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EDITORIAL

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Evidence of neuromuscular dysfunction in the early stages of the systemic inflammatory response syndrome

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Critical illness polyneuropathy (CIP) is a primary axonal degeneration of motor and sensory fibers which occurs in 50–70% of patients who have the systemic inflammatory response syndrome (SIRS) [2]. Even though it is an important cause of "unexplained" difficulty in weaning from the ventilator and may cause weakness severe enough to impair long-term rehabilitation, it still remains undiagnosed in most intensive care units (ICUs) because of difficulties in clinical assessment and failure to perform electrophysiological studies. There is still no specific treatment for CIP, but if the underlying SIRS can be successfully treated, recovery occurs in a matter of weeks in mild cases and months in more severe cases. Patients with unusually severe cases may not recover, even though the SIRS is successfully treated, and the patient is ultimately discharged from the ICU.

While there is still debate as to the precise nature of CIP, several prospective studies have confirmed the strong association between CIP and SIRS [1, 6, 9, 10]. Accepting this association, many have wondered just how soon in the course of SIRS CIP develops. This is of importance in better understanding the association and how to conduct future research. The question is addressed in a small, but well designed preliminary study by Tennila et al. (in this issue of *Intensive Care Medicine*). They performed electrophysiological studies in

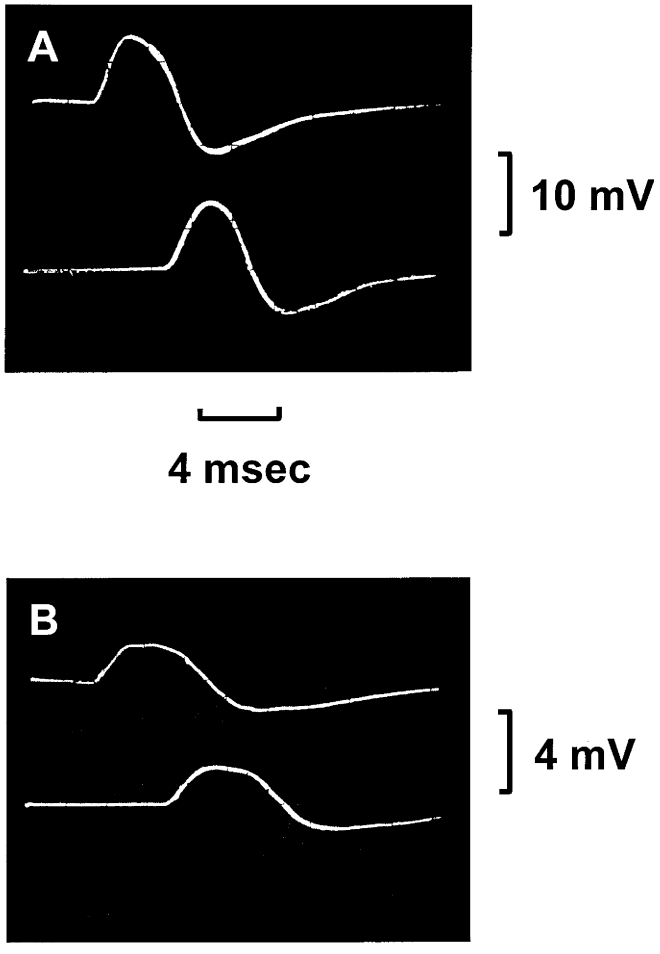

Fig. 1 Measurements of compound thenar muscle action potentials at the onset of sepsis (**A**) and 3 weeks later (**B**). Note the marked fall in amplitude and increase in duration, without change in latency, on stimulation of the median nerve at the wrist and elbow. These changes suggest primary dysfunction of the muscle fiber membrane, in addition to denervation as a secondary effect

nine patients who had moderate to severe SIRS and multiple organ dysfunctions 2, 5, and 14 days following admission to the ICU. On the second to the fifth days all nine patients developed signs of CIP, manifested as a considerable drop in the amplitude of the compound muscle action potential. One-half of the patients had fibrillation potentials and positive sharp waves (abnormal spontaneous activity) on needle electromyography. On the 14th day three of the nine patients had died. In the remainder, electrophysiological abnormalities remained.

A key observation by Tennila et al. is the fall in the compound muscle action potential amplitude, as an isolated electrophysiological event without clinical signs and occurring within the first 2 weeks of the onset of SIRS. There are several possible mechanisms for this. The most likely is that it is secondary to CIP. Even though sensory nerve action potential amplitudes are normal, it has been shown that a fall in compound muscle action potential amplitude is an early and predominant sign of CIP [10, 11]. This may involve predominantly distal motor fibers, as shown in single fiber electromyography studies by Schwarz et al. [8]. It could also have been due to a defect in neuromuscular transmission brought about by the use of neuromuscular blocking agents. However, in the present study these agents were used only briefly, and moreover there was no defect on neuromuscular transmission testing. The fall in amplitude could also have been due to a critical illness myopathy [4]. However, this has been most commonly associated with the use of neuromuscular blocking agents and steroids, which, again, were not factors in the present study. On the other hand, it has been demonstrated that muscle, as well as nerve, is affected in SIRS. Careful measurements of the compound muscle action potential amplitude during the early stages of sepsis [12] show not only a fall in amplitude but also an increase in duration without change in latency (Fig. 1), which indicates that at least some of the fall is due to primary involvement of the muscle fiber membrane. These changes, fall in amplitude and increased duration, are seen in human muscle during fatigue and are thought to be secondary to dysfunction of the energy dependent Na/K gradients [7]. There is further evidence that there are energy changes in the muscle fiber membrane associated with SIRS. P31 nuclear magnetic resonance spectroscopy of human muscle in sepsis, complicated by CIP, shows a marked fall in bioenergetic reserves, which cannot be explained by denervation alone [3]. Thus in the present study the fall in compound muscle action potential amplitude is probably a combination of dysfunction of both peripheral nerve and muscle. Electrophysiological and morphological studies of critically ill patients who had severe muscle weakness suggests functional derangement precedes structural change [5]. It may therefore be an important early biological sign in humans of cell membrane dysfunction in SIRS and may have implications for research. The information could be used in trials determining the efficacy of various interventions which attempt to interrupt the septic cascade in its early stages.

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