# 24.19.3 Myotonia 6328 David Hilton- Jones

# 24.19.3 Myotonia 6328 David Hilton- Jones

section 24 Neurological disorders 6328 entering clinical trials. Gene transfer experiments in animal models have proved the general feasibility of this approach to these genetic diseases, at least on a small scale. Modification of mutations, either by drugs or by other means, is an area of research, as is the concept of up-regulating the production of ancillary proteins. Novel and promising therapies arising from genetic manipulation concepts, targeting either DNA or RNA are currently undergoing clinical trials and may be licensed for treatment. In boys with DMD who have a nonsense mutation in the dystrophin gene, resulting in a premature stop codon, nonsense suppression therapies induce a readthrough of premature stop codons through insertion of an amino acid into the peptide chain allowing full translation. While in patients with a deletion resulting in disruption of the reading frame and absence of protein, exon skipping techniques are able to restore the reading frame and produce a shorter, though functional, protein. Other promising approaches include gene transfer through viral vectors. In view of these promising developments with mutation-specific treatments, achieving a precise genetic diagnosis is fundamental, as is the possibility for these patients to be offered participation in clinical trials, when available. Participation in research is the way forward for better understanding of the disease, identifica- tion of early signs and markers of disease progression and contri- bution to the development of novel therapeutics. Patients should be informed and encouraged to sign on to patient disease specific registries, acting as a database for all patients diagnosed with a specific condition. On top of the need for databases to collect in- formation for better understanding of these rare conditions and help developing standards of care, registries offer the possibility to identify patients for clinical trial and keep patients updated with new developments in the field of muscular dystrophy. The list of registries is available at http://www.treat-nmd.eu/resources/ patient-registries/list/. FURTHER READING With the rate of change, over the last few years, in the information available about genetically determined diseases, the most up-to-date reviews of the subject may be found on the internet rather than in traditional textbooks. Bushby K, et al. for the DMD Care Considerations Working Group (2010). Diagnosis and management of Duchenne muscular dys- trophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol, 9, 77–93. Bushby K, et al. for the DMD Care Considerations Working Group (2010). Diagnosis and management of Duchenne

muscular dys- trophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol, 9, 177–89. Engel A (ed.) (2004). Myology, 3rd edition. McGraw Hill, New York, NY. Karpati G, et al. (eds) (2010). Disorders of Voluntary Muscle 8th edi- tion. Cambridge University Press, Cambridge. Murphy AP, Straub V (2015). The classification, natural history and treatment of the limb girdle muscular dystrophies. J Neuromuscul Dis, 2, S7–S19. Nigro V, Savarese M (2014). Genetic basis of limb-girdle muscular dystrophies: the 2014 update. Acta Myol, 33, 1–12. Mercuri E, Muntoni F (2012). The ever-expanding spectrum of con- genital muscular dystrophies. Ann Neurol, 72, 9–17. Lemmers RJLF, Miller DG, van der Maarel SM (1999). Facioscapulohumeral muscular dystrophy. In: Pagon RA, et al.
(eds) GeneReviews®. Websites Leiden University Medical Center. Leiden Muscular Dystrophy pages. http://www.dmd.nl National Center for Biotechnology Information (NCBI). Online Mendelian Inheritance in Man (OMIM). http://www.ncbi.nlm.nih. gov/sites/entrez?db=omim Neuromuscular Disorders Online gene table http://www. musclegenetable.org/ TREAT-nmd network http://www.treat-nmd.eu/ Washington University Neuromuscular Disease Centre. http://neuro-muscular.wustl.edu/ 24.19.3 Myotonia David Hilton-Jones ESSENTIALS Myotonia is defined at an electrical level as repetitive discharge of the muscle fibre membrane after initial activation, which occurs due to dysfunction of the membrane’s ion channels, most commonly the chloride channel, less commonly the sodium channel. This manifests clinically as stiffness of the muscle and delayed relaxation after vol- untary contraction (e.g. difficulty relaxing the grip after clenching the fingers, and stiffness in the thigh muscles and difficulty walking on first moving after rest). Disabling myotonia may respond to carba- mazepine, phenytoin or, often most effectively, mexiletine, although supplies are now limited. Particular myotonic disorders Useful clinical distinction can be made between (1) myotonic dystrophies—multisystem disorders in which weakness is a signifi- cant feature, and (2) nondystrophic myotonias. Myotonic dystrophy type 1 (Steinert’s disease)—caused by ex- pansion of an unstable trinucleotide repeat in the myotonic dystrophy protein kinase (DMPK) gene, leading to myotonia through altered splicing of the chloride channel gene. There are four main patterns of disease: (1) congenital; (2) childhood onset; (3) classic or early adult onset; (4) late onset, asymptomatic, or oligosymptomatic. The classic form of the disease is the most frequent cause of myotonia and the most prevalent muscular dystrophy in adults (c.1 in 8000). In addition to myotonia and a characteristic pattern of weakness affecting the facial muscles and (unusually for a myopathic disorder) distal limbs, other fea- tures include premature male-pattern balding, cataracts, central nervous system involvement (cognitive change, excessive daytime sleepiness), cardiac conduction abnormalities (which may lead to sudden death), gastroenterological involvement (dysphagia and irritable bowel syndrome), and respiratory problems. Recurrent chest infections are common due to the combination of muscular

 weakness and the tendency to aspirate, and death is often sec- ondary to pneumonia. The underlying trinucleotide repeat is unstable and increases in size during meiosis, giving rise to antici- pation in which the disease has an earlier onset in the offspring of affected individuals. Myotonic dystrophy type 2 (proximal myotonic myopathy)— caused by a quadruplet repeat expansion in the zinc finger 9 pro- tein (ZNF9) gene (also called CNBP) that leads to disruption of normal RNA processing and altered splicing patterns of numerous genes. Clinical features are similar to type 1, but with proximal
(rather than distal) weakness and less evident anticipation. Nondystrophic myotonias—mutations affecting the skeletal muscle chloride channel (CLCN-1) gene give rise to the rare condition myotonia congenita, which can be inherited as either an autosomal dominant or recessive trait.

Myotonia is striking; leg stiffness causing difficulty walking is the major feature, but persistent weakness is uncommon. Introduction Myotonia can be considered as a symptom, a physical sign, or a neurophysiological phenomenon, but understanding is perhaps best served by discussing these in the reverse order. The basic neurophysiological finding is of repetitive muscle fibre action potentials following a stimulus, which may be voluntary con- traction or muscle percussion. The repetitive electrical activity causes muscle contraction, and thus myotonia is characterized by delayed muscle fibre relaxation after such a stimulus. Electromyography demonstrates the repetitive firing. Characteristically, the discharge gradually declines in amplitude and frequency, producing the so- called ‘dive-bomber’ sound in the monitoring loudspeaker. The term ‘myotonia’, and apparently related terms such as ‘paramyotonia’ and ‘neuromyotonia’, cause much confusion. Various diseases accom- panied by myotonia have different molecular origins and many as- sociated symptoms and signs As a physical sign, myotonia is demonstrated either as de- layed muscle relaxation following voluntary contraction (e.g. grip myotonia—Fig. 24.19.3.1), or as persistent muscle dimpling fol- lowing percussion (percussion myotonia—Fig. 24.19.3.2). As a symptom, complaints relating to myotonia differ between pa- tients with myotonic dystrophy, which is by far the most common cause of myotonia, and those with myotonia congenita. In myotonic dystrophy, even when grip myotonia is readily evident on examin- ation, the patient may offer no symptoms. They are more likely to complain of hand weakness than of myotonia. When the myotonia is symptomatic, the patient complains of difficulty releasing objects after a tight grip. This is sometimes striking. One patient first noted grip myotonia in early adult life, when he was appointed as a teacher at a school—as his future headmaster shook his hand to congratu- late him, he was embarrassingly unable to release his grip. In myo- tonic dystrophy, bulbar symptoms relating to myotonia are quite common—patients complain of their tongue or jaw ‘locking’ when speaking or swallowing, and tongue myotonia on percussion may be demonstrated. By contrast, in myotonia congenita weakness is absent and the myotonia, which is generalized, is problematic, particularly in the lower limbs. Patients complain of stiffness that is most evident on trying to initiate movement after rest. Thus, the patient who has been sitting in the waiting room rises and walks with profound leg stiffness, somewhat reminiscent of spasticity, into the con- sulting room. A classic presentation is the soldier on the parade ground—after a prolonged period ‘standing to attention’, the order to march results in his falling due to leg muscle stiffness. One such patient also demonstrated marked grip myotonia—on an unfor- tunate occasion he alighted from a bus but, unable to release his grip from the handrail before the bus departed, was dragged along the road. (a) (b) (c) Fig. 24.19.3.1 Grip myotonia: the patient was asked to grip the examiner’s fingers tightly for 3 s, and then to release the grip as rapidly as possible. The two photographs were taken at 3-s intervals.

section 24 Neurological disorders 6330 In most disorders, myotonia lessens with repeated activity of the muscle. Thus, the sign becomes less striking with repeated percus- sion of the thenar eminence or attempts to demonstrate grip myo- tonia. As a symptom, for example, the leg stiffness in myotonia congenita lessens as the patient continues to walk. In paramyotonia the reverse is seen, with myotonia increasing with activity—so- called paradoxical myotonia. Some, but by no means all, patients complain that their myotonia is worse in the cold. This is again a particular characteristic of paramyotonia. As the anecdotes described here indicate, severe myotonia— which is more common in myotonia congenita than the myotonic dystrophies—can be very disabling. It may respond to phenytoin, but side-effects can be problematic. Recent evidence favours the use of mexiletine, which is effective and generally well tolerated, with no adverse cardiac effects even in

the myotonic dystrophies in which cardiac conduction defects are common. Classification of myotonic disorders As with many other inherited neuromuscular disorders, nomen- clature and classification are currently in a state of flux as mo- lecular mechanisms are being unravelled. For clinical purposes a useful distinction is between those multisystem disorders in which weakness is a significant feature, and which are therefore referred to as dystrophies, and the nondystrophic myotonias (Table 24.19.3.1). Classic myotonic dystrophy was previously called dystrophia myotonica, which gave rise to the abbreviation DM. It shows no genetic heterogeneity, all cases being associated with a trinucleotide repeat expansion in the 3’-untranslated region of a novel protein kinase gene (DMPK) on chromosome 19q. This locus and clinical disorder are referred to as DM1. A closely related condition, previ- ously called proximal myotonic myopathy (PROMM), is caused by a quadruplet repeat expansion in intron 1 of the zinc finger 9 protein gene (ZNF9), also called CNBP, on chromosome 3q and is referred to as DM2. The most common nondystrophic myotonias are the autosomal dominant and recessive forms of myotonia congenita, both of which are caused by mutations of the skeletal muscle chloride channel gene (CLCN1). Different mutations of the skeletal muscle sodium channel gene (SCN4A) give rise to hyperkalaemic periodic paralysis and re- lated disorders, including paramyotonia congenita. These chloride and sodium channelopathies, together with the calcium channel dis- orders causing hypokalaemic periodic paralysis, are discussed fur- ther in Chapter 24.19.4. Schwartz–Jampel syndrome is a very rare recessive dis- order of infantile onset, characterized by skeletal abnormalities (chondrodysplasia), abnormal facial appearance, and abnormal muscle electrical activity. Electromyography shows periods of con- tinuous electrical activity, which are probably neural in origin. It is caused by mutations in the HSPG2 gene, encoding the basement membrane protein perlecan. (a) (b) (c) Fig. 24.19.3.2 Percussion myotonia: following a sharp tap, the thenar eminence muscles contract and then relax slowly (photographs taken at 3-s intervals). Table 24.19.3.1 Classification of myotonic disorders Myotonic dystrophies (multisystem myotonic myopathies) Nondystrophic myotonias DM1: myotonic dystrophy type 1 (chromosome 19q) Chloride channelopathies: myotonia congenita (chromosome 7q) DM2: myotonic dystrophy type 2 (chromosome 3q) Sodium channelopathies: paramyotonia congenita (chromosome 17q) Schwartz–Jampel syndrome: chondrodystrophic myotonia (chromosome 1p)

24.19.3 Myotonia 6331 Myotonic dystrophy type 1 (DM1) DM1 is the most frequent cause of myotonia and is also the most prevalent muscular dystrophy in adults. It is a multisystem dis- order that has very important (but sometimes rather neglected) manifestations other than skeletal muscle dysfunction, involving cardiac conduction tissues, smooth muscle, eyes, and the central nervous system. Clinical severity ranges from death in utero to a condition so mild that it may be asymptomatic and with no ab- normal physical signs in old age. The molecular basis is an expan- sion of an unstable trinucleotide repeat in a gene coding for a novel protein kinase, DMPK. There is strong evidence that the molecular mechanism in both DM1 and DM2 is disruption of normal RNA processing which causes altered splicing patterns of numerous genes, including the chloride channel gene (compare myotonia congenita)—this explains the myotonia—and the insulin receptor gene, causing insulin resistance. Myotonic dystrophy provides a dramatic example of the phenomenon of ‘anticipation’, by which succeeding generations may be much more severely affected than their predecessors, and this correlates with the size of the genetic expansion. Epidemiology The disease is seen worldwide, with a particularly high frequency in French Canadians in Quebec (originating from a single immigrant couple). Incidence and prevalence figures are unreliable, and prob- ably mostly underestimates, because of the difficulty in identifying

asymptomatic individuals. A generally accepted prevalence value is 8/100 000 population. Pathogenesis The molecular basis is the expansion of a trinucleotide (cytosine– thymine–guanine, CTG) repeat sequence in the 3′-untranslated region of the myotonic dystrophy protein kinase (DMPK) gene on chromosome 19q. In the normal population the size of the re- peat is in the range CTG5–37, with a trimodal distribution of 5, 11 to 17, and 19 to 37 repeats. Expansions in the range CTG37–49 are believed to represent premutations. Individuals with myotonic dys- trophy have repeats in the range CTG50–5000 and, as noted next, there is a correlation between the size of the repeat and clinical severity, and an inverse correlation between repeat size and age of onset. Diagnostic studies are based on measurement of the expansion size in blood lymphocyte DNA. There is only a broad correlation be- tween lymphocyte expansion size and clinical severity, in large part because other tissues may have very different expansion sizes com- pared with lymphocytes. The expansion size in lymphocytes cannot therefore be used in any meaningful predictive fashion for clinical severity and because of misunderstandings relating to this, some la- boratories will only report ‘positive or negative’ for an expansion, without stating the size. A fundamental concept is that the expanded gene is unstable. It is mitotically unstable, and so the size of the gene increases with age. There is somatic mosaicism, so that the expansion is not the same size in different tissues. More important is intergenerational CTG-repeat instability, which explains why the disease tends to increase in severity, and also show rather different clinical features, in subsequent generations. The gender of the parent of origin is important. In most trans- missions the allele size increases. However, there appears to be a threshold limit for sperm, and males never transmit the very large expansions associated with congenital myotonic dystrophy (see next), which occurs only when the mother is the gene carrier. There is some evidence of meiotic drive, which leads to preferred transmis- sion of the abnormal expanded allele. Clinical features From the previous discussion, it is apparent that there is a con- tinuous distribution of expanded allele size, and a relationship be- tween allele size and disease severity and between allele size and age of onset. While accepting that some patients will fall between these categories, for practical clinical purposes myotonic dystrophy can be considered to give rise to four main patterns of disease: • congenital • childhood onset • classic or early adult onset • late onset, asymptomatic, or oligosymptomatic As it is the best known, and illustrates the multifarious manifest- ations of myotonic dystrophy, the classic form is discussed first. Classic form Onset is in adolescence or early adult life. The principal manifest- ations are summarized in Table 24.19.3.2. Several rarer or clin- ically less important associations are also recognized, including reduced fertility, testicular atrophy, insulin resistance (but rarely overt diabetes), retinopathy, eye movement disorder, peripheral neuropathy, disturbed tests of endocrine function, hypotension, pilomatrixomas, and reduced levels of immunoglobulins and complement. Table 24.19.3.2 Main clinical features of myotonic dystrophy System Manifestations Neuromuscular Weakness Myotonia Ocular Cataract Central nervous system Excessive daytime sleepiness Low IQ Sensorineural deafness Cardiovascular Heart block Dysrhythmias Sudden death Respiratory Recurrent infections Sleep apnoea Hair Premature balding Gastrointestinal Dysphagia Irritable bowel syndrome Pseudo-obstruction

 Skeletal and smooth muscle The features of myotonia have already been discussed. The distribu- tion of muscle weakness is highly characteristic. Wasting and weak- ness of the facial muscles, combined with premature male-pattern balding (in males much more apparent than females), give rise to the typical facial appearance of the condition (Fig. 24.19.3.3). The temporalis muscle is atrophic, giving a sunken appearance over the temples. There

is ptosis. Eye closure is weak and in se- vere cases the sclera may remain visible. The jaw tends to hang down. Neck flexion is weak and in some, but not all, patients there is evident atrophy of the sternomastoid muscles. In the limbs, and in marked contrast to most other myopathic disorders, the weak- ness is predominantly distal. In the upper limbs there is weakness and wasting of the small hand muscles and of the long wrist, and finger flexor and extensor muscles in the forearm. There is often profound weakness of grip and the patient complains of difficulty with tasks such as wringing out a cloth and removing the lid from a bottle. A simple hand-held dynamometer reveals the extent of the weakness—whereas a normal woman would easily exceed 35 kg, patients of either sex may manage only 1 or 2 kg. In the lower limbs there is weakness of ankle dorsiflexion, presenting as tripping easily and foot-drop. As the disease advances, weakness becomes evident more proximally, but the marked distal predilection re- mains throughout. Bulbar muscle weakness presents with dysarthria and dysphagia. Smooth muscle involvement contributes towards the dysphagia. Symptoms akin to those of irritable bowel syndrome are frequent. Constipation is also common and pseudo-obstruction rare. There may be evidence of incoordinate uterine contraction in labour but there is little evidence that this is of any clinical significance and most women can deliver a pregnancy normally. Ocular Cataracts develop at an early age. The initial manifestation is multi- coloured opacities in the subcapsular regions, readily seen on slit- lamp examination. Identification of cataracts used to be important in screening asymptomatic family members for the disease, but that has now been replaced by DNA testing. In practice, the cataracts are managed as any other cataracts, being operated on when vision is significantly impaired. Early-onset cataracts, even in the absence of any other suggestive features, should always raise the suspicion of myotonic dystrophy. Central nervous system Central nervous system disease is expressed in two main ways. As a group, patients with myotonic dystrophy have a lower intelligence than average, but many mildly affected patients have intelligence within the normal range. They are often perceived as apathetic or lacking self-motivation. There is neuropsychological evidence of specific defects of frontal lobe functioning. The second principal feature is excessive daytime sleepiness, which affects over three- quarters of patients, some profoundly. This appears to be a central phenomenon and is only rarely attributable to obstructive sleep ap- noea/nocturnal sleep disturbance. Cardiovascular Cardiovascular dysfunction is arguably the most important extramuscular manifestation of myotonic dystrophy and is prob- ably responsible for most of the not infrequently reported cases of sudden death. The most commonly recognized pattern is of pro- gressive conduction disturbance. Thus, in very early cases the ECG is normal. Subsequently, the PR interval gradually lengthens until first-degree block is present. Left anterior hemiblock is particularly common. Later features include bundle-branch and complete heart block. Tachyarrhythmias also occur, most frequently atrial flutter or fibrillation, but also ventricular arrhythmias, which may be fatal. Symptoms include palpitation, dizzy spells, and fainting. Prolonged ECG monitoring and sometimes intracardiac electrophysiological studies are indicated if such symptoms are reported, or the standard ECG shows significant change. All patients should have an ECG annually and be advised to report any cardiac symptoms immedi- ately. Rhythm disturbances precipitated by anaesthesia or surgery are common, as are respiratory problems. For these reasons, patients should carry a medical alert bracelet/medallion and, for elective ad- missions for surgery, be reminded to inform the anaesthetist of their diagnosis. The latter is particularly important for asymptomatic in- dividuals diagnosed on the basis of DNA studies following family screening, because they may not consider themselves to be at risk; they are. Although there is some correlation between cardiac in- volvement and overall severity of the myotonic dystrophy, it is not absolute and individuals with minimal muscle involvement may have

significant ECG changes. Heart muscle disease, as opposed to disordered cardiac con- ducting tissues, is not clinically significant and routine echocardi- ography is not required. Respiratory Recurrent chest infections are common and relate to respiratory muscle weakness and the tendency to aspirate. In advanced dis- ease, death is often secondary to pneumonia. Respiratory insuffi- ciency may become apparent following anaesthesia, with difficulty in weaning from the ventilator. Chronic hypoventilation and sleep fragmentation may cause excessive daytime sleepiness, but in prac- tice are much less common than the presumed central mechanism already mentioned. However, it must be considered and excluded (e.g. by overnight oximetry) if felt to be a possibility. Particular warning features would include a history of disturbed night-time
Fig. 24.19.3.3 Adult-onset myotonic dystrophy: typical facial features (see text).

 sleep, snoring, waking with headaches, and the development of sec- ondary polycythaemia. Congenital form By definition, this form of myotonic dystrophy is evident at birth, but the spectrum of early-onset myotonic dystrophy is much wider, as noted next. The exclusive (with only very rare exceptions) maternal transmission of congenital myotonic dystrophy has al- ready been discussed. Many fetuses carrying large expansions are aborted spontaneously in early pregnancy and there is a high rate of fetal wastage. As a result of the unstable nature of the CTG re- peat and the associated phenomenon of anticipation, it is not un- common for the mother to be unaware of her own diagnosis at the time of birth. In that situation, the diagnosis in the infant is not always immediately apparent, because there are no entirely specific clinical features. There is often a history of polyhydramnios and poor fetal move- ment in the pregnancy. The child is born hypotonic (‘floppy’) and talipes is present in about half. Respiratory and feeding difficulties may necessitate assisted ventilation or an oxygen tent, and feeding by nasogastric tube. Some die in the neonatal period from respira- tory complications, but, somewhat surprisingly, there are few fur- ther deaths in the survivors until the late teens and early adult life. There is generalized weakness, including the face—the jaw hangs open and the mouth has a characteristic tented or carp-like (as in fish) appearance. Myotonia is not evident clinically and even elec- tromyographically may not appear for several years. In those who survive, hypotonia resolves and motor function im- proves over the following few years, but during adolescence the fea- tures of the classic adult form of the disease appear (Fig. 24.19.3.4). Cognitive impairment is invariable and may be severe. Most re- quire special needs schooling. Bowel involvement is common, with faecal soiling and irregular bowel habit. Curiously, cataracts are rela- tively uncommon. The overall prognosis is poor. Some 25% die in the first 18 months of life, most in the neonatal period. Half survive into the mid-30s, death most commonly resulting from respiratory involvement, but with a proportion of sudden deaths almost certainly due to cardiac conduction defects. Few achieve an independent adult life. Childhood-onset form It is only recently that the specific problems of childhood-onset disease have been recognized. By definition, such children do not have evidence of disease at birth. Motor milestones may be delayed. Problems are often first recognized around the start of schooling with evidence of cognitive delay and poor language development. Dysarthria is common. Fatigue and slowness of activities are often striking. Facial weakness is almost invariable, together with weak- ness of neck flexion. Late-onset form This form is associated with a small CTG-repeat expansion. It is typically asymptomatic or oligosymptomatic, and diagnosed during family studies or by an alert ophthalmologist when the patient presents with cataracts. Skeletal muscle disease may be absent, or confined to mild myotonia and weakness restricted to the hands. Balding may be a feature. It is not uncommon to see the parents of a patient with the classic adult form of the dis- ease and not be able to identify the transmitting parent on clinical examination. Importantly, even patients with such minimal symptoms may oc- casionally develop significant cardiac conduction problems and

they should have annual electrocardiograms. Management The essential management issues in myotonic dystrophy are: • genetic counselling • annual electrocardiogram (ECG) • anaesthetic risks • physical therapies • cataract surgery A particular concern relates to the genetic phenomenon of antici- pation and the potential for an asymptomatic mother, ignorant of the diagnosis, to give birth to a congenitally affected child. When the diagnosis of myotonic dystrophy is established in a family member it is imperative that at-risk relatives are offered screening. Reproductive options include prenatal diagnosis, by chorionic villus sampling, with termination of an affected fetus and, gradually be- coming more widely available, preimplantation genetic diagnosis. Annual ECG should be performed in all patients. They and their medical attendants must be aware of the cardiorespiratory compli- cations associated with anaesthesia. They should be encouraged to wear an appropriate medical alert bracelet or medallion. A few pa- tients require nocturnal positive-pressure ventilation by facemask, but most excessive daytime sleepiness is not related to respiratory insufficiency. Recurrent chest infections are common. Annual influ- enza immunization should be advised. Pneumococcal immuniza- tion is also given but is of uncertain value. Physiotherapy, and occupational and speech and language therapy all have a role, as does the use of orthotic devices (e.g. for foot-drop). Bowel problems in the congenital form require specific advice and counselling. Excessive daytime sleepiness may respond, sometimes dramatic- ally, to modafinil (but sleep-related breathing abnormalities should be excluded). Cataract surgery is required when vision is significantly impaired. Fig. 24.19.3.4 Myotonic dystrophy: the affected mother’s two children have the congenital form of the disease.

---

Revision #1
Created 2026-01-22 16:43:28 UTC by Omar Ayman
Updated 2026-01-22 16:43:28 UTC by Omar Ayman