An overview of muscle diseases presenting in adulthood

Patients with muscle disease present not only to neurologists, but also to rheumatologists and general physicians. This article provides a framework of how to approach patients with suspected muscle disease, and reviews the clinical features of the most frequently encountered acquired and genetic conditions in adult practice.

A large number of individually rare acquired and genetic disorders can affect skeletal muscle. Patients present with muscle weakness, stiffness or pain, usually to a neurologist or rheumatologist, but general physicians frequently need to manage patients with neuromuscular ventilatory failure, dysphagia or rhabdomyolysis, or are confronted with an elevated creatine kinase (CK) level in otherwise asymptomatic patients. Approaching a patient with suspected muscle disease can seem daunting even to general neurologists. A 'surgical sieve' approach can be useful to conceptualise potential categories of disease (*Table 1*), while the three most helpful diagnostic features are speed of onset of symptoms, the pattern of muscle weakness (*Table 2*), and the level of plasma CK (*Table 3*). Taken together the clinician will be able to form an initial differential diagnosis and guide further investigations (*Figure 1*), which may include electromyography and muscle biopsy, but increasingly use non-invasive techniques, in particular muscle imaging and targeted genetic testing. This article provides a brief overview of the most common muscle diseases presenting in adulthood.

Table 1. Aetiological classification of muscle diseases

Acquired muscle diseases	Inflammatory myopathies	Dermatomyositis
		Myositis associated with connective tissue disease
		Polymyositis
		Necrotizing autoimmune myopathy
		Inclusion body myositis
	Toxic myopathies	
	Endocrine myopathies	
	Infective myopathies	
	Amyloid myopathy	
Genetic muscle diseases	Muscular dystrophies and congenital myopathies	The dystrophinopathies: Duchenne and Becker
		Myotonic dystrophy 1 and 2
		Facioscapulohumeral muscular dystrophy
		Limb girdle muscular dystrophy
		Myofibrillar myopathies
		Distal myopathies
		Oculopharyngeal muscular dystrophy
	Metabolic/inborn error of metabolism	Mitochondrial disease
		Glycogen metabolism disorders
		Fatty acid oxidation disorders
	Muscle channelopathies	

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Acute presentations

An acute or subacute syndrome of global or proximal weakness with or without muscle pain is a common consequence of severe electrolyte imbalance, in particular hypokalaemia, as well as drugs (statins, amiodarone) or toxins such as heroin. Toxic drug effects can develop in patients long established on a specific medication when new medications are introduced. An example would be the introduction of amlodipine or amiodarone in a patient already on simvastatin (Hylton and Ezekiel, 2010), which can enhance the myotoxic effects of simvastatin. While a primary muscular cause for weakness is often obvious, the differential diagnosis may include an acute motor-predominant neuropathy such as Guillain–Barré syndrome, or a spinal cord syndrome, which require exclusion by appropriate investigations.

The term rhabdomyolysis refers to an acute severe episode of muscle breakdown, leading to significant release of CK into the blood and associated myoglobinuria, often accompanied by abrupt severe myalgias and weakness. Drugs are the most important cause of rhabdomyolysis, but when no offending agent can be identified, other causes need to be considered (Zutt et al, 2014). Genetic mutations leading to inborn errors of carbohydrate or fatty acid metabolism can cause rhabdomyolysis, and there is frequently a prior history of exercise-induced

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muscle pain. This tends to occur early in exercise in disorders of carbohydrate metabolism such as McArdle's disease (McArdle, 1951; Quinlivan et al, 2010), or relatively late in exercise in fatty acid oxidation disorders such as carnitine palmitoyl-transferase II (CPT II) deficiency (Wieser et al, 2003). Exercise and heat (or fever) are common precipitants of rhabdomyolysis caused by mutations in the ryanodine receptor gene (RYR1), the gene also responsible for causing malignant hyperthermia (Dlamini et al, 2013).

Muscle biopsies performed acutely after rhabdomyolysis will often show necrosis of muscle fibres only, and may be best deferred. However, a biopsy may point to an underlying inflammatory disorder such as a myositis which requires a different treatment approach. A muscle biopsy can also be helpful in pointing towards a metabolic myopathy by showing absence of immunoreactivity for enzymes such as myophosphorylase in the case of McArdle's disease, or an increase in lipid content in fatty acid oxidation disorders. Direct genetic testing for mutations in the myophosphorylase gene (PYGM) in McArdle's disease or RYR1 can achieve a diagnosis, but can be hampered by the occurrence of 'private mutations' (a mutation only occurring in one family, which may be difficult to distinguish from a benign polymorphism). CPT II deficiency is best screened for by acylcarnitine profiles on blood.

Subacute presentations

The main considerations in this category are inflammatory myopathies (myositides) with symptoms evolving over weeks to months (Dalakas, 2015). Weakness is usually symmetrical and proximal (limb-girdle pattern), but there can be involvement of neck extensors, and respiratory and bulbar muscles, leading in severe cases to respiratory involvement and dysphagia. The serum CK level is almost always elevated in myositis, and can be used as a biomarker of disease activity in individual patients. The acute nature of muscle fibre necrosis is reflected in the electromyography findings which, in addition to 'myopathic' motor units and recruitment pattern, often show an increase in spontaneous activity with fibrillations and positive sharp waves.

In addition to muscle involvement, there is a spectrum of autoimmunity and there may be accompanying skin, gut, lung and heart involvement, as well as underlying malignancy in a proportion of cases.

There is no universal agreement on how to classify myositis and how much weight to put on clinical features, muscle biopsy findings and auto-antibody profiles. The main types of myositis are dermatomyositis, polymyositis and immune-mediated necrotizing myopathy (also termed necrotizing autoimmune myopathy) (Stenzel et al, 2012). Inclusion body myositis is frequently included under the heading of inflammatory myopathies, but usually presents more insidiously and will be discussed in the section on slowly progressive myopathies.

Dermatomyositis is characterized by a number of skin changes including the classical heliotrope rash of the eyelids, an erythematous rash predominantly on sun-exposed areas, dilated nail fold capillaries, roughening of the palmar surface of the hands ('mechanic's hands') and subcutaneous calcification (Johnson et al, 2015). Confusingly, dermatomyositis can on occasion present with skin changes only (dermatomyositis sine myositis). Even less intuitive is the diagnosis of dermatomyositis without skin changes presenting as an isolated muscle disease, when specified as a pathological entity with specific changes on muscle biopsy, in particular peri-fascicular atrophy.

Table 2. Common patterns of muscle disease

Pattern of muscle weakness	Example
Limb girdle weakness	Endocrine and toxic myopathies
	Inflammatory myopathies
	Many muscular dystrophies
Prominent distal weakness	Distal myopathies
	Myotonic dystrophy
	Inclusion body myositis (finger flexors, quadriceps)
	Myofibrillar myopathies
Scapuloperoneal pattern	Facioscapulohumeral muscular dystrophy
	Emery–Dreifuss muscular dystrophy
	Some limb-girdle muscular dystrophies
	Acid maltase deficiency
Extraocular muscle weakness	Oculopharyngeal muscular dystrophy
	Mitochondrial myopathy (chronic progressive external ophthalmoplegia)
Neck extensor weakness	Isolated neck extensor myopathy
	Hyperthyroid or hyperparathyroid myopathy
	Inflammatory myopathies

Table 3. Creatine kinase levels as a guide to myopathies

Creatine kinase level	Example
Normal or minimally elevated	Steroid myopathy
	Facioscapulohumeral muscular dystrophy
	Inclusion body myositis
	Myotonic dystrophy
	Limb girdle muscular dystrophy 1A, 1B
	Myofibrillar myopathies
Significantly elevated	Dermatomyositis, polymyositis, necrotizing autoimmune myopathy
	Dystrophinopathies (Duchenne/Becker)
	Limb girdle muscular dystrophy 2A, 2B, 2I, 2L

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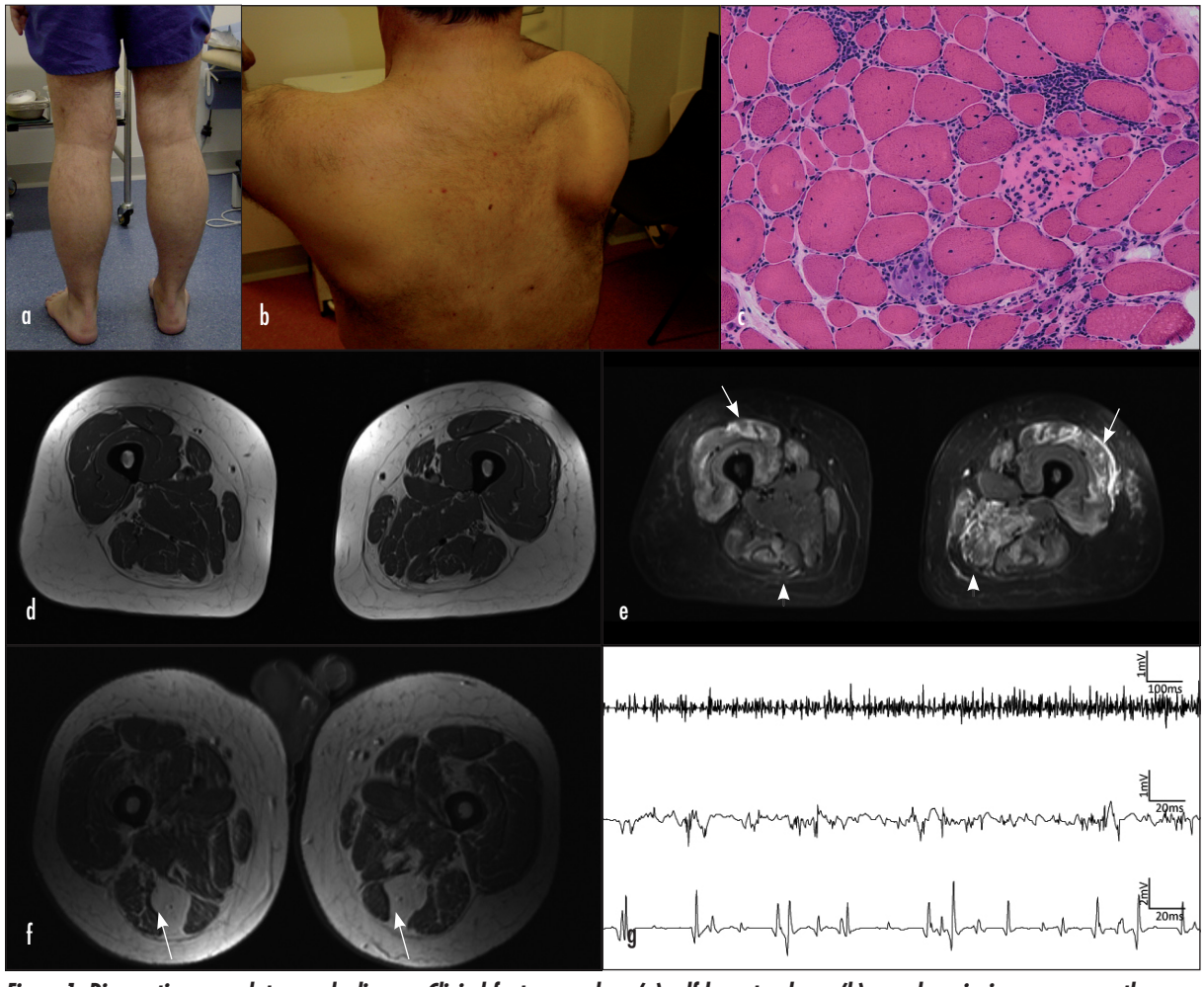

Figure 1. Diagnostic approach to muscle disease. Clinical features such as (a) calf hypertrophy or (b) scapular winging can narrow the differential diagnosis. c. Muscle biopsy showing focal endomysial inflammation, a pale necrotic fibre and a basophilic regenerating fibre, marked variation in fibre size, and increased internalized myonuclei suggestive of an inflammatory myositis. Non-invasive techniques such as muscle magnetic resonance imaging are increasingly used. d. Axial magnetic resonance imaging of the thighs showing normal muscle bulk on T1-weighted images but (e) high signal indicating oedema affecting the quadriceps (arrows) and hamstring muscles (arrowheads) on T2-weighted images with fat suppression in a case of myositis with anti-SRP antibodies. f. Complete fatty replacement of the semitendinosus muscles (arrows) in titinopathy as an example of selective muscle involvement detectable on magnetic resonance imaging. g. Three electromyography traces showing myopathic early full recruitment (top row), low amplitude short duration polyphasic myopathic motor units (middle) and normal motor units (bottom) for comparison.

Polymyositis is now considered a rare disorder presenting with proximal muscle weakness without skin changes, but with inflammatory changes on biopsy. More frequent is an 'overlap syndrome' of myositis occurring together with other clinical or serological features of a connective tissue disorder such as systemic sclerosis or mixed connective tissue disease.

Immune-mediated necrotizing myopathy presents with weakness which can be severe, high CK levels and myalgia evolving over weeks. As opposed to dermatomyositis or polymyositis, the muscle biopsy shows no prominent inflammatory infiltrates, but necrosis and MHC I upregulation (Stenzel et al, 2012; Allenbach and Benveniste, 2013).

Increasingly the classification of myositis is refined by the use of antibody panels (Casciola-Rosen and Mammen, 2012). Antibodies are either myositis-specific or myositis-associated. Myositis-specific antibodies or myositis-associated antibodies are present in about 80% of myositides. If present, they may help to define a relatively homogeneous syndrome and thus help to guide prognosis. For example, anti-Jo-1 antibodies, which are directed against histidyl-tRNA synthetase, are strongly associated with the so-called anti-synthetase syndrome consisting of myositis together with a specific skin manifestation (mechanic's hands), Raynaud's phenomenon, seronegative arthritis and a high incidence of interstitial lung disease. Anti-Mi2 antibodies occur in more typical dermatomyositis. Immune-mediated necrotizing myopathy is associated with anti-SRP and anti-HMGCR antibodies. The presence of anti-NXP2 or anti-TIF-1γ indicates a high risk of cancer.

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It is important not to make the diagnosis of myositis on the basis of inflammatory infiltrates on muscle biopsy alone, but to take into account the entire clinical picture. Inflammation on biopsy can also be prominent in some of the genetic myopathies such as the dystrophinopathies or facioscapulohumeral muscular dystrophy (see below) (Hilton-Jones, 2014).

Chronic and slowly progressive muscle disorders

A large number of individually very rare inherited disorders can present in adulthood with slowly progressive muscle weakness evolving over months or years. Among the more frequently encountered conditions are inclusion body myositis and some genetically determined myopathies including muscular dystrophies, myofibrillar myopathies and late onset metabolic myopathies. As a group, the late onset disorders are less likely to present with symmetrical limb-girdle weakness, but frequently have a selective pattern of muscle involvement that helps to narrow the initial differential diagnosis (*Table 2*).

The dystrophinopathies

The dystrophinopathies (Duchenne and Becker muscular dystrophy) are X-linked disorders caused by inherited or de novo mutations in the gene encoding the large sarcolemmal cytoskeletal protein dystrophin. Duchenne muscular dystrophy is the commonest inherited disease of childhood, leading to progressive pelvic and shoulder girdle weakness with onset by the age of 3–5 years and subsequent ventilatory failure and cardiomyopathy (Bushby et al, 2010). Becker muscular dystrophy is a milder form of dystrophinopathy usually presenting with a similar pattern of weakness in teenage years, but the onset can be delayed into adulthood (Bushby and Gardner-Medwin, 1993). Patients may present with exercise-induced pain before weakness, or with an isolated raised CK level. Cardiomyopathy is common, and may be fatal (Finsterer and Cripe, 2014). Female carriers are usually asymptomatic, but may have a raised CK level, isolated cardiomyopathy or mild limb-girdle weakness, presumably as a result of skewed X-inactivation.

Myotonic dystrophy type 1

Myotonic dystrophy is the most common adult onset muscular dystrophy (Turner and Hilton-Jones, 2014). It is caused by a triplet (CTG) repeat expansion in the DMPK gene, which can get larger in subsequent generations as a result of genetic instability, and lead to the clinical phenomenon of anticipation (worsening disease severity and earlier onset in successive generations) (Brook et al, 1992).

Myotonic dystrophy is a multisystem disease that affects not only skeletal muscle, but also the brain, eyes, heart and pancreas. Adult-onset myotonic dystrophy is often classed as a distal myopathy, but weakness has a characteristic distribution. Often, there is atrophy of the temporalis muscle and a degree of facial weakness. Ptosis occurs, but extraocular muscles are spared. Neck flexion is weak, and there may be weakness of finger flexion and small hand muscles. More generalized weakness occurs with disease progression. In addition to weakness the inability to relax muscles after contraction (myotonia) is elicitable by percussion of muscles or evident by a slowly releasing hand grip. Gastrointestinal involvement can lead to dysphagia secondary to oesophageal dysmotility, and gastroparesis. Cardiac involvement with either heart block or ventricular tachyarrhythmias, as well as respiratory muscle weakness, occur frequently and contribute significantly to an increased mortality, with a mean age of death of 54 years in one study. Insulin resistance leads to diabetes. Cataracts are common. There may be hypotestosteronism and male pattern baldness. CNS involvement with white matter changes, executive dysfunction and profound apathy can be noted. Excessive daytime sleepiness is common and may be the result of respiratory muscle weakness or centrally generated.

Facioscapulohumeral dystrophy

Facioscapulohumeral dystrophy is the second most common muscular dystrophy in adults (van der Maarel et al, 2007). It is inherited in an autosomal dominant fashion, but the underlying molecular genetic basis is complex. It is thought that incomplete suppression of the DUX4 gene in skeletal muscle leads to the facioscapulohumeral dystrophy phenotype (Ferri et al, 2015). This in turn is caused by a combination of a permissive genotype and contraction of a long tandem repeat sequence called D4Z4, allowing genetic diagnosis using a restriction enzyme digest assay.

Facioscapulohumeral dystrophy has a wide range of age of onset and clinical severity. Characteristically, weakness affects the face and periscapular muscles leading to scapular winging. The deltoid and forearm muscles are spared, but pectoralis, biceps and triceps are affected in the upper limbs. Abdominal muscles and anterior compartment leg muscle weakness including quadriceps and ankle dorsiflexors occurs. Weakness is often strikingly asymmetrical. Cardiac, respiratory or extramuscular involvement is rare in adult onset cases, but pain is very common. The CK level is usually only mildly elevated.

Sporadic inclusion body myositis

Sporadic inclusion body myositis is the most common primary muscle disease presenting in mid to late adulthood. It is often discussed in the context of other idiopathic myositides because of the presence of inflammatory changes on biopsy, but there is debate as to whether it is really a degenerative process with secondary inflammatory changes (Benveniste et al, 2015). It is exceptional to find more than a transient response to immunosuppression, and the time course is much slower than that of other inflammatory myopathies.

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The pattern of weakness is so distinctive that some muscle experts are confident about establishing a diagnosis on clinical grounds alone (Brady et al, 2013). In a typical case there is progressive weakness and wasting of the deep forearm flexors and the quadriceps. This leads to grip weakness, and early in the disease patients have difficulty in rising from a chair despite being able to walk. At later stages more widespread weakness including the facial and bulbar muscles, paraspinals and ankle dorsiflexors is seen. The serum CK level can be normal or mildly elevated. Electromyography can be confusing in showing mixed myopathic and neurogenic features. In a proportion of cases there is an associated connective tissue disorder such as Sjögren's syndrome. Anti-cN1A (cytosolic 5'-nucleotidase 1A) antibodies are thought to be about 70% sensitive and 90% specific (Larman et al, 2013; Machado et al, 2013), but should not be used in isolation to reach a diagnosis, and are not yet routinely available. A muscle biopsy is still performed in the majority of cases with suspected sporadic inclusion body myositis. Typically it shows a number of inflammatory changes (endomysial infiltration with CD8+ T-cells, mononuclear cell infiltrate of non-necrotic muscle fibres, upregulation of major histocompatibility complex I and II antigens) as well as 'degenerative' protein aggregates positive for p62, TDP-43 and ubiquitin, rimmed vacuoles and cytochrome oxidase-negative muscle fibres.

Limb-girdle muscular dystrophies

The limb-girdle muscular dystrophies are a heterogeneous group of autosomal dominant (LGMD1) or recessive (LGMD2) disorders presenting with variable patterns of weakness, myalgia, contractures, muscle hypertrophy and cardiac and respiratory involvement, and variable levels of CK from normal to highly elevated. While not uncommon as a group (limb-girdle muscular dystrophies made up about 6% of genetic muscle disease in a large clinic-based epidemiological study in north east England; Norwood et al, 2009), there are more than 30 known genes causing limb-girdle muscular dystrophies (Nigro and Savarese, 2014), so that individual disorders are rare.

Generally the recessive forms are more common, and the commonest sub-type in the UK is LGMD type 2A, caused by mutations in the calpain-3 gene. This can present from infancy to late adulthood. Frequently, there is marked involvement of the posterior leg muscles together with a degree of scapular winging. The CK level is always high, usually more than 10 times of the upper limit of normal. Cardiac and respiratory involvement is rare in this subtype, but often occurs in other forms of limb-girdle muscular dystrophy. Some of the recessive forms of limb-girdle muscular dystrophy are caused by mutations in various genes related to the dystrophin-associated glycoprotein complex including the sarcoglycans, and alpha dystroglycan glycosylation, and can resemble the much commoner dystrophinopathies with calf hypertrophy and cardiac and respiratory muscle involvement.

Adult onset metabolic myopathies

Disorders of carbohydrate and fatty acid metabolism, as well as mitochondrial disorders, can present with a slowly progressive myopathy in addition to the more acute presentations with exercise-induced muscle pain or rhabdomyolysis described above. Mitochondrial diseases are multisystem disorders than can affect most organs (Taylor and Turnbull, 2005). Neurological involvement is common. A mitochondrial myopathy, if present, can be overshadowed by other manifestations such as seizures or psychomotor retardation, but can on occasion be the sole or predominant manifestation of a mitochondrial disorder, presenting with muscle pain, exercise intolerance and/or weakness, usually in a limb-girdle pattern. Clinical clues to a mitochondrial disorder are short stature, deafness, optic atrophy, ptosis, external ophthalmoplegia, diabetes and unexplained multisystem involvement. Typical muscle biopsy findings include ragged red fibres and COX negative fibres. Mitochondrial genetics are complex and beyond the scope of this article, but it is important to note that while mitochondrial genes are inherited maternally, mutations in nuclear genes that in turn encode proteins involved in mitochondrial DNA handling, such as POLG, can lead to mitochondrial disease. The inheritance pattern can therefore be autosomal dominant and recessive, or maternal, in addition to sporadic cases.

Pompe's disease (acid maltase deficiency), a recessive disorder caused by lysosomal alpha-glucosidase deficiency, can present in the third or fourth decade, or on occasion even later (Kishnani et al, 2006; Wens et al, 2013). Weakness is usually in a limb-girdle pattern, but may be scapuloperoneal. There may be some facial weakness, and ptosis. Respiratory involvement is not invariable but may be the presenting feature. The serum CK level can be normal. Alpha-glucosidase activity assays can be used for screening.

Muscle weakness can accompany a number of systemic disorders. It is always worth checking a patient's thyroid function (Mistry et al, 2009). Hyperthyroidism can lead to a proximal myopathy with muscle wasting and a normal CK level, while hypothyroidism more commonly presents with myalgia, high CK level and a degree of proximal weakness. A steroid myopathy can occur as consequence of Cushing's disease, but is much more commonly the result of steroid treatment (Schakman et al, 2008). Doses of 40 mg or more of daily prednisolone for several months, but probably also smaller doses of longer duration, predispose to the development of a steroid myopathy characterized by painless proximal muscle weakness particularly involving the pelvic girdle and quadriceps. The CK level is normal, and muscle biopsy shows type 2 fibre atrophy.

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Table 4. Cardiac and respiratory involvement in common muscle diseases

Muscle disorder	Cardiac involvement	Respiratory involvement
Dermatomyositis/polymyositis	Arrhythmia and cardiomyopathy can rarely occur (more likely with anti-SRP and some myositis-associated antibodies such as anti-mitochondrial antibodies)	Yes (neuromuscular and interstitial lung disease). Interstitial lung disease more likely with anti-synthetase, -MDA5 -Ku,-PM Scl antibodies
Inclusion body myositis	No	No
Becker	Yes, cardiomyopathy and/or arrhythmia, can present with cardiomyopathy only	Uncommon
Myotonic dystrophy	Yes, arrhythmias (atrioventricular block, ventricular tachycardia)	Yes
Facioscapulohumeral muscular dystrophy	No	Uncommon
Limb-girdle muscular dystrophies	Yes, depending on type	Yes, depending on type
Acid maltase deficiency (Pompe's disease)	Uncommon in adult onset form	Can be presenting symptom in up to 30%

Overview of management

Inflammatory myopathies, with the exception of inclusion body myositis, are treated with immunosuppression. Prednisolone 1 mg/kg is commonly used to induce remission and slowly tapered after several weeks or months. Secondary immunosuppressants such as methotrexate or azathioprine may be needed in case of relapse or insufficient response to steroids. If elevated, the CK level is a good guide to monitor treatment together with clinical symptomatology.

Physiotherapy and exercise are probably beneficial in inflammatory myopathies, and physiotherapy and occupational therapy are crucial in the assessment and support of patients with chronic muscle disease. This includes advice on exercise and posture, fitting of ankle foot orthoses, wheelchair assessment and use of appliances such as upper limb supports.

It is important to anticipate cardiac and respiratory complications of muscle disease (*Table 4*) (Norwood et al, 2007). If the specific diagnosis is uncertain, the authors would advocate erring on the side of caution and screening for cardiac involvement with electrocardiography and echocardiogram, and respiratory involvement with vital capacity measurements.

Speech and language therapists will be able to assess swallow function and advise on the need for feeding tube placement. Occasionally, dysphagia may respond to surgical intervention such as myotomy of the upper oesophageal sphincter in oculopharyngeal muscular dystrophy.

Conclusions

While individual muscle diseases are rare and can be difficult to diagnose, an initial approach taking into account the time course of the history, the pattern of muscle involvement, and the serum CK level can go a long way to establishing a differential diagnosis. Respiratory failure can accompany many muscle disorders and in some can occur while the patient is ambulant. Vital capacity should be used to screen for respiratory muscle weakness. Cardiac involvement can lead to either arrhythmias or cardiomyopathy, and screening with electrocardiography and echocardiogram should be performed if there is any doubt. BJHM

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Allenbach Y, Benveniste O (2013) Acquired necrotizing myopathies. *Curr Opin Neurol* **26**: 554–60 (doi: 10.1097/WCO.0b013e328364e9d9)

Benveniste O, Stenzel W, Hilton-Jones D, Sandri M, Boyer O, Van Engelen BG (2015) Amyloid deposits and inflammatory infiltrates in sporadic inclusion body myositis: the inflammatory egg comes before the degenerative chicken. *Acta Neuropathol* **129**: 611–24 (doi: 10.1007/s00401-015-1384-5)

Brady S, Squier W, Hilton-Jones D (2013) Clinical assessment determines the diagnosis of inclusion body myositis independently of pathological features. *J Neurol Neurosurg Psychiatry* **84**: 1240–6 (doi: 10.1136/jnnp-2013-305690)

Brook JD, McCurrach ME, Harley HG et al (1992) Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member. *Cell* **68**: 799–808

Bushby KM, Gardner-Medwin D (1993) The clinical, genetic and dystrophin characteristics of Becker muscular dystrophy. I. Natural history. *J Neurol* **240**: 98–104

Bushby K, Finkel R, Birnkrant DJ et al (2010) Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis,

KEY POINTS

- Rhabdomyolysis is commonly caused by drugs or toxins, but inherited causes should be considered if it is recurrent or there is a history of exercise-induced myalgia.
- Muscle weakness of subacute onset with a raised creatine kinase level suggests myositis.
- Genetic myopathies present with slowly progressive weakness that can be proximal, distal or show selective muscle involvement.
- Consider the possibility of cardiac or respiratory involvement in any patient with muscle disease.

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and pharmacological and psychosocial management. *Lancet Neurol* **9**: 77–93 (doi: 10.1016/s1474-4422(09)70271-6)
Casciola-Rosen L, Mammen AL (2012) Myositis autoantibodies. *Curr Opin Rheumatol* **24**: 602–8 (doi: 10.1097/BOR.0b013e328358bd85)
Dalakas MC (2015) Inflammatory muscle diseases. *N Engl J Med* **372**: 1734–47 (doi: 10.1056/NEJMra1402225)
Dlamini N, Voermans NC, Lillis S et al (2013) Mutations in RYR1 are a common cause of exertional myalgia and rhabdomyolysis. *Neuromuscul Disord* **23**: 540–8 (doi: 10.1016/j.nmd.2013.03.008)
Ferri G, Huichalaf CH, Caccia R, Gabellini D (2015) Direct interplay between two candidate genes in FSHD muscular dystrophy. Hum *Mol Genet* **24**: 1256–66 (doi: 10.1093/hmg/ddu536)
Finsterer J, Cripe L (2014) Treatment of dystrophin cardiomyopathies. *Nat Rev Cardiol* **11**: 168–79 (doi: 10.1038/nrcardio.2013.213)
Hilton-Jones D (2014) Myositis mimics: how to recognize them. *Curr Opin Rheumatol* **26**: 663–70 (doi: 10.1097/bor.0000000000000101)
Hylton AC, Ezekiel TO (2010) Rhabdomyolysis in a patient receiving ranolazine and simvastatin. *Am J Health Syst Pharm* **67**: 1829–31 (doi: 10.2146/ajhp090299)
Johnson NE, Arnold WD, Hebert D et al (2015) Disease course and therapeutic approach in dermatomyositis: A four-center retrospective study of 100 patients. *Neuromuscul Disord* **68**(21): 1829–31 (doi: 10.1016/j.nmd.2015.04.013)
Kishnani PS, Steiner RD, Bali D et al (2006) Pompe disease diagnosis and management guideline. *Genet Med* **8**: 267–88 (doi: 10.109701.gim.0000218152.87434.f3)
Larman HB, Salajegheh M, Nazareno R et al (2013) Cytosolic 5'-nucleotidase 1A autoimmunity in sporadic inclusion body myositis. *Ann Neurol* **73**: 408–18 (doi: 10.1002/ana.23840)
Machado P, Brady S, Hanna MG (2013) Update in inclusion body myositis. *Curr Opin Rheumatol* **25**: 763–71 (doi: 10.1097/01.bor.0000434671.77891.9a)
McArdle AB (1951) Myopathy due to a defect in muscle glycogen breakdown. *Clin Sci* **10**: 13–35
Mistry N, Wass J, Turner MR (2009) When to consider thyroid dysfunction in the neurology clinic. *Pract Neurol* **9**: 145–56 (doi: 10.1136/jnnp.2008.167163)
Nigro V, Savarese M (2014) Genetic basis of limb-girdle muscular dystrophies: the 2014 update. *Acta Myol* **33**: 1–12
Norwood F, De Visser M, Eymard B, Lochmuller H, Bushby K (2007) EFNS guideline on diagnosis and management of limb girdle muscular dystrophies. *Eur J Neurol* **14**: 1305–12 (doi: 10.1111/j.1468-1331.2007.01979.x)
Norwood FL, Harling C, Chinnery PF, Eagle M, Bushby K, Straub V (2009) Prevalence of genetic muscle disease in Northern England: in-depth analysis of a muscle clinic population. *Brain* **132**: 3175–86 (doi: 10.1093/brain/awp236)
Quinlivan R, Buckley J, James M et al (2010) McArdle disease: a clinical review. *J Neurol Neurosurg Psychiatry* **81**: 1182–8 (doi: 10.1136/jnnp.2009.195040)
Schakman O, Gilson H, Thissen JP (2008) Mechanisms of glucocorticoid-induced myopathy. *J Endocrinol* **197**: 1–10 (doi: 10.1677/joe-07-0606)
Stenzel W, Goebel HH, Aronica E (2012) Review: immune-mediated necrotizing myopathies--a heterogeneous group of diseases with specific myopathological features. *Neuropathol Appl Neurobiol* **38**: 632–46 (doi: 10.1111/j.1365-2990.2012.01302.x)
Taylor RW, Turnbull DM (2005) Mitochondrial DNA mutations in human disease. *Nat Rev Genet* **6**: 389–402 (doi: 10.1038/nrg1606)
Turner C, Hilton-Jones D (2014) Myotonic dystrophy: diagnosis, management and new therapies. *Curr Opin Neurol* **27**: 599–606 (doi: 10.1097/wco.0000000000000128)
van der Maarel SM, Frants RR, Padberg GW (2007) Facioscapulohumeral muscular dystrophy. *Biochim Biophys Acta* **1772**: 186–94 (doi: 10.1016/j.bbadis.2006.05.009)
Wens SC, Van Gelder CM, Kruijshaar ME et al (2013) Phenotypical variation within 22 families with Pompe disease. *Orphanet J Rare Dis* **8**: 182 (doi: 10.1186/1750-1172-8-182)
Wieser T, Deschauer M, Olek K, Hermann T, Zierz S (2003) Carnitine palmitoyltransferase II deficiency: molecular and biochemical analysis of 32 patients. *Neurology* **60**: 1351–3
Zutt R, Van Der Kooi AJ, Linthorst GE, Wanders RJ, De Visser M (2014) Rhabdomyolysis: review of the literature. *Neuromuscul Disord* **24**: 651–9 (doi: 10.1016/j.nmd.2014.05.005)

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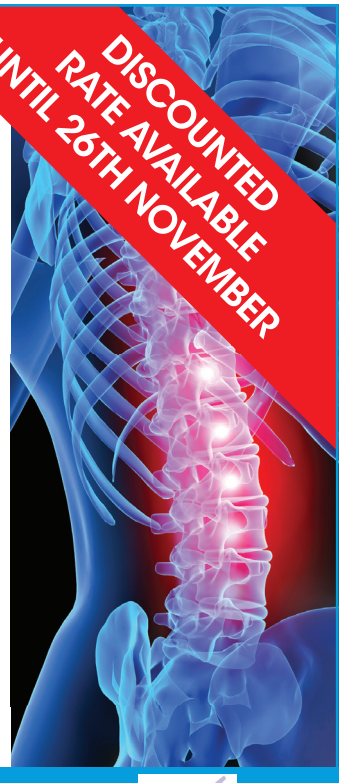

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