Muscle pain and cramps

When do muscle pain and cramps indicate a serious underlying muscle or systemic disorder? The tips in this article will aid in appropriate diagnosis and investigation.

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Muscle pain and cramping are almost invariably experienced by each of us at some point in our lives, and they constitute a frequent complaint in clinical practice. Generally, only when these symptoms are diffuse, frequent or persistent is a thorough clinical evaluation needed to establish whether the cause is benign or whether they may reflect a specific identifiable disorder. However, despite specialised investigations and a thorough clinical appraisal, the cause of muscle pain and/or cramps may remain elusive.

Mechanisms of muscle cramps and pain

Muscle cramps

It is important to ensure that what is being called a cramp by the patient is in fact a true cramp. Local pain in the calf may be due to other causes, such as intermittent vascular or neurogenic claudication in an elderly person or a stress fracture in a young athlete. Other possible causes of 'cramping' or muscle twitches are listed in the Table.

Typical muscle cramps consist of a sudden painful involuntary contraction of a muscle or group of muscles lasting from seconds up to a few minutes. Cramps arise from the anterior horn cell in the spinal cord, and electromyography during the cramp discharge reveals normal motor units firing rapidly.

The term 'benign cramp' is reserved for cramp in patients without identifiable underlying neurological disease. Typically, benign cramps occur most frequently at night and affect the calf or foot muscles, but they may also occur in exercising muscles, particularly during a forceful contraction of the muscle when it is in a shortened state. Benign cramps are also common during pregnancy and in the elderly. They may be associated with an electrolyte imbalance such as hyponatraemia.

Cramps can be followed by significant local pain for a few days. The pain is due to focal necrosis of muscle, associated with an elevated serum creatine kinase level.

In some patients (especially middle-aged men), chronic generalised cramping can be an isolated and disabling symptom with no clear cause despite extensive investigation. In contrast, frequent or diffuse cramping may be a feature of an underlying disorder such as motor neuron disease, and the associated clinical findings separate it from benign cramps.

Muscle pain

Muscle pain is commonly encountered in clinical practice. All of us are familiar with restricted muscle soreness, peaking a day or two after unaccustomed exercise, or the transient muscle

IN SUMMARY

- **Generally, only when the muscle cramps or pain are diffuse, frequent or persistent is a thorough clinical evaluation needed to establish whether the cause is benign or a specific identifiable disorder.**
- **The distribution of the pain and its relationship to exercise can aid diagnosis.**
- **Pain that is restricted to one limb or to a region is likely to have a local cause or be locally referred.**
- **Persistent 'whole body pain' from 'head to foot' is usually psychogenic.**
- **Ask about medications being take by the patient, and whether there is any family history of muscle pain or other neuromuscular disorder.**
- **Look for any associated symptoms to suggest a systemic or endocrine disturbance.**
- **Define and treat the specific cause when possible.**

pain that can accompany certain viral infections, especially influenza and coxsackie virus infections. However, muscle pain may be due to specific muscle disease or associated with serious general medical disorders.

Like visceral pain, muscle pain is a poorly localised discomfort. Muscle pain receptors are free nerve endings within the muscle, tendon, blood vessel walls and connective tissue that respond to chemical (bradykinin, histamine, prostaglandin, acid, excess potassium ions, serotonin and proteolytic enzymes), mechanical or thermal insults. Small diameter myelinated and nonmyelinated fibres transmit the pain via the dorsal roots and horn of the spinal cord ultimately to central pain pathways in the brain. The brain exerts an inhibitory influence on the input to the spinal cord from these pain receptors in muscle.

Aids in diagnosis

Diagnostic tests that may be required are listed in the box on page 22. The selection of tests will depend on what is revealed by a thorough history and examination.

Evaluating muscle cramps and twitches

A careful description by the patient or the doctor witnessing the abnormal muscle movement – combined with a thorough history and neurological examination – usually achieves the correct diagnosis. Electromyography is often diagnostic, and it enables differentiation between the various forms of muscle twitches (see the Table).

Evaluating muscle pain

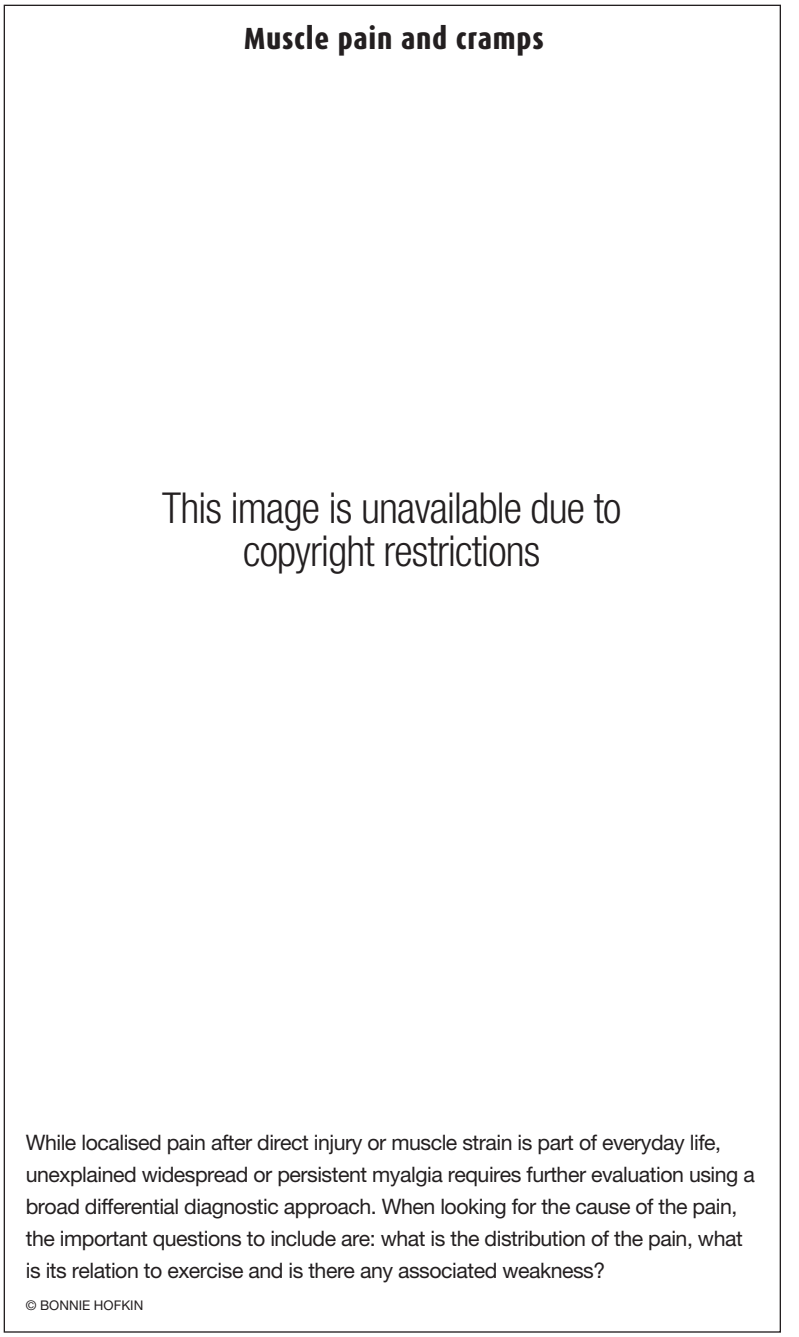
Muscle pain can vary from trivial discomfort to a severe debilitating experience. Very localised pain after direct injury or muscle strain is part of everyday life; whereas unexplained widespread or persistent myalgia requires further evaluation using a broad differential diagnostic approach.

Muscle pain may be the presenting feature of:

- systemic illness (vasculitis, sarcoidosis)
- endocrinopathy (hypothyroidism, osteomalacia)
- rheumatological disorder (polymyalgia rheumatica, systemic lupus erythematosus)
- intrinsic myopathies (inflammatory, metabolic and some mitochondrial myopathies)
- psychiatric malady (depressive equivalents)
- problems with poorly understood aetiology (chronic fatigue syndrome, primary fibromyalgia).

Hence the first step in effective treatment is to establish a precise aetiological diagnosis if possible, keeping in mind the spectrum of possible explanations.

Muscle pain and cramps



While localised pain after direct injury or muscle strain is part of everyday life, unexplained widespread or persistent myalgia requires further evaluation using a broad differential diagnostic approach. When looking for the cause of the pain, the important questions to include are: what is the distribution of the pain, what is its relation to exercise and is there any associated weakness?

A thorough clinical evaluation and generally systematic attention to the following seven questions will lead to a confident broad clinical diagnosis and can often uncover the aetiological basis of the myalgia:

1. What is the distribution of myalgia?
2. What is the relation of pain to exercise?
3. Does the patient have associated weakness?
4. Are there any associated symptoms to suggest a systemic or endocrine disturbance or is the patient taking any medications that may be relevant?
5. Are there any abnormalities on the investigation that support the diagnosis of a myopathy?
6. Is the muscle pain an isolated symptom or part of a spectrum of symptoms that suggest primary fibromyalgia or chronic fatigue syndrome?
7. Is there a family history of muscle pain or other neuromuscular disorder?

What is the distribution of myalgia?

Pain that is restricted to one limb or to a region is likely to have a local cause or be locally referred. Idiopathic inflammatory myopathies (polymyositis, dermatomyositis, inclusion body myositis) are uncommonly associated with muscle pain, but if pain is present it is usually in a similar distribution to weakness. Typically, in metabolic myopathies (e.g. McArdle's disease) pain is reproducibly linked to exercise and affects the exercising muscles. In rheumatological disorders, the emphasis of pain is usually in joints or periarticular tissues rather than muscle. Polymyalgia rheumatica has an emphasis around the axial spine and limb girdle, with symptoms most prominent in the morning.

In primary fibromyalgia, pain is usually unremitting and widespread, with characteristic fibrositic tender points that aid diagnosis. In some general medical problems (hypothyroidism, systemic vasculitis), myalgia may also be widespread. Persistent 'whole body pain' from 'head to foot' is usually psychogenic.

What is the relation of pain to exercise?

If inflammatory myopathies are associated with myalgia, it is usually not significantly influenced by exercise. In dramatic contrast, disorders of glycogenolysis (e.g. McArdle's disease) and glycolysis (e.g. phosphofructokinase deficiency) are associated with severe, disabling pain in the exercising muscles, which precludes further exercise and may be associated with severe 'cramps'. There is characteristically no inter-exercise myalgia. The very painful cramps during exercise are more correctly contractures due to the energy crisis induced by muscular work. If the person rests immediately, pain may settle within a few minutes. If the person persists in exercising, severe pain may continue for days secondary to rhabdomyolysis.

Disorders of lipid beta-oxidation can be associated with severe myalgia during or after prolonged exercise. In addition, infection or intercurrent illness can precipitate an episode of severe myalgia with rhabdomyolysis, with relatively few symptoms between events (e.g. carnitine

Suggested diagnostic tests

Blood tests

- Useful blood tests are: muscle enzymes (creatine kinase, aldolase); erythrocyte sedimentation rate; full blood examination (neutrophil, lymphocyte, eosinophil count); resting serum lactate; thyroid function tests; serum urea, creatinine and electrolytes (including potassium, magnesium and phosphate); serum angiotensin converting enzyme; rheumatoid factor; antinuclear antibody; double-stranded DNA antibodies; and antibodies to extractable nuclear antigens.
- Normal creatine kinase levels do not exclude an indolent inflammatory myopathy.
- Other medical or endocrine investigations may be indicated by the patient's history and general medical and neuromuscular examination.

Electromyography

- Electromyography results are usually abnormal in myopathies. Fibrillation potentials may indicate active segmental necrosis of muscle fibres. In a very indolent myopathy, abnormalities may be very subtle or undetectable.

Ischaemic forearm testing

- The ischaemic forearm exercise test is useful in the diagnosis of metabolic myopathies due to abnormalities in carbohydrate metabolism or myoadenylate deaminase deficiency.
- The forearm muscles are exercised for one minute under ischaemic conditions (with a blood pressure cuff on the upper arm above systolic blood pressure). Serial blood samples for serum ammonia and lactate are taken at baseline and for 20 minutes after the exercise.
- The test must be performed according to protocol by an experienced practitioner.

Muscle biopsy

- Diagnosis may require a biopsy for specific histochemistry and/or biochemical studies. These studies must be done in a specialised centre.
- One major diagnostic decision in a patient with muscle pain is whether or not to proceed with a muscle biopsy.

palmitoyltranferase deficiency).

In the myalgia of chronic fatigue syndrome and primary fibromyalgia, the pain is typically constant, and any exercise exacerbation of pain occurs after, rather than during, exercise. The inter-exercise level of pain is often high, even at times of relative inactivity. However, in these conditions there is no associated rhabdomyolysis or contractures.

Is there associated weakness?

If weakness is detected, the examiner must be careful to ascertain the distribution and whether it relates to incomplete effort. Pseudoparesis due to pain (e.g. primary fibromyalgia) is characterised by varying effort and sudden 'giveway' in muscle strength. Proximal weakness suggests a myopathy, but the absence of weakness does not exclude a myopathic disorder, especially a metabolic myopathy such as McArdle's disease.

Is there a systemic or endocrine disturbance or medication effect?

Symptoms such as malaise, weight loss or night sweats may indicate a systemic illness such as sarcoidosis, vasculitis or infection. Hypothyroidism may present with myalgia; despite laboratory confirmation, patients may not always have the additional symptoms and signs of cold intolerance, weight gain, hoarse voice, dry skin, myxoedema and delayed relaxation of tendon reflexes.

Some medications may cause myalgia, especially the newer cholesterol lowering agents such as HMG-CoA reductase inhibitors and immunomodulatory agents such as hydroxychloroquine.

Are there any investigative abnormalities supporting a myopathy?

A raised creatine kinase level is very common in myopathies (inflammatory, metabolic) although not invariable. Myopathic (small amplitude, polyphasic and short duration) motor units found on needle electrode examination during electromyography help support a diagnosis of myopathy, but their absence does not exclude a myopathic process, especially a multifocal one. Muscle biopsy is often necessary to confirm or exclude an inflammatory, mitochondrial or metabolic myopathy.

Is the pain part of a spectrum of symptoms suggesting primary fibromyalgia or chronic fatigue syndrome?

Light-headedness, paraesthesiae, memory and concentration problems, and symptoms of depression, anxiety or obsessive compulsive disorder may suggest a

Table. Differential diagnosis of muscle cramps or twitches

Benign cramps
Sudden painful contractions of calf or foot muscles – common in elderly and during pregnancy, and occur especially at night

Fasciculations
Brief shock-like twitches of isolated muscle bundles – may be benign or associated with motor neuron disease or motor neuropathies

Myotonia
Slow relaxation of muscle after voluntary contraction or after percussion of muscle belly – occurs in association with 'channelopathies' (e.g. paramyotonia congenita) or with myotonic dystrophy

Myokymia
Continuous, rhythmic, writhing and contraction of parts of muscle – persistent facial myokymia may be associated with central disorders such as multiple sclerosis, brainstem glioma or other brainstem pathology

Myoclonus
Brief, sudden muscle jerks usually significant to move the affected body part – they occur singly or repetitively and may be focal, segmental (confined to a group of muscles) or generalised. All of us are familiar with benign, physiological myoclonus, such as hiccoughs or 'sleep jerks'. Myoclonus is also associated with a number of disorders, such as myoclonic epilepsies, or as part of more widespread encephalopathy occurring in some mitochondrial cytopathies, Creutzfeld–Jacob disease, dementias, spinocerebellar degenerations, viral and toxic encephalopathies, and after focal brain damage

Indications for specialist referral

- History of chronic or recurrent muscle pain or cramps related to exercise, especially if associated with elevated creatine kinase or myoglobinuria
- Abnormal neurological examination with muscle weakness, wasting or areflexia
- Abnormal resting serum lactate or creatine kinase levels
- Elevated erythrocyte sedimentation rate, antinuclear antibodies or double-stranded DNA antibodies – may indicate a rheumatological disorder
- Abnormal electromyography

psychogenic basis for myalgia, but care must be taken not to miss an organic disorder.

Is there a family history of muscle pain or other neuromuscular disorder?

A family history of muscle pain, weakness or wasting may suggest mitochondrial disorders, muscular dystrophies, some metabolic myopathies or muscle channelopathies as the explanation for the patient's myalgia.

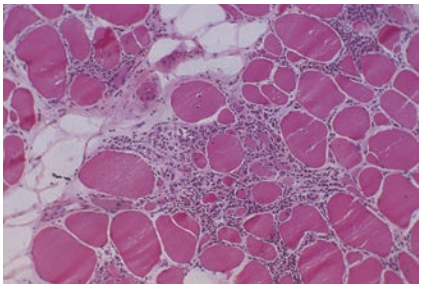


Figure 1. Inflammatory cell infiltrate seen in polymyositis.

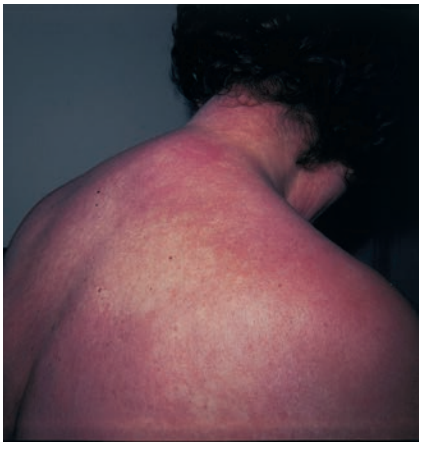


Figure 2. Typical rash seen in dermatomyositis.

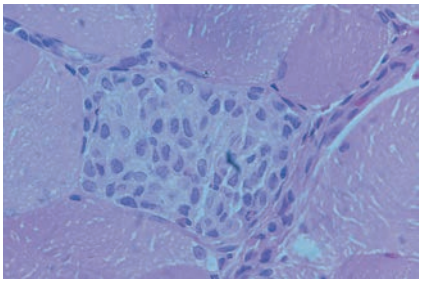


Figure 3. Granuloma in muscle, typical of sarcoidosis.

When to refer to a specialist

Indications for referral to a specialist for further assessment and investigation are listed in the box on page 23.

Common causes of muscle pain

Delayed onset muscle soreness after unaccustomed or excessive exercise

- The pain typically peaks in the exercised muscle 24 to 72 hours after exertion and is particularly associated with eccentric exercise where the muscle resists lengthening (such as the quadriceps muscle while walking down stairs).
- The high tension in the muscle produces microscopic muscle tears. No specific treatment is required because the condition is self-limiting.

Viral infections

- Typically diffuse myalgia usually occurs in the setting of an obvious viral upper respiratory tract infection or gastroenteritis. Influenza and coxsackievirus infections are most commonly associated with myalgia and are self-limiting.

Idiopathic inflammatory myopathies and sarcoidosis

- In idiopathic inflammatory myopathies (e.g. polymyositis, dermatomyositis, inclusion body myositis), there is usually an elevated serum creatine kinase and proximal weakness.
- Muscle biopsy of a moderately weak muscle typically shows inflammatory cell infiltrates (Figure 1). Biopsy is advisable to confirm diagnosis.
- Polymyositis and inclusion body myositis may be very indolent.
- Myalgia occurs in about 20 to 30% of cases.
- Be aware of underlying malignancy with adult-onset dermatomyositis. The typical rash of dermatomyositis aids diagnosis (Figure 2).
- Sarcoid myopathy may be painful and associated with rash (erythema nodosum) or sarcoid granulomas in other tissues (e.g. hilar lymphadenopathy or interstitial infiltrates on chest x-ray). Granulomas may be seen on histochemistry of muscle (Figure 3).

Rheumatological disease and systemic vasculitis

- Diffuse myalgia is not uncommon with connective tissue diseases.
- Erythrocyte sedimentation rate (ESR) and serological markers are useful in screening for these disorders (e.g. antinuclear antibodies, double-stranded DNA antibodies, antibodies to extractable nuclear antigens).
- Biopsy may show some inflammatory (especially endomysial and perivenular) infiltrates.
- There may be overlap syndromes with frank myositis (e.g. mixed connective tissue syndrome).
- Proximal limb girdle and axial pain and stiffness with a morning emphasis in an elderly person suggest polymyalgia rheumatica. ESR elevation is very typical. Urgent diagnosis is required because of the association with temporal arteritis.

Drug-induced and toxic myopathies

- HMG-CoA reductase inhibitors (pravastatin, simvastatin) may cause myalgia, especially if used with other lipid lowering agents (i.e. gemfibrozil, clofibrate). Creatine kinase is invariably elevated.
- Chronic alcohol-related myopathy is typically painless, but acute painful myopathy with rhabdomyolysis may be seen after a binge during which the patient has been recumbent for a prolonged time.
- Many prescribed drugs can cause myopathy, but it is not usually painful. Hydroxychloroquine myopathy is a rare painful myopathy.

Endocrine myopathies

- Hypothyroidism may present with myalgia as the only obvious manifestation.

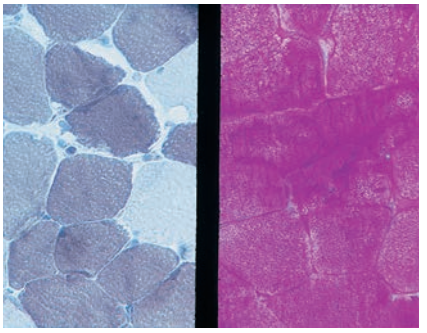


Figure 4. Periodic acid–Schiff (PAS) stain for glycogen. The left panel shows staining in normal muscle. The right panel shows excess staining in glycogen excess.

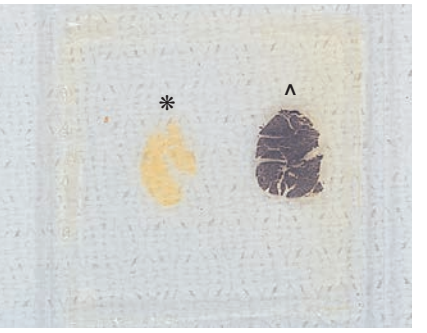


Figure 5. Histochemistry demonstrating muscle phosphorylase deficiency on the left (*) and a normal control sample on the right (^).

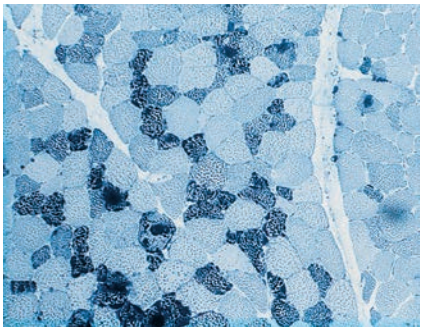


Figure 6. Sudan black stain in muscle cells, demonstrating excess fat in primary carnitine deficiency.

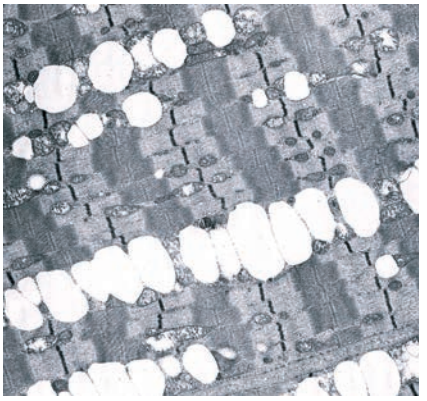


Figure 7. Electron micrograph showing large lipid collections between the myofibrils in muscle cells affected by carnitine deficiency.

Cramps, muscle stiffness and delayed tendon reflex relaxation may appear later. Creatine kinase is typically elevated.

- Osteomalacia may present with severe proximal myalgia, especially around the pelvic girdle. Typical 'pseudofractures' or Looser's zones are seen on x-ray of the femoral neck, pelvis, scapula, fibula or metatarsals.

Metabolic myopathies

Carbohydrate disorders

- Examples of carbohydrate disorders are disorders of glycogen breakdown (myophosphorylase deficiency [McArdle's disease], phosphorylase b kinase deficiency) and glycolysis (phosphofructokinase deficiency).
- Pain quickly develops in the exercising muscles and worsens with continued activity. Eventually, contractures of muscles may develop lasting for minutes to hours; they are due to profound energy supply failure.
- Prolonged postexertional pain may develop, and clinically overt rhabdomyolysis with myoglobinuria may occur if the patient persists with exercise despite pain.
- The resting creatine kinase level is typically elevated, sometimes markedly. The postexercise level is always elevated.
- A flat lactate response on ischaemic (anaerobic) forearm testing or other exercise is typical of most of these disorders.
- Muscle biopsy usually shows glycogen excess (Figure 4, right panel). Appropriate enzyme histochemistry or biochemical assay is needed to confirm a specific enzyme deficiency (e.g. muscle phosphorylase; Figure 5).
- There is usually autosomal recessive inheritance, but occasionally myophosphorylase deficiency follows an autosomal dominant pattern.

Disorders of lipid metabolism

- Examples are primary muscle carnitine deficiency and carnitine palmitoyl transferase deficiency.
- Primary muscle carnitine deficiency is very rare (secondary deficiencies are much more common). It manifests as progressive proximal weakness but is typically painless. There is marked lipid accumulation, with a low muscle carnitine level shown by biochemical assay (Figures 6 and 7).
- In carnitine palmitoyl transferase deficiency, the muscle pain develops during or after prolonged exercise. The patient commonly presents with postexertional painful muscle swelling and rhabdomyolysis. A family history may be present. The lactate rise with exertion is normal, the muscle biopsy is usually normal, and excessive lipid accumulation is not a feature. Biochemical assay of this enzyme from a muscle specimen will confirm the deficiency.

Purine metabolism myopathy

- The example here is myoadenylate deaminase deficiency – in which there is exertional muscle pain, exercise intolerance and stiffness, particularly in the calf muscles. Myalgia is not always closely linked to exercise, thereby differentiating this deficiency from disorders of carbohydrate metabolism.
- Myoadenylate deaminase deficiency follows autosomal recessive inheritance.
- There is a normal venous lactate rise but a minimal rise in venous ammonia

General approach to the treatment of chronic myalgia

- Define and treat the specific cause when possible.
- Develop specific dietary and exercise regimens in patients with metabolic myopathies, as appropriate.
- When a definite correctable cause is not identified or the cause is not clear, the following approaches may help:
  - short courses of nonsteroidal anti-inflammatory medication
  - regular simple analgesia (paracetamol or aspirin)
  - low dose antidepressant medication: amitriptyline (Endep, Tryptanol) 10 to 75 mg at night
  - low dose sodium valproate (Epilim, Valpro) or carbamazepine (Carbium, Tegretol, Teril) if excessive motor unit activity is suspected as contributing to the myalgia.
- Full antidepressant treatment may be tried empirically if a depressive equivalent is suspected.
- Physical treatment is very important in combination with medication. Feldenkrais physiotherapy in combination with a low level graded aerobic exercise program or hydrotherapy may be helpful.

with ischaemic forearm exercise testing. Muscle histochemistry can demonstrate deficient enzyme activity, which is confirmed by biochemical assay.

Mitochondrial myopathies

• Only a small number of mitochondrial disorders of oxidative phosphorylation are associated with exercise intolerance, muscle pain and/or rhabdomyolysis. Cytochrome b deficiency is one of them.

• The serum creatine kinase level is generally normal, but the resting serum lactate may be elevated.

• Electromyography often shows minimal abnormalities or mild myopathic features.

• Muscle biopsy may show an increased number of muscle fibres with an abnormal accumulation of subsarcolemmal mitochondria (known as ragged red fibres; Figure 8). Histochemistry for cytochrome oxidase shows that these and other fibres have abnormal activity (Figure 9). Electron microscopy may show structural abnormalities in mitochondria (Figure 10).

• Mitochondrial genetic studies can be performed on muscle biopsies, blood and hair follicles. They usually show characteristic associated abnormalities.

Myalgia with obscure aetiology

Depressive equivalents

• Dull persistent myalgia without exercise exacerbation may be part of the somatisation seen in depressive illness. Coincidental organic syndromes need to be excluded because secondary depressive features may arise in patients with chronic organic illness and great care must be taken not to overlook an organic trigger.

Chronic fatigue syndrome

• Muscle pain is a prominent symptom in most patients with chronic fatigue syndrome. Muscle size and strength, serum creatine kinase and electromyographic findings are typically normal.

Fibromyalgia

• Fibromyalgia is characterised by a greater than three-month history of widespread pain that is not explained by inflammatory or degenerative musculoskeletal disorder and is associated with excessive tenderness on palpation of 11 of 18 specified tender points.

• The creatine kinase level and muscle strength are normal.

• Fibromyalgia is thought to be due to centrally determined heightened pain perception in the brain from the muscle

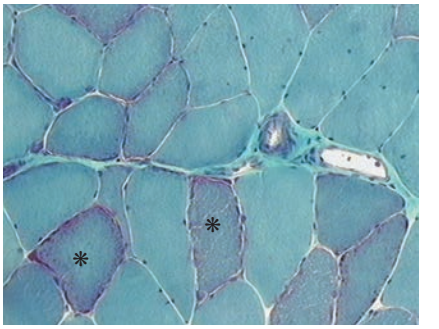


Figure 8. Ragged red fibres (abnormal aggregates of mitochondria) beneath the muscle membrane, shown by Gomori trichrome stain (*).

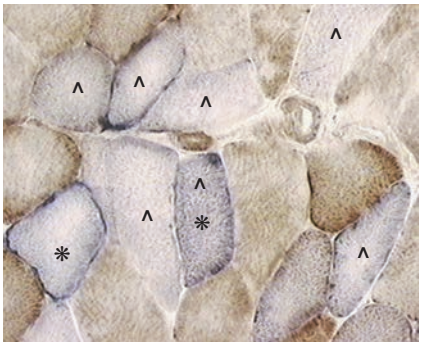


Figure 9. Muscle from a patient with a mitochondrial disorder. The cytochrome oxidase stain is demonstrating pale 'cox-negative' fibres (^). The ragged red fibres are shown (*).

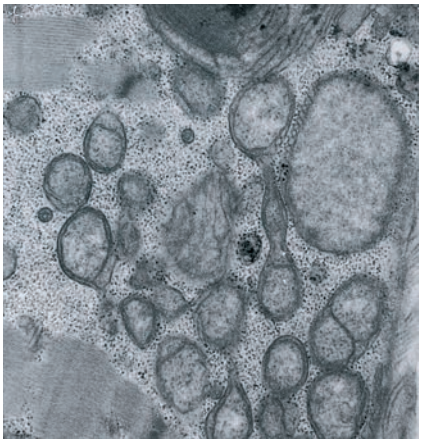


Figure 10. Electron micrograph showing abnormal appearances of mitochondria in mitochondrial myopathy.

pain receptors. Apparent associations with the onset of this disorder include physical injury, infection and endogenous factors such as emotional upset.

- Around 50 to 70% of patients with fibromyalgia report symptoms of altered mood or sleep disorder before the onset of their pain.
- Fibromyalgia often coexists with chronic fatigue syndrome, chronic headache syndromes, inflammatory bowel syndrome and depression.
- Tricyclic antidepressants are useful in 30 to 50% of patients because they improve sleep quality and modify the central mechanisms of pain perception and mood. Some patients respond to a gentle, graded, supervised aerobic exercise program.

Central causes of myalgia

- Chronic muscle pain may be evident with some central nervous system problems, especially those associated with increased muscle tone, either spasticity or rigidity.
- Syndromes of excessive motor unit activity are an unusual cause of muscle pain and cramps. Isaac's syndrome is one such condition where electromyography shows chaotic (neuromyotonic) spontaneous activity. Anticonvulsants may be helpful in this context. In some patients with myalgia and cramps with no other features, there may be a suspicion of excess of motor unit activity, and therapeutic trial of an anticonvulsant medication may occasionally be helpful.

Treatment

A general approach to the treatment of chronic myalgia is summarised in the box on page 27.

Treatment is largely dictated by the clinical diagnosis after a careful and thorough evaluation is completed. A straightforward cure for patients with chronic myalgic syndromes is not always possible. Toxic, inflammatory and endocrine myopathies usually show a good response to specific treatment. Metabolic myopathies may show some improvement with exercise manipulation (e.g. myophosphorylase deficiency). Dietary replacement is helpful only in a small number of disorders (e.g. carnitine deficiency). Coenzyme Q10 may improve symptoms in mitochondrial myopathies.

Identification of a psychogenic cause or contribution may allow some improvement with explanation, support and appropriate medication. Often, however, troublesome symptoms continue despite these measures.

Quinine is effective for the symptomatic relief of muscle cramps, particularly when the symptoms are frequent and troublesome at night. It acts directly on the muscle and the neuromuscular endplate. Quinine should always be used cautiously because of potential serious side effects, which include hypersensitivity reactions – in these situations the drug should be discontinued immediately. It is important to ensure that there is no history of previous quinine sensitivity with thrombocytopenia, haemolytic uraemic syndrome or acute renal dysfunction. Quinine is contraindicated in pregnant and lactating women. Drug interactions include a potentiation of the anticoagulant effect of warfarin. Despite these issues, many patients tolerate low doses of quinine (300 to 600 mg) at night with few side effects.

Conclusion

Although muscle pain and cramps are common in general practice and most often the cause is benign, it is important to remember that there may be a serious underlying muscle or systemic disorder that requires specific investigation to establish the diagnosis. In most cases, a thorough clinical assessment (including the seven questions discussed in this article) and simple investigations will determine if further specialised investigation, referral and treatment are necessary. MT