NEUROLOGICAL AND NEUROMUSCULAR DISEASE

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A general intensive care unit (ICU) is likely to encounter neurosurgical, neurological and neuromuscular problems fairly frequently. The management of head injury, increased intracranial pressure and coma is covered in many other texts and will not be discussed here. Rather, it is felt better to discuss a few specific, but relatively infrequent, neurological problems seen in ICU which may give rise to respiratory problems.

The act of breathing is under neurological control and lesions at any point along the neuraxis from the cortex through the brainstem to the neuromuscular junction and the respiratory muscles may cause respiratory abnormalities or respiratory failure. Problems related to neural control of breathing will be discussed first, followed by acute polyneuritis, myasthenia gravis and finally the management of chronic neuromuscular respiratory failure.

ASPECTS OF THE NEURAL CONTROL OF BREATHING

Even after many years of investigation, the neural mechanisms which control breathing are still fairly obscure and, by the vast majority of anaesthetists, the respiratory centres are regarded as vague collections of neurones situated in the "black box" of the pontine and medullary regions of the brainstem. We are aware that local trauma and disease of the brainstem and certain drugs acting on the brainstem have an effect on "ventilation", but seldom do we take the trouble to observe carefully those changes in the patterns of breathing which may reflect the particular part of the system which is at fault. It is only by observing in man the abnormality in respiration and correlating it with the nervous system pathology, that we can increase our understanding of the mechanisms which control breathing in man (Newsom-Davis, 1985).

An important point which is often forgotten is that there are two independent respiratory control mechanisms, one related to the voluntary control of breathing, which may be termed the behavioural system, and the other, the metabolic or automatic system, without conscious control, driving respiration in response to metabolic and other afferent stimuli. The importance of appreciating that there are these two systems, which interact only at the spinal level, is not just of academic interest. It is of clinical importance in interpreting the various patterns of breathing seen in neurological disorders and, therefore, in their management.

The behavioural system

Voluntary movements are subserved by the corticospinal tracts, the signals arising in the motor cortex and passing down the fibres of the internal capsule to decussate in the pons and thence, via the corticospinal tracts in the lateral part of the spinal cord, to synapse with the anterior horn cells of the motor neurones supplying voluntary muscle. Voluntary control of breathing movements uses these same corticospinal pathways (fig. 1). In general, it overrides the respiratory drive from the metabolic system. It should be noted that respiratory function tests requiring voluntary manoeuvres, for example vital capacity, peak expiratory flow, maximum breathing capacity and voluntary cough, are only tests of the behavioural system and do not tell us anything about the integrity of the metabolic system.

The metabolic system

Groups of neurones forming longitudinal columns of cells in the medulla, concentrated in the regions of nucleus tractus solitarii (NTS) just beneath the floor of the fourth ventricle, and also nucleus retroambigualis (NRA) deeper in the medulla (fig. 1), cross in the medulla and project down the antero–lateral part of the spinal cord to synapse with the anterior horn cells of respiratory
muscles, probably via an internuncial neurone. The neurones of NTS and NRA project to both inspiratory and expiratory muscles, although those of NTS are largely inspiratory to the diaphragm. They also receive projections from various other neurones in the pons and medulla.

The generation of a rhythmical pattern of breathing is a highly complex interaction between the pontine and medullary respiratory nuclei and has not been defined clearly in experimental animals, let alone in man. There is probably a pontine rhythm generator which inhibits tonic inspiratory and expiratory medullary neurone activity, which are themselves mutually inhibitory (Sears, Berger and Phillipson, 1982). These neurones may form the fundamental basis of a rhythmic breathing pattern which is further modulated by central and peripheral chemoreceptor drives, afferents from the lungs and chest wall receptors and muscle spindles, in addition to pharyngeal, laryngeal and tracheal receptors. Body temperature and the general level of activity in the reticular activating system also modify the firing thresholds of neurones, not only centrally, but also at the spinal level.

Figure 2 illustrates the breathing pattern of a man who has had the corticospinal tracts interrupted as a result of infarction of the ventral pontine region. He was unable to move voluntarily any muscle innervated below the level of the lesion and although completely aware, was able to communicate only with eye movements — an example of the “locked-in syndrome”. The breathing pattern is extremely regular, showing the metabolic system driving respiration in isolation, uninfluenced by the behavioural system. When asked to take a deep breath or stop breathing, the patient was unable to do either, and yet could augment his breathing reflexly following an increase in inspired carbon dioxide.

Figure 3 shows the irregular breathing pattern of a man who had a tumour invading the floor of the fourth ventricle with destruction of NTS bilaterally. He was unable to sleep because he feared, quite correctly, that he would stop breathing if he did not voluntarily drive his breathing. He required artificial ventilation in order that he could sleep. The irregular pattern of breathing correlates with changes in EEG pattern when lower voltage activity, indicating short lapses in attention, is associated with slow respiration. This is an example of disruption of the metabolic system of respiratory control, a true “Ondine’s Curse”. The patient could perform various voluntary respiratory manoeuvres but, when drowsy, would hypoventilate and show a slow irregular pattern of respiration with apnoeic periods.

The lesson to be learned here is that, in the
awake state, patients with a defect in the metabolic system may appear normal and be able to perform satisfactorily various voluntary respiratory tests, but, if left alone, they may severely hypoventilate and even succumb through failure on our part to recognize the abnormality in the metabolic system. Patients with medullary lesions should be observed very carefully for signs of hypoventilation, apnoeic episodes or slow irregular respiration, a situation not unlike an overdose of fentanyl, which is in effect a pharmacological disruption of the metabolic or automatic control system, with preservation of the behavioural mechanism.

The efferent and afferent neurones of the glossopharyngeal and vagal nuclei are situated close to NTS and NRA and any lesion affecting one is likely to affect the other. Thus, patients who have loss of sensation of the pharynx and trachea or difficulty with swallowing, or who develop hiccup resulting from damage to the medulla, are likely to have respiratory disturbances of the metabolic system in addition.

The descending tracts of NTS and NRA, which carry the respiratory drive to the anterior horn cells of respiratory muscles, lie in the anterolateral part of the cord in what might be described as the reticulospinal tracts (Nathan, 1963). When a high cervical cordotomy is performed for pain relief, a unilateral lesion of the spinothalamic tracts frequently also cuts the descending reticulospinal tract, giving rise to a temporary disturbance of automatic breathing. Bilateral lesions lead to death from total failure of the metabolic system, an irreversible Ondine's Curse. Similar high cervical lesions from other causes will have the same effects.

Whilst tests of the behavioural system involve tests of voluntary function, tests of the metabolic system should include observation of the breathing pattern during quiet breathing or sleep. Frequent sighs, hiccups, slow irregular breathing and apnoeic periods are indicative of disturbance of the metabolic system. Specific tests of ventilatory response to hypoxia and carbon dioxide may be useful, although difficult to interpret.

The management of a deficiency of the metabolic system depends on the prognosis, but tracheotomy with artificial ventilation, especially during sleep, are necessary in the first instance. If the patient has a reasonable prognosis, this type of central respiratory failure is one of the few indications for phrenic nerve pacing (Glenn et al., 1972).

Other disturbances of respiratory pattern

Cheyne-Stokes respiration is a characteristic pattern of breathing occurring in patients with cortical damage or ischaemia and a slow circulation time. It is seen in the presence of an intact respiratory control mechanism. Breathing progressively increases in depth to a peak and then wanes, the cycle often ending with a period of apnoea before starting again. The pattern of change is smooth and regular. Cherniack and Longobardo (1973) suggested that the combination of a decreased cerebral inhibition of carbon dioxide sensitivity and a slow circulation, causing unusual

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**Fig. 3.** Tracings from a patient with disruption of the metabolic control system of breathing, showing an irregular breathing pattern. AB = Abdominal anteroposterior movement by magnetometer; EEG = simultaneous electroencephalogram. Below: expanded portions of EEG. Note low voltage activity associated with slow respiratory rate.
delays between blood-gas exchange in the lungs and the sensing of such changes by the chemoreceptors, caused a type of hunting or instability in the control mechanism.

*Tachypnoea*, which is a regular and persistent increase in breath frequency, is almost always the result of lung complications such as pneumothorax, pulmonary oedema, lobar collapse or consolidation. Again, the neural control mechanism is intact, but the afferent discharge from the lungs and chest wall receptors is altered by disease to produce a shortening of inspiration with a decrease in tidal volume and an increase in respiratory rate.

*Cluster breathing* describes an abrupt increase in respiratory frequency for short periods which is quite unlike Cheyne–Stokes respiration. It is seen in patients with encephalitis and brainstem lesions and probably results from a disturbance of rhythm generation from a pontine tegmental lesion.

*Apeustic breathing*, when there is an involuntary breathhold in inspiration, and *Ratchet breathing*, when inspiration occurs in a series of steps, have also been described in pontine lesions.

*Neurogenic hyperventilation* is again a manifestation of a pontine lesion, occasionally following head injury. The hyperventilation is difficult to control. In order to minimize respiratory work and prevent a severe respiratory alkalosis, muscle paralysis and controlled ventilation may be necessary.

*Hiccups* can result from lesions in the region of NTS which remove an inhibitory influence which normally suppresses hiccups (Newsom–Davis, 1970). This periodic, massive inspiratory discharge is usually closely followed by glottic closure to produce the “hic”. However, in patients in whom the trachea is intubated, limitation of inspiration by glottic closure cannot occur and the inspiratory activity produces large tidal volumes and gross hyperventilation. It appears that hypocapnia perpetuates the situation which can sometimes be improved by carbon dioxide rebreathing. Strong vagal stimulation may also inhibit hiccups on occasion. It is important that hiccups in the intubated patient are recognized and not mistaken for some other form of hyperventilation. It may be picked up by the regular periodicity of the inspiration, often with a few normal breaths in between.

It is hoped that, by drawing attention to the various different patterns of breathing, this review will prompt intensive care doctors to look more carefully and observe and correlate these patterns with the neuropathology and thereby improve our understanding of the central control mechanisms which govern this important function.

**ACUTE INFLAMMATORY POLYRADICULONEUROPATHY OR GUILLAIN–BARRÉ SYNDROME**

The Guillain–Barré syndrome, noted first by Landry in 1859 and subsequently by Guillain, Barré and Strohl in 1916, may best be described as an acute inflammatory polyradiculoneuropathy (AIP) (Hughes, 1978), with a prevalence of approximately 1.5 per 100 000 of the population. It may affect individuals at any age, but the peak incidence is in the fifth decade (Lesser et al., 1973). The disease is characterized by a progressive motor weakness, usually symmetrical, with areflexia and also some sensory symptoms (Asbury et al., 1978). In approximately 60% of patients, the onset of the motor weakness is preceded by a mild non-specific viral infection, commonly of the upper respiratory tract. In about one-third of patients, high titres of antibody to *Cytomegalovirus* have been found (Dowling, Mendonna and Cook, 1977), but several other viruses have been implicated, as have inoculations, mycoplasma, bacterial infections and pre-existing illness such as Hodgkin's disease and lymphoma. The motor weakness may progress rapidly over a few days, or the deterioration may occur more gradually, and in 90% of patients the weakness will be maximum by 4 weeks. The weakness usually develops in the limbs, but may progress to involve the respiratory muscles and cranial nerves. Sensory changes are typically paraesthesia of the glove and stocking type. There is frequently autonomic dysfunction as well. The pathological changes are predominantly lymphocyte infiltration of the peripheral nerves up to the spinal roots, resulting in segmental demyelination. In severe cases there is also secondary axonal degeneration. There is marked slowing or blockade of nerve conduction as a result of demyelination and denervation; muscle fibrillation indicates axonal degeneration. An increase in CSF protein concentration is usually seen by the 2nd week, but only a few cells are seen. The disorder should be distinguished from porphyria, lead neuropathy, volatile solvent abuse, toxic neuropathy (e.g. from organophosphorus compounds), poliomyelitis, botulism and diphtheria.

Since AIP is likely to be the result of a
sensitivity reaction to Schwann cells, myelin or other peripheral nerve protein, various forms of immunosuppressive treatment have been tried. On the whole, steroids are felt not to be beneficial. There is some evidence of delayed recovery and a higher incidence of complication following steroid treatment (Hughes et al., 1978). Early use of plasma exchange may be useful in limiting the deterioration and demyelination, but further trials are required (Editorial, 1984; Greenwood et al., 1984; Osterman et al., 1984).

The disease is very variable in severity and is self-limiting. The signs of recovery of neuronal function are usually seen within 4 weeks of the onset of symptoms. The majority of patients make a full recovery over several months to a year, but about 10% are left with residual disability; mortality is about 10%. The prognosis, therefore, is good, and the aim of management is to prevent complications and thus keep the patient in good condition whilst awaiting spontaneous recovery.

Management

The main life threatening problem in AIP is acute respiratory failure resulting from respiratory muscle weakness. This is likely to occur within the first 2 weeks of the illness and usually there is a progressive deterioration of respiratory muscle power over a few days. A reasonable clinical test of respiratory muscle power is the vital capacity (VC) and if this shows a progressive decrease to less than 1 litre in an adult, then it is likely that artificial ventilation will be required.

A decreasing vital capacity together with bulbar weakness, with difficulty in swallowing and coughing, is a very dangerous combination as such patients may be precipitated into acute respiratory failure by the aspiration of small quantities of saliva. It is best to intubate the trachea under these circumstances and perhaps the best guides to the need for tracheal intubation are if the patient begins to look anxious and is restless, and if the respiratory rate increases and the accessory muscles of respiration are being used. Arterial blood-gas tensions are not helpful in making an early decision to intubate.

The function of the diaphragm may be an important determinant of the need for tracheal intubation and ventilation, since it is the prime muscle of inspiration. Severe weakness or total paralysis of the diaphragm may be recognized by observation of the anterior abdominal wall during quiet respiration in the supine posture, when paradoxical inward movement of the upper abdominal wall occurs during inspiration. Such patients are likely to be distressed by the supine position and prefer to sit upright, and it is these patients who are most likely to require intubation and ventilation. It is also likely that satisfactory respiration will take place only after some diaphragm function has returned.

Once intubation is necessary, then early tracheotomy should be considered as it usually takes at least 2, and often several, weeks before extubation can satisfactorily take place. Patients accept artificial ventilation easily and there is no need to sedate or paralyse them. The management of ventilation and care of the tracheostomy is straightforward and will not be discussed further.

Vital capacity is a reasonable guide to recovery of respiratory muscle function. A VC of 1–1.5 litre is often required before satisfactory spontaneous respiration can occur, and this is commonly when abdominal paradoxical movement disappears, signifying the return of diaphragm activity. It is probably unwise to decannulate the tracheostomy until it has been well established that bulbar function is adequate and the return of a satisfactory gag reflex and swallowing have been demonstrated. In some patients it is wise to change to an uncuffed silver tracheostomy tube with speaking attachment as an intermediate step before decannulation.

Autonomic disturbances

Second to respiratory failure, the commonest cause of death in AIP is cardiac arrhythmia (Lichtenfeld, 1971). Arrhythmias are associated frequently with autonomic abnormalities. Sinus tachycardia and persistent fluctuating hypertension are frequently observed early in the disease. Bradycardia and hypotension are also seen, particularly following vagal stimulation from tracheal suction. Prolonged episodes of hypotension can also occur with pallor and bouts of excessive sweating as a result of parasympathetic over-activity. Bladder and bowel function are seldom affected, although catheterization of the bladder may be needed for other reasons. Paralytic ileus lasting a few days, with failure to absorb feeds, may be also result from autonomic dysfunction. Postural hypotension should be suspected, particularly when patients are being mobilized during the recovery phase of the illness.

Several papers have recorded sudden death in patients showing autonomic disturbances and...
currently our policy is to try to stabilize the cardiovascular system by partial p-blockade with propranolol to prevent tachycardia and hypertension, and also to give atropine 0.6 mg three to four times a day to avoid episodes of bradycardia during tracheal toilet and physiotherapy. Marked hypertension may be treated with a hypotensive drug such as hydralazine. Should episodes of marked bradycardia be noted, we would seriously consider inserting a transvenous pacemaker.

Patients with profound muscle weakness are at risk from deep vein thrombosis and pulmonary embolus. Good nursing care, physiotherapy and hydration can do much to prevent this complication. However, we routinely prescribe a subcutaneous heparin regimen (5000 i.u. twice daily).

Many patients complain of pain, which may last several days. It is often severe and persistent and usually felt in the back or calves. This pain is not easily relieved by analgesics and can be a most distressing problem.

The aim of management is to prevent complications and permit the natural recovery process to take place. Medical interference is really secondary to good nursing care and physiotherapy. Attention must be paid to adequate nutrition and the prevention of muscle wasting. One of the most distressing problems is the inability of patients to communicate. They may be so weak that they are unable to signal with their hands or write and in some cases the facial weakness is such that they cannot even signal with their eyes. Frequent reassurance is required. Television, radio and cassette tapes help to fill the time and provide mental stimulation. Most important is the attitude and atmosphere created by the nursing staff and also the physiotherapy and occupational therapy staff who will be involved throughout.

The milestones to recovery are return of respiratory muscle function and spontaneous breathing, recovery of speech, oral intake of food, decannulation of the tracheostomy, sitting up and supporting first the head and then torso, standing and walking with aid, and finally walking unaided. Management is a team effort.

**MYASTHENIA GRAVIS**

In recent years it has become clear that myasthenia gravis (MG) is an autoimmune disease (Newsom-Davis, 1982). In the majority (85%) of individuals with the disease, it is possible to demonstrate an antibody in the IgG fraction which, through complement-mediated lysis, causes an increase in the rate of breakdown of acetylcholine receptors (AchR) on the postjunctional membrane of the neuromuscular junction (NMJ). This antibody, the anti-acetylcholine receptor antibody (anti-AchR antibody), eventually depletes the NMJ of acetylcholine receptors, giving rise to a characteristic fatiguable muscle weakness. The weakness may affect some muscle groups more than others, so that some patients only complain of ptosis and diplopia, others may have proximal limb weakness and the most severely affected can develop bulbar and respiratory muscle weakness which may require intensive care management.

The diagnosis is suggested on the history of muscle weakness which is worsened by exercise and improved by rest. An improvement in muscle power following the administration of an anticholinesterase drug such as edrophonium and a characteristic decrement of EMG on repetitive stimulation of peripheral nerves add weight to the diagnosis, but MG is confirmed by the demonstration of the anti-AchR antibody in the patient’s plasma, although the disease cannot be excluded if no antibody is detected.

The prevalence of MG is about 1 in 20 000 of the population and affects all age groups. There is a female preponderance, particularly in the group younger than 40 years of age. Compston and colleagues (1980) showed an increased frequency of certain HLA antigens in non-thymoma patients, indicating that genetic factors probably have a role in the aetiology of the disease. Occasionally, MG is associated with other autoimmune disorders such as rheumatoid arthritis, thyrotoxicosis and pernicious anaemia.

Thymoma occurs in approximately 10% of patients with MG and, although usually benign, the tumour can show malignant change and locally invade important mediastinal structures such as phrenic nerve and aorta.

**Other forms of myasthenia**

There are some rarer disorders of neuromuscular transmission which should be distinguished from the usual acquired form of MG. Neonatal myasthenia occurs in one in eight babies born of mothers with MG and results from placental transfer of anti-AchR antibody from the mother. This causes a transient muscle weakness in the baby which responds to anticholinesterases and which usually only lasts for 4–6 weeks. Following this the baby is normal. A congenital form of
myasthenia has been described, in which the abnormality is in the acetylcholine receptor itself and no immunological abnormality is found; these patients do not respond to immunosuppression.

The Eaton–Lambert myasthenic syndrome is an immunological disorder which produces a presynaptic defect in the release of acetylcholine from the nerve terminal. It is frequently associated with an oat cell carcinoma of the bronchus, although in some cases no malignancy is found. The muscle power is transiently improved with exercise and the neurophysiological characteristics are quite different from those of myasthenia gravis. No antibody has yet been identified, but the condition can be improved with plasma exchange and immunosuppression.

Treatment of myasthenia gravis

Anticholinesterase drugs. These drugs delay the breakdown of acetylcholine by cholinesterase at the NMJ and therefore presumably allow the more efficient transfer of acetylcholine to the depleted acetylcholine receptors on the postjunctional membrane. They produce symptomatic improvement, but do not alter the underlying pathology. In fact there is some evidence that prolonged, high dose anticholinesterase drugs themselves produce undesirable changes at the NMJ. Too much anticholinesterase produces a cholinergic muscle weakness in addition to excessive salivation, colic, diarrhoea and other symptoms of parasympathetic overactivity. It is best to keep the patient suboptimally dosed, that is slightly myasthenic, rather than run the risk of cholinergic problems. Pyridostigmine bromide is the drug of choice, 30–120 mg 3-hourly, taken by mouth in tablet form or as an elixir via nasogastric tube. Atropine may be given to reduce the parasympathetic side effects, but if the side effects are troublesome, reduction in anticholinesterase therapy would be wise since the patient may be cholinergic, and alternative methods of management should be considered. Edrophonium (Tensilon) may be used as a test of the myasthenic or cholinergic state. After prior treatment with atropine 0.3–0.6 mg i.v., usually not more than 5 mg of edrophonium i.v. is required to produce a satisfactory response. If the patient is myasthenic then, within 30 s, there should be a marked improvement in muscle power which lasts for 2–3 min. The useful bedside tests of improved muscle power are loss of ptosis, recovery of facial muscle power, speech and voice, increased arm or leg outstretched time and improvement in vital capacity. If the improvement is marked then it would be reasonable to increase anticholinesterase therapy. However, if the response is marginal one should contemplate a reduction in medication, bearing in mind that not all muscle groups behave equally and that some muscles may show a cholinergic response at the same time as others are myasthenic.

Thymectomy

Thymectomy alone produces an improvement in myasthenia gravis in approximately 60–70% of patients. The precise role of the thymus gland in MG is not clear, but it may be that some antigenic stimulus in the gland perpetuates the anti-AchR antibody production. It has been demonstrated that, over a period of months, anti-AchR antibody concentrations decrease following thymectomy. Thymectomy is the treatment of choice in patients younger than 50 years, when the thymus usually shows hyperplasia. Thymectomy is indicated in cases of thymoma.

The thymus gland is removed most satisfactorily through a median sternotomy incision. The hazards of thymectomy are reduced considerably if patients come to operation in a good clinical state. Prior treatment with steroids or plasma exchange can improve the preoperative situation. The postoperative management is simplified by maintaining complete control of the airway with nasotracheal intubation for the first few days after operation. Anticholinesterases are often stopped before operation and reintroduced when indicated, usually at a lower dose, but guided by clinical state and edrophonium testing. If comfortable, patients are allowed to breathe spontaneously through the nasotracheal tube, but at the first sign of respiratory distress, artificial ventilation is easily instituted. Extubation occurs when vital capacity is satisfactory and it is judged that respiratory assistance is unlikely to be required.

Immunosuppression

Immunosuppression with steroids can produce a remission of symptoms in approximately 80% of patients. This can be achieved using an alternate day regimen of prednisolone, starting at a low dose of 10 mg and slowly increasing over a period of weeks up to a maximum of about 120 mg on alternate days. Thereafter the dose may be very
slowly reduced to a minimum dose which will maintain the improvement. If steroids are introduced too rapidly at high dose, a temporary deterioration in muscle power can occur which may require intubation and ventilation for a few days, but in this way, remission can be attained sooner. It may thus be justified to use a high dose steroid regimen in those patients already in a poor clinical state and requiring artificial ventilation. Azathioprine can also be used for immunosuppression with a starting dose of 2.5 mg/kg body weight. The improvement is slow and can take up to 1 year, but the side effects are probably less than with steroids. Regular checks on the blood picture and liver function are required.

Quite frequently, steroids and azathioprine are used in combination, steroids being used to produce a more rapid improvement and azathioprine for long term immunosuppression. It seems that immunosuppression needs to be continued indefinitely. Because of the side effects of steroids and azathioprine there is a reluctance to use these drugs in the younger age group, especially in women of child bearing age. Thymectomy is still the treatment of choice in this younger age group since, if thymectomy alone produces a good remission, the problems of immunosuppression can be avoided.

Plasma exchange

Plasma exchange can very effectively reduce the anti-AChR antibody concentrations in blood and produce a remission of MG within a few days by allowing the effective regeneration of acetylcholine receptors. A series of approximately five daily exchanges removing ca 50 ml/kg body weight of plasma each time can produce a marked clinical improvement, but it is relatively short lived, lasting only about 3–4 weeks. Since the technique is very costly it should be reserved for patients with severe disease who are awaiting the benefits of immunosuppression.

ICU problems

To the anaesthetist the most significant fact regarding MG is the severe reduction in the number of acetylcholine receptors, which means that these patients are exceptionally sensitive to non-depolarizing muscle relaxants, but from the point of view of the intensive care specialist, the main problems are those of acute respiratory failure. The respiratory failure usually results from either a myasthenic or cholinergic crisis, but may be steroid-induced or the result of thymectomy. The majority are cholinergic crises.

Myasthenic crisis

This occurs in patients with severe myasthenia who suddenly deteriorate as a result of an acute infection or stress of some other kind and in whom the anticholinesterase requirements increase. However, recovery may not be achieved by an increase in anticholinesterase alone. It is also necessary to deal with the precipitating factor (such as infection). The safest course is to ensure an adequate airway by intubation and to ventilate until an improvement is achieved. Plasma exchange may be performed for a rapid improvement and the opportunity to introduce more effective immunosuppression should be considered.

Cholinergic crisis

This frequently occurs from overdose with anticholinesterase drugs. The situation commonly arises following a myasthenic crisis in which only partial improvement with anticholinesterases occurs and more and more drug is administered. This results in a cholinergic weakness which is not recognized as such. Eventually the patient develops respiratory and bulbar muscle weakness, excessive salivation and abdominal cramps. Should aspiration of secretions occur, a dangerous and acute respiratory failure can rapidly follow. Intubation and ventilation should be performed early and the anticholinesterase drugs withdrawn. Given time, the patient returns to a myasthenic state and anticholinesterases can be reintroduced and the process of weaning from the ventilator started. It is unwise to expedite tracheal extubation and in general patients should be able to breathe without assistance for at least a full 24 h before extubation. As with a myasthenic crisis, plasma exchange and more effective immunosuppression should be considered.

It is worth a reminder that myasthenic patients may be made weaker by antibiotics of the aminoglycoside group such as streptomycin, gentamicin and neomycin, which reduce acetylcholine release at the nerve terminal. Similarly, procainamide causes a reduction in acetylcholine release and quinine and quinidine reduce the spread of excitation along a muscle fibre, also making myasthenics weaker. In addition, a low
serum potassium should be avoided, since this potentiates muscle weakness.

CHRONIC NEUROMUSCULAR RESPIRATORY FAILURE

There are a number of neuromuscular disorders, the result of either neuronal damage such as poliomyelitis, or primary muscle disease as in the various myopathies and muscular dystrophies, which result in respiratory muscle weakness. Sometimes the muscle weakness is such that a state of chronic respiratory failure develops in which the lungs are relatively normal, but the bellows function of the chest wall is impaired. If the condition is allowed to progress unrecognized, the patient may present in an intensive care unit with unexplained respiratory failure. Occasionally, such patients are admitted having failed to breathe following anaesthesia or as difficult weaning problems and some are admitted in congestive heart failure from chronic pulmonary hypertension. These neuromuscular problems can also be diagnosed as out-patients, provided one is attuned to the characteristic history. The patients often complain of breathlessness on exercise and often on assuming the supine posture, so that they sleep either propped up or in the lateral posture. A common feature is hypersomnolence with excessive sleepiness during the day, and yet disturbed sleep at night with frequent arousal and sometimes with nightmares. They are often difficult to rouse in the morning and wake up with a headache which clears shortly after getting up. These are symptoms of marked nocturnal hypoventilation with severe hypoxia and hypercapnia. On examination, there is evidence of neuromuscular weakness frequently affecting the shoulder girdle and neck muscles in addition to other muscle groups. In the majority of patients who suffer from this problem, there is evidence of marked diaphragm weakness (Newsom-Davis et al., 1976).

As mentioned earlier, diaphragm weakness may be seen best in the supine posture during quiet breathing, when the upper anterior abdominal wall moves paradoxically inwards during inspiration (Loh, Goldman and Newsom-Davis, 1977). This paradoxical movement is the result of the diaphragm failing to develop sufficient tension to prevent the abdominal contents moving up into the chest in the face of the more negative intrapleural pressure generated during inspiration. Awake resting blood-gas tensions reveal hypoxia and hypercapnia which can be corrected to a degree by voluntary hyperventilation and there is normally an increased bicarbonate concentration, indicating a long-standing respiratory acidosis.

Lung function tests may reveal a reduced vital capacity which may decrease further in the supine position. Ventilatory responses to hypoxia and hypercapnia are blunted and exercise tolerance is poor. Pulmonary hypertension is another feature and, as mentioned above, signs of congestive heart failure may be present. One of the problems in making a correct diagnosis is that the patients often appear relatively normal when upright and awake and the problem reveals itself only during sleep. During sleep the patient is at a gross disadvantage, both from a mechanical point of view because of the recumbent posture and from the respiratory drive to the breathing muscles.

Patients with diaphragm weakness in the upright posture may use abdominal muscle contraction to drive the abdominal contents up into the chest at end-expiration and then augment the inspiratory tidal volume by relaxing the abdominal muscles and allowing passive descent of the diaphragm and abdominal contents out of the chest in early inspiration. This mechanism is largely lost in the horizontal position. In addition, in the supine position the inspiratory muscles tend to be shorter and the mechanical advantage of extending the spine in the upright position is lost. During sleep, the central drive to the breathing muscles is normally directed largely to the diaphragm and if this muscle is non-functional, hypoventilation is to be expected. Also because the ventilatory responses to hypoxia and hypercapnia are obtunded, there is a change in the threshold for arousal and severe hypoxia and hypercapnia are allowed to persist. For these reasons, patients with diaphragm weakness are at risk during sleep and the correct diagnosis can only be made with certainty by observing what happens during sleep and making the relevant measurements.

Once the diagnosis is made appropriate treatment in the way of assisted ventilation during sleep can be attempted, with the aim of permanent use by the patient at home. This type of management should be undertaken by respiratory specialists and may be best initiated in an intensive care unit. The aims of treatment are: (a) to prevent hypoxia and hypercapnia during sleep; (b) to reduce pulmonary hypertension; (c) to allow satisfactory sleep; and (d) to rest fatigued respiratory muscles.
The results of satisfactory treatment are: (a) abolition of hypersomnolence; (b) reversal of congestive heart failure; (c) induction of more normal blood-gas tensions; (d) improved quality of life and (e) prolonged survival.

Nocturnal assisted ventilation

There are several ways of augmenting respiration during sleep. Rocking beds, which tip the patient head-up and then head-down regularly, assist respiration by moving the abdominal contents in and out of the thorax, causing the diaphragm to act passively as a piston. Not all patients can tolerate the motion and, in some, ventilation is inadequate. Positive pressure ventilation via a tracheostomy or negative pressure respiration with a cuirass type device are more commonly used for long term home ventilation (Dunkin, 1983).

Positive pressure ventilation

Positive pressure ventilation is particularly suitable for the severely disabled patient who might find difficulty using a negative pressure device; for patients for whom there is minimal assistance at night; and if there is need for a tracheostomy to overcome the problem of upper airways obstruction during sleep. A small, reliable, relatively cheap, positive pressure ventilator such as the East Radcliffe RP4 ventilator (H. G. East & Co Ltd, Sandy Lane West, Littlemore, Oxford OX4 5JT) is very suitable for home use (cost approximately £2000). The disadvantage of positive pressure ventilation is that it does require a tracheostomy and, if an uncuffed tracheostomy tube is used, the leakage of air into the pharynx during the inspiratory phase may not be well tolerated. However, with perseverance this problem can usually be overcome.

Negative pressure respiration

Negative pressure respiration is suitable provided the patient has a competent larynx, is able to breathe reasonably well on his own and is not entirely dependent on the device, and has adequate help at home. The advantage of negative pressure devices is that tracheostomy may be avoided. Unfortunately, most of the devices are cumbersome, some may not be very efficient at ventilating and they may encourage upper airway obstruction during sleep.

Most of the apparatus available for home ventilation is of ancient design and, because of the small demand, commercial companies are reluctant to invest finance in the research and development of such apparatus. Specially tailored cuirass shells (S. Thomas & Co., 3 Cholmeley Crescent, Highgate, London N6 5EZ) are available, as is the Tunnicliffe jacket (Watco Services, 24 Lingfield Close, Basingstoke, Hants). It is possible to provide a patient with such equipment and a respirator pump for approximately £3000. At considerably more cost, a small tank respirator suitable for home use is available from Cape Warwick Ltd (Birmingham Road, Warwick CV34 4TX).

In order to pursue this type of therapy, one has to have adequate medical expertise, adequate finance, good engineering back up and interested and understanding nursing staff, so that the patient feels that he can rely on the support of the hospital.

Many of the neuromuscular disorders which can be helped by assisted ventilation are only very slowly progressive and often the condition affects young adults who have dependants. It can be extremely worthwhile and rewarding to assist these patients to lead happier, more productive and longer lives (Loh, 1983).

REFERENCES


