range 5.0–17.1, SD 3.96) compared with 5.0 ms in 21 controls (range 3.2–6.7, SD 0.9, mean + 2 SD = 6.8 ms), also significant \((P < 0.0005)\). In 10 of 16 (63%) patients, tibial CMAP duration values exceeded the mean + 2 SD of the control group. No significant difference in CMAP duration was noted between proximal and distal stimulation sites; that is, there was no abnormal temporal dispersion of nerve origin.

SNAP Amplitude and Duration. SNAP amplitude and durations were not statistically different between patients and controls. Mean SNAP durations in patients were 1.1 ms, 1.2 ms, and 1.2 ms on median, ulnar, and sural nerve stimulation. The corresponding values for the controls were 1.1 (SD 0.11) ms, 1.1 (SD 0.08) ms, and 1.3 (SD 0.16) ms, respectively.

EMG. Needle EMG studies revealed spontaneous activity, usually fibrillation potentials and positive sharp waves, in 15 (47%) patients. Twenty-four patients (75%) had short-duration, low-amplitude motor unit potentials and early recruitment patterns at some stage during their illness. In seven patients it was not possible to assess motor units due to severe weakness. In severely affected patients, no volitional electrical activity was seen and the muscle was inex-citable to direct simulation. Some of these patients did, however, have abnormal spontaneous activity.

MFCV. We measured MFCV in 7 CIM patients and 5 controls. Two of the 7 patients had repeat examinations during the recovery phase of the illness. Several fibers were assessed in each patient and the MFCV for each muscle fiber was calculated. In total, 146 muscle fibers were assessed in patients and 66 fibers in controls. The mean MFCV in patient fibers was
2.32 m/s (SD 1.12, range 0.4–4.8), compared with a mean of 4.02 m/s (SD 0.6, range 3.0–5.5) in controls ($P = 0.004$). However, this average value included data from patients with a spectrum of clinical severity ranging from mild–moderate to very severe. In addition, this value only included data when muscle fibers were excitable; hence, data from the most severely affected muscle fibers were not included. In 2 patients, muscle fibers were inexcitable at any distance. In 3 others, muscle-fiber action potentials could only be obtained at shorter interelectrode distances (25 mm). Plotting MFCV values against the CMAP duration values obtained during the same examination for individual patients reveals an inverse correlation between them (Fig. 5). The mean (±SD) ratio of fastest to slowest fibers was 3.02 (±0.71) in CIM patients compared with 1.65 (±0.15) in controls. This implies significantly larger variation in MFCV in CIM patients ($P < 0.003$). No significant difference in this ratio was observed between the moderate and severe groups of patients.

**Excitability Studies.** We defined muscle-fiber excitability using the interstimulus interval (ISI) at which the fiber identified became inexcitable to the second of the paired stimuli. This reflects the absolute refractory period of the fiber. The higher the ISI value, the less excitable the fiber. We assessed 11 fibers in 6 patients and 12 fibers in 5 controls. The mean ISI at which the second stimulus failed to generate an action potential in patient fibers was 4.7 ms (range 2.2–20 ms) with more than half of the values being >3.0 ms. This value included one outlier where the ISI was 20 ms. This is in comparison to a mean of 2.5 ms (SD 0.33) for controls. To give a more meaningful comparison of the groups, we recalculated the statistics with this outlier excluded; the calculated patient mean was 3.18 ms (SD 1.14). When the two groups were compared, either with or without the 20-ms outlier, there was no significant difference ($P > 0.05$) between them, but in some patients’ muscles the fibers were completely inexcitable and these data could not be included in the aforementioned analysis.

**Case History.** We include a brief case history to emphasize the overall pattern of electrophysiological findings in relation to the evolution of the illness. A 30-year-old man was admitted to the ICU with liver failure. He developed severe weakness diagnosed as CIM. We examined him on three occasions. Normal SNAPs were recorded on each of these examinations. Needle EMG on the first examination revealed electrical silence and inexcitable muscle fibers to direct stimulation. On this occasion, CMAP durations were 14.5 ms (median), 9.9 ms (ulnar), and 13.0 ms (tibial), with amplitudes of 0.2 mV, 0.3 mV, and 1.2 mV, respectively. On the second examination 1 month later, when he was still very weak, motor studies revealed a median CMAP amplitude of 0.1 mV with a duration of 30.3 ms, and tibial CMAP amplitude of 1.5 mV with a duration of 17.1 ms. At this stage, needle EMG revealed fibrillation potentials and positive sharp waves in TA and biceps brachii. Voluntary recruitment of APB was possible and revealed low-amplitude, early-recruited motor unit potentials. Muscle fibers remained inexcitable to direct stimulation. A third examination after a further 2 months during rehabilitation showed a median CMAP amplitude of 3.3 mV with a duration of 7.7 ms, and tibial CMAP amplitude of 1.4 mV with a duration of 8.6 ms. Muscle fibers at this stage were excitable and the mean MFCV at this time was 3.4 m/s. Clinically, the patient had power graded at 1 in the right TA, 3 in left APB, and 4 in right AH. EMG of the right TA and biceps brachii revealed early motor-unit recruitment but no spontaneous activity and no evidence of chronic partial denervation.

**DISCUSSION**

In this study we have demonstrated dysfunction at the level of the muscle-fiber membrane in CIM. We found a significant reduction in MFCV in CIM muscle, which correlates inversely with significant prolongation of the surface-recorded CMAP duration. We also found that muscle-fiber excitability is affected in CIM.

CIM and CIP were both first described over 20 years ago. Both have been reported with a relatively high incidence in ICU patients. In a series of 92 patients with neuromuscular disorders in the ICU, a myopathy consistent with CIM was three...
times as common as axonal polyneuropathy (42% vs. 15%).

Severe illness in itself can cause acute quadriplegic myopathy. Neither sepsis nor multiorgan failure is a prerequisite to developing CIM. Mortality rates of 50% have been reported. In our series, mortality was 38%, usually as a consequence of the underlying illness. When biopsies are performed, CIM patients have clear histological evidence of myopathy, in the presence of normal nerves. It is possible that some patients have a "neuromyopathy." Differentiating muscle disease from a pure motor neuropathy is challenging and relies on direct demonstration of muscle dysfunction. There is dispute over which are the most useful tests to distinguish CIM and CIP.

Nerve and muscle biopsy, including electron microscopy, can aid in the differentiation of CIP from CIM, revealing normal peripheral and intramuscular nerves and selective loss of myosin in CIM. However, this is frequently neither available nor practical in most ICUs. Myosin loss in itself cannot explain muscle inexcitability, and myosin loss itself lags behind the development of weakness. Calpains may increase degradation of myosin filaments and show enhanced expression in CIM muscle biopsies. Additionally, severe illness, sepsis, glucocorticoid therapy, and paralysis also stimulate muscle protein catabolism. Weakness in CIM can develop very rapidly but can also show rapid improvement. Despite rapid early improvement, however, recovery can be prolonged. Severe CIM paralysis may result in greater muscle protein loss, and regaining ambulation after CIM may take several months, presumably in part due to secondary muscle atrophy. Atrophy is a likely consequence of the systemic illness but cannot account for the sudden onset of paralysis or the electrical inexcitability of the muscles. Secondary atrophy, however, is likely and is commensurate with the delayed recovery and chronically reduced MFCV, reflecting the now smaller muscle-fiber diameter.

Although serum CK may be elevated, it is frequently normal or only mildly increased in CIM. In the recent study by Lefaucheur et al., the single patient with a serum CK of 12,000 IU/L was excluded, most patients with pure or predominant myopathy had an average CK of 127 IU/L, with a range of 17–700 IU/L. It appears that an elevated serum CK should be considered a supportive but not a major diagnostic finding. Coexistent scattered necrosis has been noted in CIM muscle biopsies.

It is likely that this causes the increased serum CK observed in some CIM cases. This, in turn, is probably related to critical illness as opposed to primary muscle pathology. In the present series, the serum CK elevation was disproportionately low relative to the degree of weakness. This further supports the notion that weakness is due to muscle-fiber membrane dysfunction and not to structural muscle changes at onset. Subsequent structural changes may occur due to changes at the level of the muscle-fiber membrane and other factors.

Some investigators suggested that myopathic-appearing motor units, associated with an often nearly normal serum CK, could be due to a distal axonopathy, an argument potentially supported by abnormal single-fiber EMG findings. These findings, however, could also be explained by abnormalities of the postsynaptic membrane. Normal intramuscular nerves have been demonstrated on biopsy. MUP duration analysis in CIM has indicated myopathic changes, whereas mean MUP amplitudes, quantitative electromyography, and motor unit number estimates were within normal limits in one study. In common with other acquired muscle disorders, the pathology is likely to be diffuse, affecting most skeletal muscles, but patchy in any given muscle. This would explain why some fibers are nearly normal but others are very abnormal with respect to MFCV and excitability.

Direct intramuscular stimulation of muscle fibers is not a new technique. Rich et al. reported that the motor nerve stimulation (MNS)/DMS ratio was useful in distinguishing myopathy and neuropathy in ICU quadriplegia. A ratio of >0.5 was associated with myopathy. Others have also used the DMS technique to distinguish myopathy and neuropathy. However, there are potential disadvantages to DMS. The whole muscle is not necessarily stimulated and the CMAP amplitudes used in the calculation are likely derived from unequal or different muscle-fiber populations. The results are semi-quantitative, only indirectly demonstrating dysfunction of muscle. DMS also has limited utility in mildly affected patients, as only large changes in amplitude can be detected and there is a lack of normative data in ICU controls. A high ratio will not distinguish between abnormal and normal muscle.

Estimation of MFCV using methods based on voluntary contraction will be biased toward the slowest fibers, which are recruited first. However, invasive MFCV study is a relatively easy technique to perform, provides objective, quantitative results, and has been found to be more sensitive than surface EMG measurement in hypokalemic periodic paralysis (HPP) carriers. Using an invasive method, Troni et al. found normal values of MFCV to be 3.53–4.24 m/s (male) and 2.96–3.74 m/s (female). Also,
using an invasive technique, normal values of 2.6–5.3 m/s (mean 3.7) were reported specifically for the TA muscle.\textsuperscript{1} Our normal control data agree, providing a mean of 4.0 m/s, with a range of 3.0–5.5 m/s. Trojaborg et al. used an invasive DMS technique to measure the MFCV and the evoked response amplitude. MFCV was 30\% lower in 5 CIM patients compared with controls (4.5 ± 0.2 m/s vs. 6.4 ± 0.3 m/s).\textsuperscript{43} Although their study showed a relative difference between these two groups, the absolute MFCV values were higher than those reported by us and others for controls and by us for CIM patients. This may reflect technical differences in measurement and possibly differences in the spectrum of CIM severity assessed.

The technique used could introduce error in the form of interelectrode distance variation. Although inserted at a measured distance (usually 50 mm), needle angulation within the tissues could result in the needle tips being closer together or further apart than the surface measurement. We estimated that, on visual inspection, a 5-degree angle of the needle could be missed and not corrected by re-placement. This would result in a 4\% shortening of the distance (4\% of 50 mm) with needle insertion to a depth of 20 mm. If both needles were angulated their relative separation would be reduced or exaggerated by approximately 8\%. If it was assumed that this effect overestimated MFCV by 8\% for all control subjects and underestimated the MFCV by 8\% for all patients, we calculated that the new mean for controls would be 3.84 m/s (SD 0.23) and for patients would be 2.56 m/s (SD 1.17). This difference would still be 2.56 m/s (SD 1.17). This difference would still reach a statistically significant level ($P = 0.0278$). This scenario is, however, unlikely as we took care to maintain perpendicular needle positions during the studies.

Reduced MFCV values can be obtained from histologically normal muscle, such as in HPP.\textsuperscript{11,46} Small atrophic fibers would be expected to show a reduced MFCV,\textsuperscript{5} but the commonly observed rapid deterioration and resolution as seen in CIM would not be expected if atrophy were the cause. Furthermore, the degree of slowing is greater than that found in other myopathies, which is further evidence of sarcolemmal dysfunction. Inaccuracy of MFCV calculation could result from uncertainty regarding the site of muscle-fiber activation. However, evidence suggests that, with weak stimulation, muscle fibers are activated at discrete low-threshold sites close to the needle tip.\textsuperscript{47} In the presence of a normal nerve and neuromuscular junction, the amplitude of MUPs can be affected by dispersion between action potentials of fibers in single motor units, amplitude decline of a single fiber action potential due to a decrease in MFCV, and blocking of action potentials.\textsuperscript{13} We believe that all three of these mechanisms may play a role in CIM. We found in several patients that muscle fibers were unable to conduct action potentials over the standard 50-mm distance. They were, however, able to conduct action potentials over shorter distances, albeit at reduced velocities, suggesting that there might be conduction block along muscle fibers. This finding has not been described prior to our study, at least to our knowledge.

With respect to the excitability of normal human muscle fibers, a few studies have found a mean absolute refractory period of 4.12 ms (range 2.69–8.13 ms) and a relative refractory period of 5.99 ms (2.88–12.40 ms).\textsuperscript{30} Our data fall within these limits, with our mean normal absolute refractory period being 2.5 ms and that for patients tending to be higher at 4.7 ms, notably above the normal mean for the other studies. The method used by us is likely to stimulate the fibers close to the stimulating electrode with the lowest threshold for activation. This technique may therefore underestimate the degree of inexcitability of muscle fibers in close proximity to the needle tip, as the most inexcitable fibers may simply not be activated.

Trojaborg et al. recently highlighted previous studies showing CMAP prolongation in CIM.\textsuperscript{14} One patient with histologically confirmed CIM had normal intramuscular nerves and marked CMAP prolongation. The smoothly outlined but prolonged CMAPs were thought to be due to slowing of MFCV, as a result of impairment or blockade of voltage-gated ion channels, although this was not demonstrated.\textsuperscript{9} Another study of 9 possible CIM cases revealed prolonged CMAP duration, again with smooth and synchronous waveforms. The investigators suggested that this observation might be useful as a simple diagnostic test.\textsuperscript{31} However, those findings could not be replicated in a subsequent study,\textsuperscript{45} perhaps reflecting milder CIM severity. As we have shown, abnormalities in CIM, namely reduced MFCV and prolonged CMAP duration, are inversely correlated and related to the clinical severity and clinical phase of the illness.

The smooth contour of the markedly prolonged CMAP probably reflects the synchronous depolarization of muscle fibers, which are not only slowed but also have a wider-than-normal distribution of MFCV. Another feature seen in these patients is that the positive phase of the CMAP is often prolonged or even replaced by a long “tail” of the negative phase. This is probably the effect of the few muscle fibers within the diseased muscle with markedly slowed conduction velocities (Fig. 4). However, altered
membrane repolarization dynamics, as part of the overall membrane dysfunction, may also contribute. CMAP measurements represent the whole muscle and, although the MFCV studies sample only a very small proportion of fibers within a single muscle, it is logical that these findings are complementary.

In vitro studies have shown that serum fractions from patients with CIM affect the excitability of intact muscle-fiber membranes and calcium release from the sarcoplasmic reticulum. Rich and Pinter demonstrated that depolarization of the resting membrane potential and a hyperpolarizing shift in the voltage dependence of sodium-channel gating is the principal factor underlying inexcitability in an animal model of CIM. In their model, depolarization of the resting membrane potential following denervation was one of the most important factors because it increased inactivation of sodium channels. In the critically ill, denervation may not be a prerequisite, as the resting membrane potential may be reduced (depolarized) due to raised intracellular sodium, possibly due to a generalized cellular dysfunction related to critical illness. In vitro intracellular recording of individual muscle fibers by Rich and Pinter showed failure of muscle fibers to generate action potentials when stimulated electrically, possibly due to reduced sodium current. Sodium-channel dysfunction in the muscle-fiber membrane can lead to inexcitability and is well known in type 2 HPP, which is associated with SCNA4 mutations. These mutations also result in enhanced inactivation and reduced current through the muscle sodium channel.

Drawing parallels between CIM and HPP may help to define the pathophysiology of CIM and also offer common therapeutic opportunities. In HPP, surface recordings between attacks revealed reduced MFCV, and sensory and motor nerve studies between attacks are normal as are needle EMG findings, although chronically some may develop myopathic changes. During a paralytic attack the CMAP amplitude declines secondary to muscle-membrane inexcitability and invasive recordings show low MFCVs (mean 2.0, range 0.9–3.0 m/s), which improves within hours to days. Early during an attack, fibrillation potentials are evident, indicating depolarized muscle membranes. Single-fiber EMG during an attack shows an increase in jitter and occasional potential blocking, but there is no jitter between attacks. Troni et al. reported that DMS in one patient was not possible for a long period during recovery from paralysis. Muscle showed near electrical silence during paralysis. When power increased to MRC grade 3 in biceps, the MFCV was still slow at 1.7 m/s. In HPP, paralysis is caused by membrane depolarization triggering sodium-channel inactivation, rendering the muscle membrane inexcitable.

In CIM, a similar shift in membrane potential, due to critical illness and perhaps serum factors, may contribute to sodium-channel inactivation and a similar pattern of pathophysiology. Depolarization of the muscle membrane initially gives rise to spontaneous activity, and slowed MFCV; as this progresses, conduction block ensues, and finally the fibers become inexcitable.

“Synchronized dispersion” of the CMAP, in contrast to the well-known asynchronous dispersion seen in demyelinating neuropathy is, we suggest, a characteristic feature of CIM. We agree with previous studies that monitoring of this is simple to perform and may be useful for diagnosis. It may also predict recovery but requires further systematic study. The techniques used for MFCV and excitability measurement are technically demanding. They are powerful research tools but are unlikely to become standard diagnostic testing techniques. Our experience suggests that CIM is more common than CIP and that there is a spectrum of severity within CIM. Some patients are moderately weak, have characteristic neurophysiological changes, and improve quickly. Other patients have more profound weakness, which requires a longer recovery period. These patients have inexcitable muscles, reduced MFCV, and predictable CMAP abnormalities. In CIM, changes at the level of the muscle-fiber membrane correlate with CMAP parameters and the clinical phases.

REFERENCES


