Anaesthesia and myotonia

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The myotonias are a group of uncommon disorders. All display a characteristic electromyographic picture and some of the disorders have systemic manifestations. They are important to the anaesthetist for several reasons. Anaesthetic and surgical interventions may induce myotonia which, when initiated, may complicate the course of anaesthesia and be difficult to abolish. Furthermore, patients often display extreme sensitivity to some drugs and abnormal reactions to others. During anaesthesia, the extramuscular manifestations that occur in some myotonic disorders may assume greater importance than the myotonia, but may be masked before operation by the patient's reduced exercise tolerance. Finally, patients with myotonic disorders may be susceptible to malignant hyperpyrexia and have an increased incidence of malignant hyperpyrexia-like reactions.

Most myotonic patients survive into adult life with little impairment and it is common for them to conceal their symptoms. They may present for totally unrelated surgery and the diagnosis may therefore not be considered.

**MYOTONIA**

Myotonia is a clinical sign or symptom which occurs in several disorders (table I). The term describes a persistent contraction of a muscle observed after cessation of voluntary contraction or stimulation of the muscle. In "action myotonia", the patient is unable to relax the muscle for some seconds after use. This is demonstrated classically in handgrip myotonia, in which patients are unable to release their grip after shaking hands. "Percussion myotonia" describes the sustained contraction of a muscle body either after it is trapped directly or after stimulation of the tendon reflex. In some subjects, for example apparently unaffected siblings, the phenomenon may only be elicited and detected electromyographically.

In the non-dystrophic myotonias, in which myotonia is the only manifestation of the condition, the patient's main complaint is that of stiffness. This tends to be most prominent when the muscle is exercised after a period of rest, and improves with repetitive muscle activity (the so-called "warm-up" phenomenon). However, in paramyotonia (paradoxical myotonia) myotonia is exacerbated by exercise. Characteristically, most subjects feel that myotonia is made worse by cold, but this has been confirmed electromyographically only in patients with paramyotonia congenita and the acetazolamide-responsive subtype of myotonia congenita.

Myotonic contractions are usually painless, are not related to serum potassium concentrations and are not usually accompanied by weakness. However, these features may be present, as there is considerable overlap between the various clinical subtypes.

In contrast with the non-dystrophic myotonias, the presenting feature of patients with myotonic dystrophy may not be myotonia, but symptoms associated with muscle weakness and the extramuscular manifestations of the disease.

**Electromyography**

The electromyographic (EMG) findings in myotonia are characteristic [29]. During recording with a concentric EMG electrode, a myotonic burst can be detected immediately after cessation of voluntary contraction. The frequency of this burst increases gradually to 100-150 Hz before decreasing. As the frequency changes, so too does the amplitude and this waxing and waning produces the characteristic "dive-bomber" sound when auditory amplification is used (fig. 1). In order to aid diagnosis, myotonia may be accentuated by the i.v. administration of potassium, salbutamol or fenoterol, or in some cases the topical application of ice.

**Pathophysiology**

Myotonia is an intrinsic disorder of muscle, and not of the peripheral nerve or neuromuscular Table I. The myotonias

<table>
<thead>
<tr>
<th>Disorder</th>
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<tr>
<td>Myotonic dystrophy (dystrophia myotonica, myotonia atrophica, Steinert's disease)</td>
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<tr>
<td>Myotonia congenita (Thomsen's disease)</td>
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<tr>
<td>&quot;Classical&quot; Thomsen's disease</td>
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<td>Myotonia fluctuans</td>
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<td>Acetazolamide responsive myotonia congenita</td>
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<td>Recessive generalized myotonia (Becker's)</td>
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<td>Paramyotonia congenita</td>
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<td>Hyperkalaemic periodic paralysis (adynamia episodica heredita)</td>
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<td>Acid-maltase deficiency (Pompe's disease)</td>
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<td>Schwartz-Jampel syndrome (chondrodystrophic myotonia)</td>
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**KEY WORDS**

Complications: myotonias, Muscle, skeletal.
physiology differs between the various myotonic and Cl− syndromes, the result is a defect in Na+
channel function which produces electrical instability of the muscle membrane and self-sustaining runs of depolarization. Recent studies have provided further information regarding the genetic mapping of these syndromes and the association between them. The locus for myotonic dystrophy is present on chromosome 19 [57], whereas the locus for myotonia congenita, paramyotonia congenita and hyperkalaemic periodic paralysis has been traced to chromosome 17. More specifically paramyotonia congenita, hyperkalaemic periodic paralysis and acetazolamide-responsive myotonia congenita all map to the Na+ channel locus. There is increasing evidence to suggest that they may be allelic disorders [1, 58, 77, 78].

Treatment
In some disorders, myotonia is only a minor component of the disease and may be managed without specific treatment. However, in some cases of myotonia congenita and paramyotonia congenita the myotonia may be severely disabling and require treatment. The most effective drugs stabilize the muscle membrane by inhibiting the development of Na+ currents in response to depolarization. Early studies demonstrated the effectiveness of quinine in myotonia congenita [54] and subsequently quinidine, procainamide, mexilitine and tocainide have been used. Phenytoin is another first line drug and acts by reducing Na+ influx during activation while leaving resting Na+ conductance unchanged [5]. Some patients, especially those sensitive to K+ concentrations, are responsive to acetazolamide (see below). Successful abolition of myotonia has also been achieved with dantrolene [70], lithium [37] and tricyclic antidepressants [17].

Similar principles apply to the treatment of paramyotonia congenita, although quinine, procainamide and phenytoin are less effective [93]. Pretreatment with tocainide abolishes or ameliorates cold-induced stiffness in all patients [91] and patients may adjust their dose according to anticipated requirements. Side effects are rare, but if they occur mexilitine is a useful alternative.

THE CLINICAL SYNDROMES (table II) [92]

Myotonic dystrophy was described first by Steinert in 1909 [89] and is the most common of the myotonic syndromes with a prevalence of about 3–5 in 100000. It is inherited as an autosomal dominant trait with the gene responsible residing on the long arm of chromosome 19 [22].

Unlike the other myotonic syndromes, myotonic dystrophy is a multisystem disorder. Although there is a rare congenital form of the disease, most patients present between the ages of 15 and 35 yr. Although myotonia is a common feature, there is often weakness of grip and difficulty in walking because of impaired foot dorsiflexion. It is not uncommon, however, for patients to present with bilateral cataracts or with infertility. Cataracts are found in the majority of myotonic dystrophy patients older than 20 yr, are of specific morphology and do not
occur in the other myotonic syndromes. Patients have a characteristic facial appearance, with the lips parted and forming an “inverted smile”. Marked wasting of the muscles of mastication produces hollowing of the cheeks and temporal fossae [56]. Ptosis is almost invariable, but patients are unable to close their eyelids tightly. Frontal baldness, especially in males, and sternomastoid wasting are common. In contrast with the weakness found in the face, neck and distal muscle groups, limb girdle muscle power is well preserved until late in the disease. Bulbar muscle weakness may result in pulmonary aspiration and recurrent chest infection [11].

Myotonia may affect any muscle group, but usually presents with difficulty in releasing handgrip. Percussion myotonia is best elicited by tapping the muscles of the thenar eminence or long finger extensors. The myotonia decreases with age as the muscles become progressively weaker. Although patients complain that cold aggravates the muscle stiffness, this is not confirmed by EMG studies.

Extramuscular involvement is almost invariable in myotonic dystrophy. Cardiac abnormalities are usual [33] and may precede other symptoms [40]. Most commonly, there is a progressive deterioration of the conducting system resulting in first degree heart block, bundle branch block and widening of the QRS complex [24, 34]. Sudden death has been associated with the development of third degree heart block [45, 47]. Cardiac muscle is affected by the dystrophic process and cardiomyopathy and cardiac failure occur [67, 76, 98]. There is also an increased incidence of septal defects and valvular abnormalities, including mitral valve prolapse. Little correlation exists between the severity of the cardiac defects and the severity of the skeletal muscle disease.

Ventilatory involvement in myotonic dystrophy is multifactorial [13, 38]. Muscular weakness may affect both the diaphragm and other respiratory muscles, leading to poor cough, restrictive lung defect and alveolar hypoventilation [9]. There is little evidence that myotonia of the respiratory muscles is a significant factor. A central abnormality may contribute to hypoventilation and reduce the ventilatory response to carbon dioxide [44]. Central and obstructive sleep apnoeas may be demonstrated [14]. There is undue sensitivity to various anaesthetic and sedative agents including opioids, barbiturates, benzodiazepines and propofol [53, 64, 88].

Gastrointestinal manifestations are present in 80% of patients [52]. In addition to dysphagia [11, 39], there is also a reduction in the rate of gastric emptying [50]. Intestinal pseudo-obstruction oesophageal aperistalsis and spontaneous pneumatoneumone have been reported [30].

Endocrine involvement may include hypothyroidism, primary gonadal failure and abnormalities of glucose and insulin metabolism, often with clinical diabetes mellitus [6, 74].

Although pregnancy is uncommon, as a result of ovarian failure, when it does occur it may cause exacerbation of the muscle weakness, myotonia and muscle wasting [49, 85] and of the extramuscular manifestations [32]. This deterioration may be caused by effects of progesterone on the intracellular/extracellular K+ ratio [49]. There is an increased incidence of spontaneous abortion, premature and prolonged labour. The uterus is often atonic with poor uterine contraction, and postpartum haemorrhage requiring hysterectomy has been reported [48].

The myotonia is demonstrable on EMG, but myotonic discharges are less abundant than in the non-dystrophic myotonias. They are best demonstrated by examining the facial or distal limb muscles [93].

Myotonia congenita was first described in 1876 by Dr A. J. T. Thomsen, in himself and his family, and was subsequently mapped through seven generations by his great grandson Karl Nissen. Thomsen's disease is an autosomal dominant disorder with an incidence of about 2 in 50000, characterized by the presence of generalized muscular hypertrophy. The major presenting complaint, however, is of stiffness on initiating voluntary movement, and this is relieved by exercise (the “warm up” phenomenon). The disease is not usually considered a handicap and may be concealed deliberately. All muscle groups are affected and handgrip and percussion myotonia are easily elicited. Severe blepharospasm may occasionally be disabling. There is no muscular weakness and extramuscular manifestations are absent.

Electromyographically there are widespread, intense discharges in all muscle groups. Adaptation resulting in decrement of frequency and amplitude of discharges is demonstrated easily, producing the classic myotonic EMG. Cooling the muscle does not alter the response.

More recently, several variants of this condition have been classified [79].

Myotonia fluctuans was described in 1990 in five
family members extending over three generations [81], and follows an autosomal dominant mode of transmission. In contrast with classical Thomsen's disease, patients show considerable fluctuation in severity of the condition throughout life. Handgrip myotonia is rare and the myotonia increases following a potassium load. EMG studies show a characteristic picture of exercise-induced, delayed onset myotonia. Relaxation of muscles is normal immediately after exercise, but within a few minutes a minor stimulus may provoke severe myotonia. The mechanism is unclear, but may result from the change in intracellular pH on exercise acting initially to stabilize the cell membrane.

Acetazolamide-responsive myotonia congenita was first described in 1987 [97] and is also inherited in an autosomal dominant manner. This variant is characterized by painful contractions which are provoked by fasting and by oral potassium administration (some patients require a banana-free diet), and relieved by administration of carbohydrate. The myotonia is relieved by acetazolamide and exacerbated by cold but, in contrast with paramyotonia congenita, not by exercise.

Recessive generalized myotonia was described first by Becker in 1973 [7]. It may be more common than classical Thomsen's disease. This autosomal recessive variant is characterized by severe myotonia predominantly affecting the legs, and weakness predominantly affecting the forearms [83]. Dystrophic features may be seen on muscle biopsy. The EMG may show decremental response to repetitive stimulation which may be more pronounced than in myotonia congenita. Heterozygotes may demonstrate the EMG features of the disease.

Paramyotonia congenita is a rare autosomal dominant disorder described first in 1886 by Eulenberg. The condition is characterized by generalized myotonia which is recognized in early childhood and, as in myotonia congenita, generalized muscular hypertrophy may occur. The myotonia is termed paradoxical because, in contrast with other myotonias, the muscular stiffness is often exacerbated by exercise. Cold markedly aggravates the myotonia and mothers can often tell which children are affected by the effect of washing the face in cold water. Episodes of flaccid paralysis, lasting several hours after the muscle has rewarmed, may be present. These resemble the paralysis seen in hyperkalaemic periodic paralysis. Some patients with paramyotonia congenita may develop paralysis independent of myotonia and this may be related to serum potassium concentrations. For this reason doubt has arisen whether paramyotonia congenita and hyperkalaemic periodic paralysis are separate entities [58, 78, 87].

The EMG may be normal at room temperature, but typical myotonic discharges become evident as the muscle is cooled. The myotonia may become difficult to elicit as fatigue of the muscle develops [21]. Although the membrane abnormality has been shown to lie in the sodium channel, and to affect extramuscular membranes [63], there are no clinically evident extramuscular manifestations.

Hyperkalaemic periodic paralysis was described first in 1955, and called adynamia episodica heredita. The condition is characterized by episodes of flaccid paralysis associated with increased serum potassium concentrations and precipitated by cold, hunger and emotional stress. Most patients have clinical and EMG evidence of myotonia and this may occasionally be severe and disabling. Myotonia is not a feature of hypokalaemic periodic paralysis and this difference may aid diagnosis.

Schwartz–Jampel syndrome is also known as chondrodystrophic myotonia and is a rare and progressive disorder of childhood comprising muscular stiffness, atrophy and hypertrophy, myotonia and ocular, facial and skeletal abnormalities. There is blepharospasm and tense puckering of the mouth. It is probably an autosomal recessive condition with variable expression. The myotonia may be widespread and the EMG findings differ widely. In common with the other myotonic conditions, the defect appears to lie in Na+ and Cl− conductance [62].

Acid-maltase deficiency is a glycogen storage disease (Cori type II, Pompe's disease) presenting typically in the second or third decade, with pelvic girdle weakness and respiratory failure as a result of respiratory muscle weakness [55, 82]. Myotonic discharges are demonstrable, especially in the muscles of the neck, but are rarely a predominant feature.

ANAESTHETIC CONSIDERATIONS

The preoperative assessment and subsequent conduct of anaesthesia in the patient with myotonic dystrophy have been well documented [2, 53, 68, 75] and are directed to the management of the extramuscular manifestations of the disease which may be life-threatening. Problems include undue sensitivity to premedicant drugs [2], induction agents [2, 53, 88], opiates [2] and non-depolarizing neuromuscular blocking drugs [4]. Obstetric anaesthesia [8, 27, 49, 72, 85, 90] and cardiac anaesthesia [95] pose particular problems. Postoperative complications are usually the result of pulmonary and cardiac dysfunction and of pharyngeal muscle weakness leading to increased risk of aspiration.

Myotonia congenita [46] and Schwartz–Jampel syndrome [86] are associated with malignant hyperpyrexia (MH), although it is difficult to determine the extent of the association [15]. Haberer, Fabre and Rose [43] reported the death of a 5-yr-old child with myotonia congenita who developed a clinical syndrome suggestive of MH 7 h after operation. Worryingly, the anaesthetic technique involved the avoidance of known triggering agents and a vapour-free machine. Difficulty in interpretation of the caffeine–halothane contracture test in myotonic patients further complicates the nature of the association [46, 61].

Patients with hyperkalaemic periodic paralysis develop weakness in association with changes in serum potassium concentrations and independently of myotonia. Concerning anaesthesia for these patients, Ashwood, Russell and Burrow [3] recommended preoperative potassium depletion with frusemide and mentioned that thioule diuretics,
while they may treat the weakness, may worsen the myotonia. Potassium-containing fluids and drugs which release potassium from cells should be avoided and the ECG should be monitored continuously. Calcium gluconate is suggested for the emergency treatment of hyperkalaemia-induced weakness. I.v. glucose should be given to avoid carbohydrate depletion during fasting. As in other myotonic syndromes, temperature monitoring and the maintenance of normothermia are recommended.

**Perioperative factors associated with the development of myotonia**

Induction and maintenance of anaesthesia with propofol has been reported as successful [64, 100]. However, Speedy reported a prolonged recovery time of 120 min after an induction dose of propofol 50 mg in an adult patient [88]. Furthermore, generalised myotonia has been precipitated by the use of propofol [12].

The depolarizing neuromuscular blocking drugs pose a particular problem for the myotonic patient. Although some authors have reported a normal response to suxamethonium [53, 80], others report a generalized myotonic response resulting in difficulties in tracheal intubation and ventilation [26, 96]. The response appears to be dose dependent [71]. Suxamethonium in the myotonic patient has a dual effect. It blocks neuromuscular transmission in the normal manner [4], but also acts directly on the muscle causing contraction [65, 71]. In addition, the increase in serum potassium concentration after administration of suxamethonium may further contribute to the development of myotonia. Several reports describing relaxation of myotonia after suxamethonium have appeared [25, 94], but the mechanism is unclear. A typical generalized myotonic response to suxamethonium consists of the rapid development of jaw, abdominal and chest rigidity with arching of the cervical and lumbar spines [96]. Ventilation and intubation may be difficult or impossible for 4-5 min. Furthermore, because the myotonia is caused by a primary defect of the muscle, non-depolarizing neuromuscular blocking drugs do not abolish the generalized contractions. It is therefore recommended that suxamethonium is avoided in myotonic patients.

Non-depolarizing neuromuscular blocking agents, when effective, appear to behave normally [4, 10, 65]. However, in the myotonic conditions in which muscle wasting occurs (myotonic dystrophy, recessive generalized myotonia) there may be an exaggerated response. Perioperative neuromuscular monitoring should be used in all patients if these drugs are used.

**Anticholinesterase drugs** used to antagonize the effects of the non-depolarizing neuromuscular blocking drugs may also precipitate myotonia [23], presumably because myotonic muscle has increased sensitivity to the stimulatory effects of acetylcholine [71]. If myoneural block is required, it would seem prudent to use short acting agents such as atracurium [10] or vecuronium, which do not require antagonism. In many cases, the use of neuromuscular blocking agents is unnecessary, as volatile agents provide some degree of relaxation in the myotonic patient [59].

Several other pharmacological agents may cause initiation or exacerbation of myotonia. Although both clofibrate and propranolol may exacerbate myotonia when examined electromyographically, these drugs rarely produce difficulty in clinical practice [29]. The administration of potassium worsens clinical myotonia. Normal and myotonic muscle respond differently to increased serum concentrations of potassium [31]. In normal muscle, an increase in serum potassium concentration increases muscular excitability and spontaneous discharges. Myotonic muscle shows a biphasic response. Initially, a decreased excitability can be demonstrated, but as serum potassium increases, increased sensitivity is seen. Durelli and colleagues [31] suggested that there is a differential effect of potassium on potassium channels on the muscle membrane surface and on the T-tubules of myotonic muscle. It would seem wise to avoid potassium-containing solutions.

A number of physical factors may also precipitate myotonia. Cold and shivering independently induce myotonia. Application of ice may reveal electrical myotonia and has been used to aid diagnosis [20]. Cold may worsen symptoms in myotonia congenita [41] and may produce prolonged paralysis in paramyotonia congenita and this may continue for many hours after rewarming [93].

Shivering may also produce myotonia [53]. The incidence of postoperative shivering has been reported as being 5-65% [28]. Although shivering may be associated with hypothermia, there is a poor correlation with body temperature [99]. Nevertheless, the maintenance of normothermia reduces the incidence and duration of postoperative shivering [73]. Shivering is more common if large concentrations of volatile agents are used [66] and these should therefore be avoided in myotonic patients. The incidence of shivering may be reduced by the use of doxapram, methylphenidate and pethidine [16, 28]. Management of the myotonic patient should therefore include careful monitoring of core temperature, the use of warming mattresses and warming of i.v. fluids.

Myotonic contraction during surgical manipulation and electrocautery is a major management problem. The myotonia is not responsive to neuromuscular block, regional block or peripheral nerve block. Drugs such as procainamide [36] and phenytoin [69], which stabilize muscle membranes, may be useful. Similarly, topical application of local anaesthetics to cut nerve bundles has been reported as successful [27]. Although large concentrations of volatile anaesthetic agents may abolish myotonic contraction, this may be at the expense of cardiovascular depression and an increased incidence of postoperative shivering.

**REFERENCES**


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