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Preliminary observations on the neuromuscular abnormalities in patients with organ failure and sepsis*

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Abstract. *Objective:* To estimate the incidence and nature of neuromuscular abnormalities in a representative group of ITU patients.
Design: Prospective sequential study.
Setting: Teaching hospital ITU.
Patients: 23 patients who eventually stayed >7 days on ITU who had no contraindication to muscle biopsy and whose relatives gave informed consent.
Measurements and results: Muscle histopathology, neurophysiological studies, record of all drugs administered, APACHE II score, organ system failure score, presence or absence of sepsis, clinical evaluation of neuromuscular problems, time to hospital discharge. Heterogeneous neuromuscular abnormalities were present in 22 out of 23 patients studied and included axonal neuropathy, denervation, generalised fibre atrophy, non-specific myopathy and necrotising myopathy.
Conclusion: Neuromuscular abnormalities are almost invariable in longstay intensive care patients and the resulting weakness may seriously delay hospital discharge. Various abnormalities were seen but no obvious aetiological factors were identified. The origin of the abnormalities is probably multifactorial.

Key words: Critical illness – Neuromuscular abnormalities – Organ failures – Sepsis

Weakness and muscle wasting has been recognised as a complication of acute severe illness at least since the time of Hippocrates who suggested more than 2000 years ago that physicians were not acquainted with the ways in which the various causes of weakness during the course of an illness could be distinguished [1]. Traditionally, muscle wasting complicating serious disease or injury has been attributed to inadequate nutrition in the face of increased metabolic demands [2]. It is now generally accepted, however, that even with optimal nutritional support a negative nitrogen balance may be inevitable [3], and despite the routine provision of enteral or parenteral feeding severe weakness still frequently complicates recovery from critical illness.

In some of the most seriously ill patients, weakness may be due to an acquired neuropathy, [4–8], and more recently a necrotising myopathy affecting patients with failure of one or more vital organs has been described [9, 10]. In the original descriptions of critical illness neuropathy [4–8] patients were selected for study on the basis of clinically obvious weakness [5, 6] particularly respiratory muscle weakness, and difficulty in weaning from ventilatory support [4, 7, 8]. In the larger series mortality was high; 58% of patients with neuropathy died [4] and in those with necrotising myopathy mortality was more than 70% [9, 10]. These patients were not therefore typical of the general population of intensive care patients. It was our impression that significant weakness following critical illness was more common than previously thought. We therefore preformed a preliminary prospective study to establish the incidence and nature of neuromuscular abnormalities in a representative group of intensive care patients.

Patients and methods

Patients who had been, or were expected to remain on the intensive care unit for 7 days or more, with failure of one or more organs and who did not have demonstrable weakness or wasting at the time of admission to the unit were recruited over an 11 month period. We excluded patients with severe clotting abnormalities and those receiving therapeutic anticoagulation. Consent was obtained from the patient or the next of kin. The study was approved by the Hospital Ethical Committee.

Muscle biopsies were obtained under local anaesthesia (5 ml lignocaine 2%) using the percutaneous conchotome technique [11] from the right vastus lateralis muscle. Samples were processed according to standard techniques [12]. Frozen sections were stained with haematoxylin

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and eosin, the modified Gomori trichrome method, and periodic acid Schiff stains. ATPase stains with preincubation at pH 9.4 and 4.6, NADPH-TR, and succinic dehydrogenase enzyme histochemistry were performed. Morphometric analysis of fibre size was carried out with an IBAS-2 image analyser. A sample was processed for electron microscopy.

Electromyography and nerve conduction studies were performed in 10 patients recruited into the latter part of the study. Serum creatine kinase activity was estimated in 15 patients at the time of muscle biopsy. The muscle histology and neurophysiology were reported by Dr. Honavar and Dr. Nagendran respectively, who were unaware of the diagnoses, numbers of organs failed or drugs administered.

Apache II scores [13] were calculated on admission to ITU. Organ failures (scheme devised by Dr. C. Ferguson, unpublished) and the presence or absence of sepsis were documented according to predefined criteria [14] (Table 1). A record was kept of all drugs given to the patients prior to muscle biopsy and neurophysiological examination. All patients received nutritional support either enterally (70 g protein and 2000 kcals per day) or parenterally (14 g nitrogen and 2000 kcals per day). Patients were followed until death of discharge from hospital.

Table 1. Criteria for diagnosing organ system failures

1. *Cardiovascular* One of:
   Mean arterial pressure <60 mmHg
   Fall in blood pressure of >40 mmHg from baseline
   Life threatening arrhythmia
   pH <7.24, PCO_2 <6.5 kPa
   Vasoactive drug required
2. *Respiratory* One of:
   Rate <5, >40 min
   PCO_2 >6.6 kPa
   A-a O_2 >46.6 kPa
   Ventilator dependant >60 h
3. *Renal* One of:
   Urine output <8 ml/kg/24 h
   Urea >30 mmol/l
   Creatinine >300 µmol/l
   Renal support
4. *Hepatic* Two of:
   AST >80 µ/l
   Alk. phos. >200 µ/l
   Bilirubin >34 without obstruction or haemolysis
   Unexplained hypoglycaemia
5. *Digestive* One of:
   Frank haemorrhage
   Ileus (excluding 5 days after abdominal surgery)
   Persistant diarrhoea
   Perforation/obstruction of viscus
   Pancreatitis
   Acalculous cholecystitis
   Gut infarction or ischaemia at laparotomy
6. *Haematological* One of:
   White cell count <1000
   Platelets <20000
   Packed cell volume <0.2
   Prothrombin time $>$ twice control
7. *Central nervous system*
   Glasgow coma score <10 without sedation
8. *Sepsis* Two of:
   Two episodes of core temperature >39 °C or <36 °C
   White blood cell count <3000 >12000
   Positive blood culture
   Pus in closed space
   Known or suspected source of systemic infection
   And One of:
   Unexplained systolic blood pressure <90 mmHg for over 2 h
   Unexplained metabolic acidosis
   Base defecit >5
   Systemic vascular resistance <800 dynes/s/cm^5

Results

Over the 11 month period of the study 62 patients were on ITU for 7 days or more but the majority either had abnormal blood clotting studies of platelet counts, or relatives refused consent for the study. A total of 23 patients were studied (8 female; age range 20–72 years).

A summary in Table 2 outlines the patients' age, sex, diagnosis, organ failures and the presence or absence of sepsis at the time of muscle biopsy. The outcome for each case is given as is the admission APACHE II score.

Median number of organ failures at the time of muscle biopsy was 3 (range 1–6). The organs which had failed (numbers of patients) were respiratory (23), renal (11), gastrointestinal (10), cardio vascular (8), liver (6),

Table 2. Patient numbers together with age, sex and principle conditions for which intensive care admission was necessary. The organs which failed as defined in Table 1 are shown in brackets after the admitting diagnoses. The abbreviations are as follows: Rs – respiratory, Rn – renal, CVS – cardiovascular, CNS – central nervous system, GIT – gastrointestinal tract, haem – haematological, + patients with sepsis, – patients without sepsis. Patients who died are marked *. APACHE II scores are also given at the time of ITU admission

No.	Age/sex	APACHE II	Diagnosis
1	38 M	24	Self poisoning, convulsions, respiratory arrest (Rs, Rn, CNS) –
2	70 M	23	Respiratory arrest (Rs, Rn, liver) +
3	42 F	17	Burns, acalculous cholecystitis (Rs, Rn, CVS, liver, GIT) +
4	61 M*	12	Elec. aortic aneurysm repair (Rs, Rn) –
5	58 M*	15	Head injury (Rs, CNS) –
6	64 M	13	Pneumonia (Rs, CVS, liver, GIT) +
7	54 F	9	Multiple trauma, fat embolism syndrome (Rs, CVS, liver, GIT) +
8	54 M	18	Aortic embolus (Rs, Rn, CVS, GIT) –
9	69 M*	23	Wegener's granuloma (Rs, Rn) –
10	69 F	29	Respiratory arrest, renal failure, amyloid (Rs, Rn, haem) –
11	69 M	13	Head and chest injury (Rs) –
12	34 F	8	Pelvic actinomycosis (Rs, Rn, liver, GIT) +
13	29 M	14	Chickenpox encephalitis, convulsions (Rs, Rn, CNS) –
14	66 F*	20	Chronic airflow limitation (Rs, Rn, CVS, haem, GIT) +
15	67 M	21	Chronic airflow limitation (Rs, haem, GIT) +
16	20 M	8	Multiple limb fractures (Rs, haem, GIT) +
17	70 M	10	Peritonitis post renal transplant (Rs, GIT) +
18	70 M	14	Head and chest injury (Rs, CNS) –
19	57 F	22	Chronic airflow limitation (Rs) –
20	31 M	8	Chest injury, ruptured spleen (Rs) –
21	72 F	21	Chronic airflow limitation (Rs, CVS) +
22	63 F*	19	Septic shock post laparotomy (Rs, Rn, CVS, haem, liver, GIT) +
23	47 M	6	Myocardial infarction, cardiac arrest, flail chest (Rs, CVS) –

haematological (6), central nervous system (4). Eleven patients had sepsis and 5 patients (22%) died. The number of days following ITU admission on which the biopsies were taken is given in Table 3.

Histopathology

Muscle biopsies were obtained a median of 10 days (range 3–37 days) after intensive care admission. In only one patient was muscle histopathology normal. Abnormal histological features were demonstrated in 22 patients (Table 3). In 4 cases (patients 2, 4, 17, 21) the muscle showed evidence of neurogenic atrophy with reinnervation. Muscle biopsies from 8 patients demonstrated myopathic features with atrophy and degeneration. In 2 biopsies from this group (patients 7 and 9) there were, in addition, scattered single necrotic fibres undergoing myophagocytosis. No regenerating fibres were seen. Two patients (1, 18) showed only mild type 2 fibre atrophy. The rest (8 cases) showed diffuse atrophy of both fibre types. This ranged from severe atrophy with intra-fascicular fibrosis seen in patient 3, from whom two biopsies were taken (12 days apart, taking care to avoid sampling areas affected by burns) to mild atrophy, appreciated only on morphometric analysis. The muscle abnormalities are summarised in Table 3. Electron microscopy showed atrophic muscle fibres in all the abnormal biopsies. Scattered degenerating fibres were seen in those classified as myopathic. In 3 of these there were additional features: swollen mitochondria were seen in otherwise normal fibres in one; in another paracrystalline mitochondrial inclusions were found in fibres that had disorganised myofibrils, and in a third cytoplasmic tubular aggregates were present. In one biopsy that showed mild diffuse atrophy, there were prominent subsarcolemmal aggregates of morphologically normal mitochondria.

Table 3. Histological features seen on muscle biopsy for individual patients. The numbering of patients is the same as in Table 2. The number of days following ITU admission on which the biopsy was taken is given in column two. The creatine kinase activities at the time of muscle biopsy are given in column 5. In patients with myopathy, the sign + indicates the presence of muscle fibre necrosis

Patient	Day of biopsy	Muscle histology	Discharge delay	CPK	Weakness at time of ITU discharge
1	9	Type 2 fibre atrophy	8	6665	+
2	7	Neurogenic atrophy	11[b]	3178	+ + +
3	7	Diffuse atrophy	7[a,b]	29	+ + +
4	18	Neurogenic atrophy	NS	–	NS
5	3	Myopathy	NS	–	NS
6	14	Myopathy	60[b]	19	+ + +
7	10	Myopathy +	32	200	+ +
8	10	Diffuse atrophy	31[a,b]	6170	+ + +
9	23	Myopathy +	NS	–	NS
10	21	Diffuse atrophy	61[b]	–	+ + +
11	4	Diffuse atrophy	10	161	+
12	37	Diffuse atrophy	33[b]	–	+ +
13	6	Myopathy	12	4659	+ +
14	26	Myopathy	NS	172	NS
15	34	Myopathy	29[b]	17	+ + +
16	19	Diffuse atrophy	44[a]	394	+ + +
17	9	Neurogenic atrophy and myopathy	30[b]	–	+ + +
18	7	Type 2 fibre atrophy	5[a]	–	+ +
19	5	Myopathy	15[b]	100	+ +
20	3	Diffuse atrophy	10	112	+
21	9	Neurogenic atrophy	14[b]	831	+ + +
22	11	Diffuse atrophy	NS	–	NS
23	11	Normal	10	1000	+

The time delay from ITU discharge to hospital discharge, and the degree of weakness at the time of ITU discharge is also noted, with + indicating mild, + + moderate and + + + severe weakness
NS, non-survivor
[a] transferred to other hospital – for further rehabilitation
[b] prolonged ITU stay because of respiratory muscle weakness

Electrophysiological studies

The following studies were carried out.

1. Median and sural sensory action potential (SAP) amplitudes.
2. Lateral popliteal motor conduction study
Motor conduction velocity (MCV) and the amplitude of compound muscle action potential (CMAP) from the Extensor Digitorum Brevis (EDB) were measured.
3. Median nerve motor conduction study
Motor conduction velocity and the amplitude of CMAP from the Abductor Pollicis Brevis (APB) were measured.
4. Concentric needle electromyography (CN-EMG) of Tibialis Anterior (TA).
5. CN-EMG of Biceps Brachialis (BB) or Vastus Medialis (VM).
Only 4 patients were co-operative enough to study motor unit potentials.

The most striking abnormality in the nerve conduction study was an absent or abnormally small sural SAP with severely reduced or unrecordable CMAPs from the EDB. The lateral popliteal motor conduction velocity showed mild slowing. These are features of a primarily axonal sensory motor peripheral neuropathy. The presence of coexisting myopathy is more difficult to assess. Only 4 patients were conscious enough co-operate, to study voluntary motor units. Patient 21 showed normal SAPs and markedly abnormal CMAPs from EDB and APB. Other nerves studied, including ulnar and posterior tibial nerves showed similar abnormalities. Follow up studies over the next 8 weeks showed progressive return to normality. Although repetitive stimulation at 3 Hz carried out in one of the studies showed no abnormality, the severe pure motor features with subsequent rapid improve-

Table 4. Results of neurophysiological studies

Patient number	Sural SAP μV	Median SAP μV	LPN MCV M/s	EDB CMAP mV	Med MCV M/s	APB CMAP mV	EMG TA	EMG VM/BB
7	0	17	–	0.33	–	–	–	mns
8	2	–	45	0.1	58	2.5	n++	–
10	0	20	36	0.2	–	–	n+	mns
11	16	10	–	–	55	2.0	N	N
12	3	3	0	0	36	3.0	n+	–
16	0	10	0	0	–	–	n++	–
17	0	6	43	0.5	–	–	n+	m
19	0	20	–	0.6	–	–	N	N
21	10	12	0	0	42	0.3	n+	–
22	0	10	41	0.5	–	3.0	n+	N

(–) not done, (mns) minor nonspecific abnormality, (m) myopathy, (0) absent, (n+) mildly neurogenic, (n++) severely neurogenic, (N) normal, (LPN) lateral popliteal nerve, (Med) median

ment may well be primarily due to a neuromuscular junction disorder.

In summary, all but one patient showed neurophysiological abnormalities. In 8 there was evidence suggesting a primary axonal neuropathy, and 2 of these also had evidence of a myopathic process. One (patient 21) had a predominantly motor syndrome associated with a neurogenic atrophy on muscle biopsy which we have previously reported [15].

Creatine kinase activities were variable, with a median value of 200 but a range from 17–6665 u/l (normal range < 170 u/l). The creatine kinase activities for individual patients are given in Table 3.

A wide variety of drugs were administered to these patients, including antibiotics, muscle relaxants, sedatives, inotropic and vasoactive drugs, and prophylaxis against gastrointestinal haemorrhage and venous thrombosis. There appeared to be no relationship between corticosteroid administration (hydrocortisone 20 mg/h by continuous infusion to patients 9, 10, 14, 15, 19, 21 from admission to time of biopsy) or the prolonged (> 48 h) infusion of non-depolarising muscle relaxants and the development of histological abnormalities in muscle (Table 5). Neither did the presence or absence of sepsis seem to influence the incidence of neuromuscular disorders.

Clinical features following withdrawal of sedative drugs and/or muscle relaxants at the time of ITU discharge were variable. The weakness was generalised in most cases, with relative sparing of the facial muscles. Weakness was severe in 9 patients, moderate in 5, and only mild in 4. Tendon reflexes were absent in one patient, reduced in 4, normal in 10 and brisk in 3. There was no evidence in any of the patients of asymmetrical neurological involvement and there were no clinically detectable sensory abnormalities. In all the survivors weakness progressively improved. The weakness at the time of ITU discharge is outlined in Table 3.

The median delay from leaving the intensive care unit to hospital discharge in the survivors was 15 days with a range from 5–61 days. In those with the longest delay, muscle weakness was a major contributory factor. The delay from leaving intensive care to hospital discharge is

Table 5. The relationship between the administration of steroids (20 mg/h of hydrocortisone by continuous infusion from admission to time of biopsy) or muscle relaxants (> 48 h by continuous infusion) and the presence of sepsis and the muscle histological abnormalities. The numbers of patients with each muscle abnormality are shown, with the percentages in brackets. There is no evidence that steroids or muscle relaxants are responsible for abnormal muscle histology, $p > 0.05$ for association of myopathy with steroids, $p > 0.1$ for association of neurogenic atrophy with sepsis and myopathy with relaxants, $p > 0.2$ for all other associations (χ^2)

	Sepsis		Steroids		Relaxants	
	Yes	No	Yes	No	Yes	No
Type 2 atrophy	0	2 (17)	0	2 (12)	0	2 (25)
Neurogenic atrophy	3 (27)	1 (8)	1 (17)	3 (18)	2 (13)	2 (25)
Generalised atrophy	4 (36)	4 (33)	1 (17)	7 (41)	5 (33)	3 (37)
Myopathy	4 (36)	4 (33)	4 (67)	4 (24)	7 (47)	1 (13)
Normal	0	1 (8)	0	1 (6)	1 (7)	0
Total	11	12	6	17	15	8

given in Table 3. The delay may have been underestimated because some patients were transfered for rehabilitation to hospitals nearer to their homes. In some patients there was prolonged ventilator dependence and these cases are indicated in Table 3.

Discussion

In this heterogeneous group of critically ill patients, selected solely on the basis of their length of stay in the intensive care unit, neuromuscular abnormalities, not initially apparent on clinical examination, were almost invariably demonstrable on histological and neurophysiological investigation. These abnormalities occurred in patients with or without sepsis, and with numbers of organ system failures ranging from 1–6. Unfortunately many of the patients who were on ITU were excluded because of abnormal clotting studies. Furthermore, many of the relatives involved did not consent to the study because they could see no clinical benefit accruing to the patient. The investigators were at pains to point out to all relatives that the recruitment to the study would not alter the clinical outcome and would not be beneficial to the individual patients. No pressure was applied to the relatives to give consent, and this accounts for the relatively low recruitment rate. Nevertheless the patients studied were representative of the general long stay intensive care unit population of this hospital as judged by admission Apache II scores, organ failure and sepsis scores, and overall mortality.

The development of a neuropathy characterised by primary axonal degeneration involving both motor and sensory nerves is now a well recognised complication of critical illness. This 'critical illness neuropathy' was originally described in a series of patients with multiple organ failure and sepsis who presented with difficulty in weaning from ventilators due to respiratory muscle weakness following varying periods of intensive care; in those who died histological examination revealed abnormalities in muscle suggestive of denervation atrophy and confirmed

the presence of an axonal neuropathy [7, 8]. The existence of this syndrome has been confirmed by others, in one patient with multiple organ failure who survived [5] as well as in a series of 15 patients with a variety of organ system failures and a mortality of at least 33% [6]. In all of these studies [4–8] investigation of neuromuscular disease was prompted by the development of profound weakness often manifesting as difficulty in weaning from ventilatory support. More recently neurophysiological studies have been performed prospectively in a consecutive series of patients with multiple organ failure and sepsis [16]. In this group of patients the incidence of axonal neuropathy was over 70% but again mortality was high, more than 50%. The aetiology of this neuropathy remains unclear [4] but there appeared to be an association between the presence of neuropathy and reduced serum albumin, elevated glucose, and length of stay in the intensive care unit [16].

In a previous study muscle biopsies, obtained from 31 intensive care patients for the purpose of biochemical studies, were also examined histologically. Most had combined renal and respiratory failure. Histological examination revealed a necrotising myopathy in 17 and muscle fibre atrophy in 12, including 4 patients without necrosis [9, 10]. Mortality was greater in those with necrotising myopathy (70%) than in those without (30%), and there was a greater incidence of renal failure in those with muscle necrosis [9]. Although muscle abnormalities occurred more frequently in our study, muscle necrosis was less common, possibly because our patients were less severely ill. Also in the previous study samples were obtained from the tibialis anterior muscle, and it is possible that muscle swelling within this relatively restricted compartment may have impaired intramuscular blood flow leading to ischaemic necrosis. Nevertheless, necrosis was seen in the quadriceps muscle of two of our patients, as well as in some of Helliwell's patients in whom quadriceps was sampled at the same time as anterior tibial muscle [9].

The histological abnormalities seen in the muscle are varied and it is difficult to attribute them to a single aetiology. Nevertheless it is possible that at least some of the changes may be secondary to the development of a neuropathy and there is evidence of neurogenic atrophy with reinnervation in biopsies from 4 of our patients. Neurophysiological studies were not performed in Helliwell's study, but in ours neurophysiological abnormalities were always associated with abnormal histological muscle features. Although one of our patients with diffuse atrophy had normal electrophysiology all those with evidence of axonal neuropathy had abnormal muscle biopsies, the most common finding being diffuse muscle fibre atrophy. It is possible that patients showing diffuse atrophy of both fibre types consist of a mixed group. In a proportion of these, the atrophy may have been neurogenic in origin, the small sample of muscle examined failing to reveal the typical histological features. Similarly others may be myopathic, the biopsy failing to show the focal muscle fibre degeneration. Also, there were 4 patients in whom there was histological and neurophysiological evidence of both a neuropathy and a myopathy. Preferential atrophy of type 2 fibres as a result of disuse is well recognised and documented since it was first reported [17], but such changes were seen in only 2 of our patients. It seems unlikely that immobility along could account for the development of neuropathy. The mitochondrial abnormalities on electron microscopy seen in a few of our cases have been reported in a wide variety of muscle disorders and lack specificity, but raise the possibility of disordered mitochondrial metabolism in the pathogenesis of the neuromuscular abnormalities.

The creatine kinase activities were only marginally raised or normal in most patients and in those with very high activities there were other factors which may have contributed such as prolonged convulsions (patients 1 and 13) and ischaemic damage to the legs (patient 8). Normal creatine kinase activity does not of course exclude significant neuromuscular disease.

Malnutrition may also cause abnormal muscle histology. In a study of the effects of deliberate undernutrition for 2 weeks on the muscle composition of obese patients, the most striking abnormality was a decrease in type 2 fibre diameter [18] which was found in only 2 of our patients. All of our patients were fed enterally or parenterally from a few days after admission to intensive care, although formal nitrogen balance studies were not performed. Specific deficiencies known to result in excess muscle breakdown, such as glutamine deficiency cannot be excluded [19], nor can insulin-like growth factor deficiency, which has been described in septic patients after as little as 4 days of mechanical ventilation [20].

Our patients all received a wide variety of drugs including antibiotics, inotropes, vasoconstrictors, sedatives and muscle relaxants, and we wondered about the possibility of drug induced neuromuscular damage, since this has been described previously [21–24]. We kept a complete record of all drugs administered during ITU stay and were particularly interested in the effects of prolonged administration of corticosteroids [23] and muscle relaxants [24]. We could find no evidence that either of these 2 groups of drugs was associated with the muscle abnormalities (Table 3). It has been suggested that prolonged infusions of non-depolarising neuromuscular blocking agents may cause a neuropathy [24] but the axonal neuropathy described by these authors has subsequently been documented in other patients with critical illness [4–8] many of whom had not received neuromuscular blockers. Furthermore it is difficult to explain the sensory abnormalities seen in the critical illness neuropathy on the basis of prolonged motor blockade. Others have suggested that infusion of non-depolarising muscle relaxants may cause weakness after as little as 48 h [25].

Many of our patients subsequently showed evidence of weakness on clinical examination. Since muscle force is proportional to cross sectional area [26, 27], atrophy of muscle fibres leads to weakness irrespective of other abnormalities, but is compounded by the presence of muscle necrosis, as well as neuropathy. Such weakness will inevitably prolong both weaning from ventilatory support and rehabilitation following discharge from intensive care. In our series survivors remained in hospital for up to 61 days after ITU discharge, and in many cases hospital stay was prolonged purely because of weakness.

In conclusion, neuromuscular abnormalities were almost invariable in our long stay intensive care patients, and in contrast to previous studies were not exclusively associated with multiple organ failure and sepsis. If the neuromuscular apparatus is accepted as an organ system capable of failing, it was numerically second only to respiratory failure in our patient population. The abnormalities are heterogeneous, and probably multifactorial in origin. Aetiological factors may include nutritional deficiency, immobility, underlying disease and the effects of drugs, although other, as yet unidentified causes, are also likely to be responsible. Overall the commonest abnormality was diffuse muscle fibre atrophy, associated with a critical illness type axonal neuropathy. The ensuing weakness may cause delay in weaning from ventilatory support and hospital discharge, and is thus potentially both expensive and demanding of medical, nursing and physiotherapy time. Further research is needed to identify the causes of neuromuscular weakness in the critically ill since prevention may only be possible once the aetiology has been established.

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