Management of acute neuromuscular paralysis

ABSTRACT – The diagnosis of acute neuromuscular paralysis includes central nervous system disorders, peripheral neuropathy, neuromuscular conduction block and muscle disease. Identification of the cause is largely a clinical problem but neurophysiological investigations are often essential and a few specific tests are helpful. The commonest cause is Guillain-Barré syndrome. Special precautions, especially monitoring vital capacity, must be taken to detect respiratory failure and avoid atelectasis and chest infection. In acute neuropathy there is an additional danger of cardiac arrhythmias which requires continuous electrocardiographic monitoring. Prolonged artificial ventilation should be supervised by a specialist multi-disciplinary intensive care team. Specific treatment depends on the diagnosis: for Guillain-Barré syndrome, intravenous immunoglobulin is preferred to plasma exchange on the basis of similar efficacy but greater convenience; steroids are not helpful; for myasthenia gravis, anticholinesterases and prednisolone may need to be supplemented with intravenous immunoglobulin or plasma exchange; for polymyositis, steroids are the mainstay of treatment. During convalescence patients require understanding and support in coping with residual disability.

Differential diagnosis

Central nervous system disorders mimicking acute neuromuscular paralysis

Acute neuromuscular paralysis presents as acute flaccid weakness with diminished or absent tendon reflexes. This sometimes occurs with brainstem or spinal cord lesions. Although brainstem disorders usually cause increased tendon reflexes, critically placed rostral lesions may cause transient hyporeflexia. In acute spinal cord lesions the injury initially inhibits intrinsic spinal cord relays and so depresses the tendon reflexes, a condition called ‘spinal shock’. The principal causes of central nervous system disorders mimicking acute neuromuscular paralysis are listed in Table 1.

Polioymelitis deserves special mention because of the current World Health Organisation (WHO) effort to eradicate the disease. Although it is uncommon in UK practice, we must continue to consider and investigate the possibility of poliomyelitis in all relevant cases of acute flaccid paralysis.

Recent vaccination or contact with a recently vaccinated individual, asymmetric paralysis, absence of sensory deficit and cerebrospinal fluid (CSF) pleocytosis all raise the suspicion of poliomyelitis, and proof or exclusion requires the submission of two stool samples for viral culture within two weeks from the onset of symptoms. The Americas have already been declared free of wild-type paralytic poliomyelitis and efforts are under way to eradicate it also from Europe. We will not achieve this aim without investigating suspect cases to exclude the possibility of the diagnosis.

Disorders of neuromuscular transmission

Myasthenia gravis is usually easily diagnosed from the characteristic history of fatigue and paresis, but fulminating cases can be difficult to recognise and other disorders of neuromuscular transmission are frequently overlooked (Table 2). The rarity of botulism makes the diagnosis particularly difficult: clues are abdominal pain and vomiting soon after an appropriate meal; appearance of neurological symptoms within a few hours; dryness of the mouth; loss of visual accommodation; constipation; bulbar palsy; and descending paralysis. Repetitive nerve stimulation elicits an incremental pattern of evoked muscle action potential amplitudes. Proof comes from culturing Clostridium botulinum from the affected food and paralysis of mice injected with serum from the patient. The diagnosis of myasthenia gravis will usually be obvious but can be confirmed by a decremental pattern of evoked muscle action potential amplitudes, positive acetylcholine receptor antibodies, and response to intravenous edrophonium (which should always be performed with atropine cover and precautions to cope with the asystole that it may produce).

Muscle disorders

The commonest missed cause of acute neuromuscular paralysis is hypokalaemia. Blood electrolytes should therefore be checked immediately in every case. Muscle disorders usually pursue a chronic course but sometimes rapid deterioration and decompensation of respiratory muscles first bring the patient to hospital. In acute rhabdomyolysis the rapid development of weakness and renal failure with a markedly elevated creatine kinase may be dramatic (Table 3). The diagnosis of muscle disease will be suggested by muscle weakness without sensory symptoms or signs and can be confirmed electromyographically by the presence of small amplitude, polyphasic motor units. Identifying the cause may need a muscle biopsy, which can be readily performed under local anaesthesia by inserting a needle into the vastus lateralis muscle under local anaesthesia.
Table 1. Central nervous system disorders mimicking acute neuromuscular paralysis.

| Disorder                                      |
|-----------------------------------------------|
| Locked-in syndrome                            |
| Brainstem infarction                          |
| Brainstem encephalitis                        |
| Poliomyelitis                                 |
| Spinal cord compression                       |
| Acute transverse myelopathy                   |
| Paralytic rabies                               |
| Conus/cauda equina compression                |
| Motor neuron disease                          |

Acute neuropathies

The clinical diagnosis of peripheral neuropathy will be suggested by the presence of sensory symptoms and especially signs, as well as weakness and loss of tendon reflexes at an early stage, cranial nerve involvement, and, in some cases, autonomic features. The presence of peripheral neuropathy can be confirmed by the neurophysiological findings of diminished sensory nerve and motor action potentials and slowed nerve conduction velocity. Acute neuropathy occurs in the course of many systemic diseases and may sometimes be their presenting feature. Careful enquiry about antecedent events, drug history and toxin exposure, and consideration of the clinical setting will be sufficient to narrow the differential diagnosis (Table 4) to manageable proportions.

Guillain-Barré syndrome

The diagnosis of Guillain-Barré syndrome (GBS) can only be achieved by exclusion of other causes of acute neuromuscular paralysis, because there is no absolute diagnostic test and even the characteristic clinical picture can be mimicked by the conditions in Tables 1-4. The annual incidence is between 1 and 4 per 100,000 worldwide. In the most recent population-based study in South East England the incidence was 1.5 per 100,000; of the 79 patients in this study, 25% required ventilation, 8% died and 13% were unable to walk one year later.

Neurophysiological investigation is the most helpful diagnostic test because it both establishes the presence of peripheral neuropathy and characterises its type. During the past decade it has become accepted that GBS includes at least three separate entities: acute inflammatory demyelinating polyradiculoneuropathy, which accounts for the large majority, and two forms of axonal neuropathy, acute motor and sensory axonal neuropathy and acute motor axonal neuropathy, which between them account for the remainder. Distinguishing these pathological entities during life is difficult but can be attempted with early and, if possible, sequential neurophysiological studies. In the demyelinating form, slowed nerve conduction velocity, partial conduction block and dispersion of compound muscle action potentials are present. In the axonal form, these features are absent but the compound muscle action potentials diminish in amplitude despite relative preservation of conduction velocity. According to criteria based on these principles, 69% of 369 patients participating in a worldwide multicentre trial had demyelinating neuropathy, 3% axonal neuropathy, and 3% inexcitable nerves (which could not therefore be classified as axonal or demyelinating). In the remainder the findings were equivocal, not allowing a distinction between axonal or demyelinating, or within normal limits.

The chief usefulness of CSF examination is that the presence of a marked pleocytosis suggests alternative diagnoses, such as poliomyelitis, Lyme disease or associated HIV.

Table 2. Neuromuscular conduction disorders causing acute neuromuscular paralysis.

| Disorder                                      |
|-----------------------------------------------|
| Myasthenia gravis                             |
| Eaton-Lambert syndrome                        |
| Botulism                                      |
| Hypermagnesaemia                              |
| Tickbite paralysis                            |
| Snake, scorpion and spider bites              |

Table 3. Muscle diseases causing acute neuromuscular paralysis.

| Disorder                                      |
|-----------------------------------------------|
| Hypokalaemia                                  |
| Hypophosphataemia                             |
| Periodic paralysis                            |
| Acute rhabdomyolysis                          |
| Polymyositis                                  |
| Critical illness myopathy                     |

Table 4. Peripheral neuropathies causing acute neuromuscular paralysis.

| Disorder                                      |
|-----------------------------------------------|
| Toxins: heavy metals, eg arsenic, thallium, lead; organophosphates; hexacarbons |
| Alcohol                                       |
| Drugs: nitrofurantoin, isoniazid, vincristine, taxol |
| Metabolic: diabetes, porphyria, tyrosinaemia   |
| Nutritional deficiency: thiamine              |
| Vasculitis: polyarteritis nodosa, Churg-Strauss syndrome, systemic lupus erythematosus |
| Sarcoidosis                                   |
| Lymphoma                                      |
| Infections: diphtheria, Lyme disease          |
| Critical illness polyneuropathy               |
| Guillain-Barré syndrome:                     |
| Acute inflammatory demyelinating polyradiculoneuropathy |
| Acute motor and sensory axonal neuropathy     |
| Acute motor axonal neuropathy                 |

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infection. The CSF protein is famously increased in GBS, but unhelpful because it is often normal during the first two weeks. Additional investigations need to be directed to exclude systemic disorders which are possible in the clinical setting. Neuropathy may be the presenting feature of porphyria and systemic lupus erythematosus, so that testing the urine for porphyrins and the serum for antinuclear antibodies should be routine. Although there are no clinically useful immunological tests for GBS, immunoglobulin G (IgG) antibodies against ganglioside GM₁, a component of myelin and axonal membranes, are present in 25% of patients. The commonest antecedent events are Campylobacter jejuni infection (25%), cytomegalovirus (10%), and Epstein-Barr virus (EBV), Mycoplasma and herpes zoster (each in 1–5%). Each of these may be diagnosed retrospectively by serological tests but their identification is only of research interest because it does not lead to any alteration in treatment. However, GBS following Campylobacter jejuni infection does have a worse prognosis than GBS from other causes.

**Neuromuscular paralysis in the critically ill**

Neuromuscular paralysis occurring in the critically ill patient presents as failure to wean from the ventilator in a patient in the intensive care unit (ITU) who has usually had a combination of major trauma or operation, multiorgan failure, sepsis, high fever and sometimes prolonged high dose steroid and muscle relaxant treatment. The differential diagnosis includes persistent neuromuscular conduction block, critical illness polyneuropathy, necrotising myopathy and the acute inflammatory demyelinating form of GBS. Critical illness polyneuropathy is a predominantly motor axonal polyneuropathy of unknown pathogenesis. The problem is being recognised with increasing frequency in intensive care units throughout the world: prospective clinical and neurophysiological studies have identified an incidence as high as 50 to 70%. The severity is variable and although many severely affected patients die, recovery in three to six months is possible. Acute necrotising myopathy causes a clinical and electrophysiological picture that may be difficult to distinguish unless the patient is well enough to report the absence of sensory impairment or unless sensory nerve action potentials can be shown to be absent (which may be difficult for technical reasons in the ITU). The serum creatine kinase is usually elevated. Needle muscle biopsy will reveal either diffuse necrotising myopathy with myosin loss or multifocal muscle fibre necrosis.

**Investigation**

The investigation of acute neuromuscular paralysis needs to be guided economically by the clinical features and undertaken urgently so that specific treatment can be instituted. It is wise to check the plasma electrolytes immediately since correction of hypokalaemia may avoid the need for further investigation or treatment. The investigations that usually need to be considered are listed in Table 5.

**Neuromuscular respiratory failure**

**Recognition**

Neuromuscular respiratory failure is dangerous because patients die quietly without the obvious shortness of breath or loud wheezing that accompany serious lung or airway disease. The vital capacity falls to low levels before hypoxaemia develops from neuromuscular respiratory failure, and hypercapnia is a late event. Impairment of vital capacity causes loss of the ability to make the intermittent deep sighing breaths that preserve the potential patency of peripheral alveoli. When hypoxaemia does develop, the respiratory muscles fatigue, increasing the weakness and accelerating the deterioration. Failure of expansion of the alveoli permits the development of atelectasis, a tendency that is aggravated by failure to clear secretions in the presence of a bulbar palsy, which often coexists with respiratory muscle weakness. Consequently any patients with progressive weakness of the limbs, especially the upper limbs, and bulbar musculature, should be considered at risk and their ventilation monitored.

Watching for the need for ventilatory support chiefly requires serial observation by experienced personnel. Patients at risk usually admit to shortness of breath, especially on exertion, talking and swallowing, but their

| Table 5. Investigation of acute neuromuscular paralysis. These tests will be appropriate in most cases where the clinical picture is an acute neuropathy. |
| --- |
| **Blood tests** |
| Full blood picture |
| Erythrocyte sedimentation rate (ESR) |
| Electrolytes, especially potassium, and including magnesium and urea |
| Liver function |
| Antinuclear factor, possibly acetylcholine receptor antibodies |
| Store serum for subsequent antibody studies* |
| **Neurophysiological tests** |
| Nerve conduction |
| Electromyography |
| Repetitive stimulation |
| **Urine** |
| Porphobilinogen |
| **Chest radiograph** |
| ECG |
| Stool |
| Bacterial culture for Campylobacter jejuni* |
| Viral culture for poliomyelitis virus* |
| **Cerebrospinal fluid** |
| Cell count and morphology |
| Protein |

*These tests, and others, may also be indicated depending on the clinical picture.
breathing is quiet, rapid and shallow. They are more breathless lying flat if their diaphragm is principally affected, and more breathless sitting up if the weakness predominantly affects the intercostal muscles. They have a rapid respiratory rate, rapid pulse and use their accessory muscles of respiration. With diaphragmatic palsy there is paradoxical indrawing of the abdominal wall during inspiration, and with intercostal weakness inward movement of the chest wall. If swallowing a few millilitres of water makes the patient more breathless, or causes coughing or nasal regurgitation, then intubation and ventilatory support should be instituted promptly. Passing a nasogastric tube in this situation will only aggravate the problem and is usually contraindicated.

The most practical measurement of the need for ventilation is the forced vital capacity. Herein lies a problem, because few acute medical wards in the UK are equipped with a vital capacity monitor and measuring the peak expiratory flow with the universally available peak flow meters is not a satisfactory substitute. The volume of air that the weak chest can move, not the speed of movement, is important in neuromuscular respiratory failure. Inexpensive portable vital capacity monitors (Fig 1) are now available and can be used, even in patients with facial weakness and poor lip seal, by attaching a face mask to the monitor. The level at which respiratory support is needed depends on many factors, including the rate at which the vital capacity is falling and the presence of bulbar palsy. It is our practice to move patients into the ITU if the vital capacity is falling towards 20 ml/kg body weight, about 1,500 ml in an adult, and to institute artificial ventilation when it falls to 15 ml/kg, about 1,050 ml in an adult. However, the decision to intubate and ventilate should not depend on any single measurement but on assessment by an experienced clinician of the whole clinical picture including the rate of deterioration, the likelihood of further deterioration, and fatigue.

Management of the ventilated patient

The patient at risk of respiratory failure should be moved to the ITU and intubated and ventilated prophylactically. The endotracheal tube should be inserted through the mouth rather than the nose because nasal intubation risks the development of sinusitis. If ventilation is likely to be needed for more than a few days, a tracheostomy should be placed. A percutaneous tracheostomy with a dilator system usually leaves a much more acceptable scar than the traditional surgical incisions. It is important not to use depolarising drugs such as suxamethonium when the patient is anaesthetised for the intubation and tracheostomy because of the risk of inducing immediate, fatal hyperkalaemia. The ventilator needs to be adjusted to deliver a tidal volume adequate to maintain normal blood gases using a positive end expiratory pressure to preserve the aeration of the peripheral alveoli. In addition, a regular programme of disconnection of the ventilator, tracheal suction, maximal chest inflation with a bag, and chest physiotherapy in order to clear secretions is important to avoid atelectasis and pneumonia. Regular disconnection from the ventilator and vital capacity measurement are helpful in assessing the course of the disease and predicting when the patient will be able to discontinue ventilatory support.

In patients with acute neuropathy, as in GBS, there is a significant risk of cardiac arrhythmias, especially bradycardia, and even asystole. The arrhythmias may precede the onset of respiratory failure or occur after weaning from the ventilator. Bradycardia and asystole are commonest at the time of tracheal suction and can usually be avoided by hyperoxygenation, but they may require insertion of a

![Fig 1. Vital capacity should be monitored in all patients with neuromuscular paralysis threatening the respiratory muscles. Despite the need, many medical wards do not have the equipment. Simple portable monitors, such as this, can be carried in a medical bag.](image-url)
temporary pacemaker. The occurrence of cardiac arrhythmias mandates continuous electrocardiographic monitoring from the time of admission with GBS until it is clear that the nadir of the illness has been reached without autonomic involvement, or until normal ventilation has been restored and the tracheostomy tube has been removed.

Careful attention to all the details of long-term intensive care lasting weeks or months requires a different approach from that for the usual acute surgical or medical ITU patient. A recent population-based study suggested that the outcome from GBS is better when patients are admitted to regional units with neurology departments. The risk of development of deep vein thrombosis should be reduced by giving heparin 5,000 units subcutaneously twice daily for as long as patients are bedbound. Careful positioning, intermittent splinting of wrists, fingers and ankles, and passive full range joint movements are needed to prevent contractures. Hydration and nutrition are often best achieved in severe cases with a percutaneous enteroscopic gastrostomy. Artificial tears for corneal exposure, prevention of pressure sores, bladder catheterisation, laxatives, help with communication, sleep deprivation, counselling, consistent information and reassurance are all required. Pain is a difficult problem. Careful, frequent repositioning, supportive mattress design and good nursing are often more helpful than drugs. Standard analgesics may not be sufficient and opiate analgesics may be necessary but cause hypotension and aggravate constipation. Either amitriptyline or carbamazepine may help painful paraesthesiae; amitriptyline may also help by virtue of its hypnotic and antidepressant properties.

Weaning the patient from ventilatory support can be achieved by gradually reducing the amount of pressure support delivered by the ventilator and eventually by trials of self-ventilation of increasing duration. The patient is unlikely to maintain self-ventilation safely until vital capacity has returned to about 15 ml/kg. Abandoning the ventilator after being dependent on it for weeks or months involves overcoming psychological as well as physical dependence and requires patience and reassurance.

Specific treatments

Guillain-Barré syndrome

Plasma exchange has been shown to hasten recovery from GBS in three large randomised controlled trials. Two large controlled trials have shown that intravenous immunoglobulin is as effective, and it has justifiably become the preferred treatment because it probably has fewer side-effects and is certainly more convenient and more widely available. The standard regimen is 0.4 g/kg daily for five consecutive days. About 10% of patients relapse within two to ten weeks after either plasma exchange or intravenous immunoglobulin. It is conventional to treat these patients again, usually with the same treatment as was used first. Further relapses or gradual progression raise the likelihood that the patient is developing subacute or chronic inflammatory demyelinating polyradiculoneuropathy for which repeated treatment or steroids may be necessary. In typical GBS, steroids have not been found beneficial and their use is discouraged. The combination of plasma exchange immediately followed by intravenous immunoglobulin was no more effective than either alone (Fig 2).

Myasthenia gravis

The response of myasthenia gravis to anticholinesterases is so dramatic that no randomised trial has ever been undertaken. In severely affected patients it is often appropriate to introduce steroids, which are also effective but may cause an early temporary deterioration with a need for ventilation. This risk may be reduced by introducing steroids slowly. If the patient has already required artificial ventilation, there is no point in delaying and a full dose, such as prednisolone 60 mg by nasogastric tube, can be started immediately. Both plasma exchange and intravenous immunoglobulin seem effective in most cases and a randomised trial suggests that they have equivalent efficacy.

Fig 2. Rate of recovery to unaided walking in a randomised trial of treatment in Guillain-Barré syndrome. Patients were randomly allocated to intravenous immunoglobulin (IVIG) (n=130), plasma exchange (PE) (n=121) or combined treatment (n=128). The graph shows the proportion of patients who were unable to walk at different times after randomisation. There was no significant difference between the treatments on this or any other outcome measure. (Reproduced from reference 3 by permission of the Lancet.)
Steroids are the mainstay of treatment for acute polymyositis. Randomised controlled trials have shown benefit from intravenous immunoglobulin in dermatomyositis, but not from plasma exchange in polymyositis and dermatomyositis. Anecdotal reports of favourable responses to azathioprine, methotrexate, cyclophosphamide and cyclosporin all require confirmation in randomised trials.

Follow-up

Some patients recover well, others are left with persistent impairment and disability or chronic illness requiring continued medical supervision and treatment. Following discharge from intensive care, it is important to have a plan for supervised rehabilitation. Persistent disability is not necessarily directly due to the physical deficit, and a better outcome can be achieved by a multidisciplinary, holistic approach to behavioural attitudes, coincidental medical disorders, anxiety, depression and social problems.

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Address for correspondence: Professor R A C Hughes, Department of Neurology, UMDS, Guy's Hospital, London SE1 9RT.