Skeletal muscles

Symptoms

Myotonia

Sustained muscle contraction (myotonia) is a distinctive aspect of myotonic dystrophy. The presence of myotonia is not the most disabling aspect of DM, but it is the recognized hallmark of the condition, and the aspect of the disease that distinguishes it from other forms of muscular dystrophy.

Myotonia stems from an abnormality of the muscle fiber membrane (sarcolemma) that results in an extended delay before muscles can relax after a contraction. A muscle starts its contraction on cue, but the electrical activity continues after the nerve signal has ended, causing a stiffness or "locking up" of the muscle.

Myotonia can be observed by having a patient grip tightly with the fingers. It may take the hand muscles 20 seconds or more to fully relax after a sustained grip (grip myotonia). Myotonia can also be demonstrated by tapping a muscle with a reflex hammer (percussion myotonia). Current research indicates that myotonia may be related to decreased chloride ion conduction across the sarcolemma.

Myotonia in DM1
• Most prominent in the forearm and finger muscles, causing grip lock • Sometimes affects tongue and jaw muscles, leading to difficulty with speech and chewing • Commonly worse in cold weather
Myotonia in DM2
• Affects finger grip muscles • Also noticeable in leg muscles, especially in thighs, and in the back and shoulders • Quick movements may trigger muscle stiffness (e.g. hitting a baseball and running to base; sprinting up stairs)

Muscle weakness and atrophy

Muscle weakness is the main cause of disability in myotonic dystrophy. The problem tends to affect some muscles more than others; it is common for certain muscles to be severely weak while others have normal strength. Muscle weakness often affects mobility, hand dexterity, and lifting. Serious problems in DM1, such as difficulty with breathing or swallowing, are caused by weakness of the muscles in the throat and chest.

Muscle weakness generally worsens over time, but the rate of deterioration is slow. The severity of muscle atrophy and weakness varies considerably among individuals with myotonic dystrophy, even among members of the same family. (See Patterns of Muscle Weakness in DM1, p.48) For some people the weakness is obvious in childhood, but for others it remains mild even into the 6th decade. Most people experience weakness on a spectrum between these two extremes.

For most people, noticeable increases in weakness occur year-to-year, or season-to-season. Weakness that accelerates more rapidly (i.e. week-by-week or month-by-month) is not typical in myotonic dystrophy. In these cases other explanations should be considered, such as medication side effects, or an illness unrelated

to myotonic dystrophy. Many people will experience extended periods when the condition seems to remain relatively stable.

Researchers still do not have a clear understanding of what causes muscles to become weak and atrophic in myotonic dystrophy. Although this is an area of active research, so far there are no treatments to prevent or slow muscle weakness. Assistive devices such as braces, canes, walkers, and wheelchairs can help individuals maintain independence and mobility.

Muscle pain

Myotonic dystrophy can be associated with pain. In some cases the pain originates inside the muscles. In other cases, the pain originates in the joints, ligaments, or spine. Muscle weakness may predispose individuals to arthritic changes or strain in these areas.

Patterns of Muscle Weakness in DM1

Congenital DM1
Prenatal • Lower than normal fetal movement • Buildup of fluid (edema) in fetus organs and tissues (hydrops fetalis) • Increased amniotic fluid in mother (polyhydramnios). Breech presentation, placental abruption, and umbilical cord prolapse may result.
Newborn • Severe muscle weakness in newborns • Substantial improvement in children who survive the first six months, often with delayed motor development in infancy and childhood • Development of symptoms that mimic adult onset DM1 in the later years
Childhood/Adolescence • Gradual improvement of newborn hypotonia and feeding issues (only rarely present at age 3-4 years) • Delayed gross motor skill development. Nearly all children learn to walk independently, although great variability exists as to when they achieve this milestone. • Delayed fine motor skill development: grasping a toy or finger; transferring a small object from hand to hand; pointing out objects; following movement with the eyes; self feeding • Myotonia is typically not present at birth, but typically begins in adolescence or early twenties. • Weakness in muscles (including the hands, feet, and face) that may interfere with mobility and necessitate the use of assistive devices (such as ankle braces or canes) • Lack of facial expression due to weakness of facial muscles • Muscle impairment in the mouth, palate and jaw that can delay speech development and inhibit proper pronunciation (may be exacerbated by hearing loss)
Adulthood • Gradual worsening of symptoms; symptomatic progression similar to that seen in adult onset DM1
Childhood Onset DM1

Childhood/Adolescence

- Normal or slightly delayed early motor development
- Facial and neck muscle problems, typically without the facial appearance that is associated with the congenital form
- Foot drop (lower leg, foot and ankle dorsiflexor weakness) leading to a characteristic high-stepping, toe-dragging, or shuffling gait that may result in an increased number of falls
- Weakness in distal muscle (including hands, feet, and face) that may interfere with mobility and necessitate the use of assistive devices (such as ankle braces and canes)
- Myotonia, particularly in hand intrinsic muscles (leading to difficulty relaxing grasp, especially in the cold) and the tongue (leading to slurred and slow speech, exacerbated by weakness of the facial muscles)
- Additional symptoms of adult onset myotonic dystrophy DM1 will appear in later years.

Adulthood

- Gradual worsening of symptoms; symptomatic progression similar to that seen in adult onset myotonic dystrophy DM1

Adult Onset DM1

Classic form

- Commonly starts in the teens, twenties, or thirties with myotonia of the hand grip.
- Symptoms progress to weakness of gripping or pinching with the fingers, or moving the ankles.
- Examination at this point usually shows weakness and wasting in the long finger flexors and weakness of the facial and neck flexor muscles.
- Typical effects of adult-onset DM1 include:
    - Weakness and atrophy of the jaw (masseter and temporalis) and facial muscles, leading to thinning of the facial contour and reduced facial expression
    - Indistinct speech and problems with articulation due to weakness of facial, tongue, and palatal muscles, and myotonia of the tongue
    - Drooping of the eyelids (ptosis) due to weakness of muscles levator palpebrae and Mueller muscle
    - Limitation of lateral and vertical eye movements due to weakness of the other ocular muscles
    - Weakness in distal muscles that interferes with dexterity, handwriting and mobility. The combination of finger weakness and myotonia is particularly challenging for jobs that require rapid, repeated, or forceful finger movements.
    - Characteristic high-stepping, toe-dragging, or shuffling gait due to difficulty lifting the toes and foot ("foot drop")
    - Difficulty jumping or rising up on the toes due to weakness of the calf muscles. When combined with foot drop, this can lead to instability of the ankles, difficulty standing still, and frequent falls.
    - Weakness of neck flexor muscles, causing difficulty raising head from pillow
    - Dropped head posture and difficulty holding head upright due to weakness in the neck extensor muscle
    - Shortness of breath due to weakness of the diaphragm and other breathing muscles. Breathing problems may occur during exercise but are most prevalent during sleep. It is important to identify weakness of the breathing muscles before attempting surgery.
    - Reduced muscle stretch reflexes
    - Decline in myotonia as muscle weakness increases

Mild form • Minor weakness and very mild myotonia that begins in a person's fifties, sixties, or seventies. This form of the condition can be so mild that a person never seeks medical attention, explaining how the disease may be inherited even if neither parent was known to be affected.
DM2
• Muscle symptoms in DM2 may begin in the teenage years, but more commonly symptoms develop in the twenties, thirties, forties, or fifties. The congenital and childhood-onset forms of the disease probably do not occur in DM2. • Initial symptoms may relate to grip myotonia. Alternatively, myotonia may be inconspicuous, and the initial symptoms may involve weakness of muscles around the hips or shoulders. • Common symptoms are difficulty standing up from a low chair, rising from the ground or a squatting position, or climbing stairs. Reaching up or working with the arms overhead also may be difficult. People with DM2 often experience unusual fatigue with exercise. • Muscle atrophy is present but less noticeable than in DM1 and occurs later in life. • Muscle pain in the neck, back, shoulders, hip flexors, and upper legs may be a prominent symptom. • Severity of pain can fluctuate from day to day.

Diagnosis

Neuromuscular assessment

Careful neurological and sometimes ophthalmological examination is the most important element in making a diagnosis of DM1. When the characteristic changes of myotonia and muscle weakness have occurred, the examination can provide strong evidence for DM1, and the physician can be reasonably confident of the diagnosis.

Checking for myotonia is not routine for most general physicians. Neuromuscular specialists generally check for this symptom either by having a person make a tight grip or using a percussion hammer to tap the muscles in the hand or forearm.

Delay in reaching a diagnosis is common because people with DM1 may not recognize the exact nature of their symptoms. Physicians in several specialties are often consulted before the diagnosis of DM1 is even considered. Congenital DM1 is more difficult to recognize because there can be multiple causes of weakness and hypotonia in newborns. DM2 can be difficult to differentiate from other types of late-onset muscular dystrophy, especially when the myotonia is not readily apparent and cataracts are not recognized. Other diagnostic procedures can be helpful in establishing a definitive diagnosis:

Electromyography (EMG)

A needle electrode placed in the muscle can record myotonic discharges. Extended bursts of electrical discharges in a saw tooth-like pattern are indicative of the abnormal electrical signals associated with slowing of muscle relaxation. This procedure shows myotonia in a high proportion of people with DM1 or DM2.

Muscle biopsy

Pathological features observed on muscle biopsy can strongly indicate the presence of DM but are not definitive in making the diagnosis. However, research techniques which can provide a highly accurate analysis are

becoming more widely used in non-research pathology laboratories. Muscle biopsies are performed less frequently in the diagnosis of DM1 because of increased availability of genetic testing.

Identifying DM2 can present a greater diagnostic challenge. Abnormal muscle biopsy results may be the initial indicator of the presence of DM2.

Serum CK concentration

The enzyme creatine kinase (CK) leaks into blood when muscle tissue is damaged. Serum CK concentration may be mildly elevated in individuals with DM1 with weakness, but is normal in asymptomatic individuals.

Other blood tests

Enzymes such as ALT or AST can leak into the blood when there is muscle damage. Tests for these substances are a routine part of a general physical to screen for liver health. If a muscle condition is not suspected, the presence of ALT or AST is attributed to liver damage rather than muscle abnormalities. This assumption can create confusion when DM2 is present.

Genetic testing

Confirmation of a DM1 or DM2 diagnosis can be achieved through molecular genetic testing. The presence of the characteristic genes indicates that the person has DM or is at risk for developing it; the absence of the mutations means the disease is not present.

Treatment

Weakness

There are currently no medications available that address myotonic dystrophy weakness. Symptomatic treatments include:

- Occupational therapy and physiotherapy
- Molded ankle supports and leg braces to reduce foot-drop and enhance gait stability
- Fitted collar to reduce the effects of neck muscle weakness
- Low-intensity exercise strength training, to the extent that individuals are capable and without undue physical or cardiac stress (see Patterns Of Cardiovascular System Problems, p. 52)

Pain

Conventional pain medications may be useful in treating the painful aspects of myotonic dystrophy.

Myotonia

Drugs affecting ion channels, such as mexiletine, can improve myotonia. Although additional testing of these medications is needed, it may be reasonable for people with moderate to severe DM or symptoms to consider use of these medications if the condition sufficiently interferes with the individual's daily activities. Potential side effects need to be carefully considered, however. Symptomatic relief may be achieved by using regular or heated gloves to keep hands warm in cold temperatures.

Future directions in treatment

A major focus of current research, including research supported by the Myotonic Dystrophy Foundation, is to clarify why muscles become weak, and find treatments that can prevent the onset of weakness or restore

strength to weakened muscles.

The pace of research progress has accelerated rapidly in the last decade. Researchers are focusing for the first time on correcting the chemical irregularities that exist in muscle cells of people with myotonic dystrophy. Although initial studies in this area are encouraging, it is difficult to predict when therapies may become available to patients. The Myotonic Dystrophy Foundation will make every effort to encourage these efforts and track their progress.