INTRODUCTION

Myalgia, or muscle pain, is a common complaint among adults presenting for medical care. In fact, nearly everyone will experience muscle soreness at some point in their life. Excessive exertion, trauma, and viral infections are among the most common causes. While many causes are benign and self-limited, myalgia may be the harbinger of disorders associated with significant morbidity.

A thorough review of the patient's history and a complete physical examination can usually narrow the list of potential causes of myalgia to a manageable few. For persistent or severe myalgia without a known cause, selected testing may be necessary to identify or exclude specific diagnoses and to direct treatment.

It is important to differentiate myalgia from myopathy (muscle disease) and myositis (muscle inflammation). Although myopathy and myositis may cause myalgia, most individuals with myalgia have neither. It is also useful to separate diffuse from localized symptoms. This review will discuss the approach to myalgia as a presenting symptom to a primary care clinician, focusing on etiology, history, physical examination, laboratory studies, and management. Specific disorders characterized by prominent myalgia are covered elsewhere. (See "Differential diagnosis of fibromyalgia" and "Myopathies of systemic disease" and "Drug-induced myopathies").
ETIOLOGY

Most etiologies of myalgia can be divided based upon diffuse versus focal symptoms, although myalgia may also be multifactorial. For example, a patient may have concomitant rheumatoid arthritis, fibromyalgia, and pes anserinus pain syndrome (formerly anserine bursitis). (See "Bursitis: An overview of clinical manifestations, diagnosis, and management" and "Overview of soft tissue musculoskeletal disorders", section on 'Myofascial pain syndrome' and "Clinical manifestations of rheumatoid arthritis".)

Diffuse myalgias — The most common causes of diffuse myalgia are (table 1):

- Systemic infection, including viral, bacterial, and spirochetal diseases [1-6]. As a prominent example, dengue fever is sometimes called "break bone fever" due to the severe muscle and joint pain associated with this virus. Prominent myalgia is also a typical feature of influenza [7] and coronavirus disease 2019 (COVID-19) [8]. Moreover, myalgia at the time of hospital admission for COVID-19 may be associated with persistent post-COVID musculoskeletal pain [9].

In addition, vaccination may also cause significant, though short-lived, myalgia.

- Rheumatic disease, especially polymyalgia rheumatica (PMR), inflammatory myopathy [10,11], or autoinflammatory disease [12]. (See "Clinical manifestations and diagnosis of polymyalgia rheumatica" and "Clinical manifestations of dermatomyositis and polymyositis in adults".)

- Noninflammatory conditions, such as fibromyalgia and chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) [13]. (See "Differential diagnosis of fibromyalgia" and "Clinical features and diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome".)

- Medications, particularly the use of statins (with or without creatine kinase elevation) [14,15], ciprofloxacin [16], bisphosphonates [17], aromatase inhibitors [18,19], or withdrawal from antidepressant therapy [20]. (See "Drug-induced myopathies".)

- Metabolic disorders, such as mitochondrial myopathy [21,22], vitamin D deficiency [23,24], and scurvy [25], can lead to myalgias, although these are rarer causes. (See "Approach to the metabolic myopathies" and "Mitochondrial myopathies: Clinical features and diagnosis".)

- Liver disease, such as chronic viral hepatitis and autoimmune hepatitis [1,2,26].
Localized myalgia — The most common causes of localized myalgia are (table 2) [32-36]:

- Overuse or strenuous exercise
- Soft tissue disease (such as bursitis, trauma, or infection)
- Pyomyositis
- Myofascial pain syndrome
- Muscle infarction or compartment syndrome

DIAGNOSIS

For patients presenting with myalgia, it is common that the diagnosis cannot be established at the initial visit. This may relate in part to the need to follow symptoms over time and to obtain laboratory or other diagnostic studies. In fact, the course of symptoms and signs over time may be particularly helpful. (See 'Muscle symptoms' below.)

The list of conditions associated with myalgia is long (table 1 and table 2). In patients with a characteristic pattern of symptoms, the diagnosis may be established promptly. However, considerable uncertainty is common after initial evaluation. Selective testing and vigilant follow-up may be necessary for several months to narrow the list of potential explanations.

Serious conditions — Early in the evaluation of patients with myalgia, the clinician should attempt to identify those patients with a serious or life-threatening condition. Conditions causing myalgia may cause significant suffering, but true medical emergencies presenting with myalgia are rare. Prompt diagnosis and treatment are required for bacterial infections, especially endocarditis and impending sepsis, which may present with diffuse myalgia, fever, chills, arthralgia, fatigue and back pain [4]. Rhabdomyolysis with renal failure may complicate a number of myalgic conditions, including crush injury or compression, exertion, hyperthermia, toxins, or systemic infection. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis" and "Rhabdomyolysis: Clinical manifestations and diagnosis" and "Acute compartment syndrome of the extremities".)
History — The patient's history provides a useful starting point in narrowing down the long list of potential causes for myalgia. Particular attention should be given to mode of onset, location of pain, and associated symptoms.

Muscle symptoms — The first step in determining the cause of myalgia is to inquire about the specific nature of the patient's muscle pain:

- Did the muscle pain begin suddenly or gradually? If sudden in onset, did it follow trauma or an unusually strenuous activity? Is the muscle pain worse in the morning?

As an example, acute onset with prominent constitutional symptoms suggests infection (such as bacterial sepsis, pyomyositis, influenza or acute hepatitis B). Acute onset of myalgia in the neck, shoulders, upper arms, buttocks, and thighs in an older adult is characteristic of polymyalgia rheumatica (PMR), especially if accompanied by morning stiffness.

Subacute myalgia is typical of a medication-induced cause (such as statin-induced myalgia) and can occur weeks to months after initiating therapy. (See "Statin muscle-related adverse events", section on 'Management'.)

Insidious onset and chronic symptoms are typical of infection with chronic hepatitis C, hypothyroidism, hypercalcemia, and vitamin D deficiency. This is also the typical pattern for patients with fibromyalgia, chronic fatigue syndrome (CFS), myofascial pain syndrome, and a somatization disorder.

In addition, muscle pain and stiffness in the morning is highly suggestive of PMR or other inflammatory arthritis.

- Is the muscle pain associated with pain elsewhere? Is it near joints? If so, are they axial joints, such as the shoulder and hips? Shoulder and hip pathology, in particular, tend to cause referred pain to proximal muscles. Referred pain accounts for the prominent myalgia described by patients with PMR and rheumatoid arthritis involving the shoulders.

- Is there a particular distribution of muscle pain? Statin-induced myalgia typically presents as proximal, symmetric muscle weakness and soreness. By contrast, diffuse myalgia, fever, headache, malaise, and a nonproductive cough are typical of a viral infection, such as influenza. (See "Statin muscle-related adverse events" and "Seasonal influenza in adults: Clinical manifestations and diagnosis".)
- Is there redness, swelling, or warmth in the area of the muscle pain? Is the muscle painful to touch? Pyomyositis, abscess, muscle infarction, or compartment syndrome may cause focal muscle tenderness. Pyomyositis and abscess may cause localized inflammatory findings as well.

- Is the myalgia associated with muscle weakness? Is it difficult to arise from a chair or reach above the head? Objective muscle weakness is not expected with fibromyalgia, myofascial pain syndrome, or PMR; these common causes of muscle pain can be placed lower on the list of possibilities in the face of demonstrable muscle weakness. (See "Approach to the patient with muscle weakness".)

- Have there been muscle cramps? The etiology of muscle cramps is often not found, but they can be caused by several conditions:
  - Structural disorders such as flat feet
  - Unusual positioning during work or sleep
  - Neurologic disorders such as Parkinson disease
  - Muscle injury such as trauma or fall
  - Dehydration
  - Exercise-associated muscle cramping or spasm
  - Electrolyte abnormalities
  - Medications such as diuretics, statins, and beta agonists.

Leg cramps occurring at night are discussed separately. (See "Nocturnal leg cramps".)

**Associated symptoms** — The presence or absence of associated symptoms can be quite helpful in pointing toward or against a particular cause. The clinician should undertake a detailed review of systems with particular attention paid to:

- Constipation
- Depression
- Fatigue
- Fever
- Joint pain or swelling
- Paresthesias
- Rash or hyperpigmentation
- Weight change
- Nausea, vomiting or diarrhea

Constipation, fatigue, and weight gain are common symptoms of hypothyroidism, whereas
rash or hyperpigmentation are suggestive of infection or adrenal insufficiency, respectively. Fever raises the possibility of infection or systemic rheumatic disease (such as systemic lupus erythematosus) or autoinflammatory disease (such as familial Mediterranean fever) while joint swelling suggests inflammatory arthritis. Paresthesias suggest a neuropathic condition, which may cause myalgia due to referred pain or indicate the presence of a vasculitic process.

**Other history** — The cause of myalgia may not be apparent until additional details of the patient's medical history are considered. These include:

- Patient demographics, such as age and sex. For example, newly diagnosed systemic lupus erythematosus and rheumatoid arthritis are most common among young adult women, while PMR is seen exclusively among adults over the age of 55.

- Past medical history, such as a prior diagnosis of thyroid disease, hepatitis C, diabetes, or hyperparathyroidism.

- Recent exposure to individuals who have symptoms suggestive of influenza, COVID-19, or other viral illness.

- Medication use, especially statin administration, can lead to myalgias. Myalgia due to statin or fibrate medications may be associated with weakness and an elevation in creatine kinase, but these features are often absent [37]. Drug interactions account for many cases of medication-induced myalgia or myopathy, particularly in patients taking statins and inhibitors of CYP3A4 (table 3). A number of other common medications may be associated with myalgia, including bisphosphonates and aromatase inhibitors.

In addition, abrupt discontinuation of serotonin-reuptake inhibitors with short half-lives (such as venlafaxine or paroxetine) may cause significant myalgia [30,31]. Muscle symptoms that follow the administration of a new medication should prompt the clinician to consider drug-induced muscle pain. (See "Statin muscle-related adverse events" and "Drug-induced myopathies".)

- Trauma, a change in activity or function, recent injury, or unusually strenuous exercise may trigger muscle pain, which is typically localized.

Understanding the functional status of the patient or a recent change in function can help determine the pace and direction of the evaluation. For example, the possibility of myopathy is raised by a patient with myalgia who has difficulty arising from a chair or...
Physical examination — While the history can provide important clues to the cause of myalgia, the physical examination can provide compelling, objective evidence for myopathy (muscle disease) or an alternative explanation for the symptoms.

Muscle examination — Although it can be difficult for a patient with myalgia to cooperate fully with a muscle examination, the finding of weakness can be particularly helpful in narrowing down the list of possible causes of symptoms by excluding many. For example, the finding of proximal muscle weakness in all four extremities in a patient with myalgia should turn the focus of diagnostic considerations to inflammatory myopathy (such as polymyositis), hypothyroidism, drug-induced myopathy, or hypercalcemia. Identifying objective weakness is important because weakness (with or without myalgia) is a common complaint even in the absence of demonstrable loss of motor function.

Even patients with significant pain can usually give maximum effort at least briefly to provide the examiner with a sense of whether muscle strength is normal. Besides assessing muscle strength in the usual proximal and distal muscle groups (including deltoids, wrist extensors, grip, thigh flexors, and ankle flexors and extensors), assessment of neck flexor strength may be useful as these muscles are a powerful and often overlooked proximal muscle group.

Besides the assessment of weakness, helpful findings on muscle examination may include focal swelling or erythema, which should raise the possibility of pyomyositis or other localized infection. Severe, localized tenderness without inflammatory features suggests muscle infarction or compartment syndrome. (See "Diabetic muscle infarction" and "Acute compartment syndrome of the extremities".)

It should be noted that muscle weakness without pain includes a much broader differential diagnosis discussed elsewhere. (See "Approach to the patient with muscle weakness".)

General physical examination — The source of myalgia may lie far from the muscles. For this reason, as well as the fact that diseases causing myalgia may affect other organ systems, a thorough physical examination should follow, with particular attention to the presence of the following physical findings:
• Fever (which may suggest viral infection, pyomyositis, endocarditis, or impending sepsis).

• Hypotension (as may be found in patients with sepsis).

• Hyperpigmentation and postural hypotension (as may be present in adrenal insufficiency). (See "Clinical manifestations of adrenal insufficiency in adults", section on 'Musculoskeletal'.)

• Cutaneous lesions (such as those found in systemic lupus erythematosus, vasculitis, Lyme disease, psoriasis, or endocarditis).

• Ecchymoses (suggestive of recent trauma).

• Limited shoulder and hip range of motion (consistent with PMR) or spinal disease (as may be noted in patients with spondyloarthropathy).

• Joint inflammation (swelling, heat, warmth, and/or limited motion) in the peripheral joints (as is typical of rheumatoid arthritis, psoriatic arthritis, or systemic lupus erythematosus).

• Bursal or tendon tenderness with more limitation of active motion than passive motion (compatible with bursitis or tendonitis).

• Tender points (as with fibromyalgia) or trigger points (suggestive of myofascial pain syndrome), although the ability to distinguish tender and trigger points is controversial. While the presence of multiple tender points in characteristic locations is highly suggestive of fibromyalgia, their absence does not exclude the diagnosis (figure 1). The clinical manifestations and diagnosis of fibromyalgia are discussed in detail elsewhere. (See "Differential diagnosis of fibromyalgia", section on 'Myofascial pain syndromes' and "Clinical manifestations and diagnosis of fibromyalgia in adults".)

• Severe, focal muscle pain should suggest the possibility of muscle infarction, compartment syndrome, or pyomyositis. (See "Diabetic muscle infarction", section on 'Clinical manifestations' and "Acute compartment syndrome of the extremities", section on 'Clinical features' and "Primary pyomyositis".)

• Delayed relaxation of reflexes, slowed speech, dry skin, hoarse voice, or other signs of hypothyroidism. (See "Clinical manifestations of hypothyroidism", section on 'Musculoskeletal symptoms'.)

• Depressed or flattened affect (as an indication of depression or as associated with a
Laboratory studies — For mild symptoms, watchful waiting without laboratory evaluation may be appropriate, as symptoms often resolve on their own with time. However, for more significant symptoms (e.g., severe pain or muscle weakness), selected laboratory studies may be quite helpful in ruling in or ruling out conditions that remain in the differential diagnosis after a detailed history and physical examination.

As an initial assessment, complete blood count, urinalysis, and measures of renal and liver function are appropriate for most patients with significant myalgia. Depending upon the specific symptoms, risk factors and physical findings, measures of serum calcium, albumin, phosphate, TSH, creatine kinase, and 25-hydroxyvitamin D may be appropriate to assess, especially if symptoms are prominent, persistent, and otherwise unexplained. Weakness should prompt creatine kinase measurement while bone pain and/or abnormal measures of serum calcium make it important to test for hypovitaminosis D. Cold intolerance, fatigue, and delayed reflexes may suggest hypothyroidism as a cause of myalgia.

The following tests may also prove helpful in certain clinical situations (table 1):

- Blood cultures and serologic testing for viral infections (such as parvovirus and viral hepatitis).

- Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) – These may be helpful to identify the presence of systemic inflammation, as with infection and systemic rheumatic disease (especially PMR and inflammatory myopathy). On the other hand, a normal ESR is the expected finding in patients with fibromyalgia.

However, caution must be taken in interpreting these test results as elevations in the ESR and CRP are not specific. In addition, normal or unimpressive results rarely rule out a particular cause of myalgia.

- Autoantibodies, such as antinuclear antibodies (ANA) for suspected systemic lupus erythematosus, anti-neutrophilic cytoplasmic antibodies (ANCA) for suspected ANCA-associated vasculitis, as well as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies for suspected rheumatoid arthritis, should be limited to those patients for whom there is at least a moderate pre-test probability of disease. Widespread testing with these autoantibody tests for all patients with myalgia is likely to produce an unacceptably high rate of false-positive results. (See "Measurement and clinical significance of antinuclear antibodies" and "Biologic markers in the diagnosis and assessment of rheumatoid arthritis".)
Other studies

- Testing of cortisol production, such as morning serum cortisol or adrenocorticotropic hormone (ACTH) stimulation test, are helpful to diagnose or rule out adrenal insufficiency. (See "Diagnosis of adrenal insufficiency in adults".)

- Imaging – Radiographs, magnetic resonance imaging (MRI), and other imaging tests are not routinely necessary in the evaluation of myalgia. Utility is limited to assessment of erosive arthritis (rheumatoid arthritis and others), fracture, inflammatory muscle disease, or localized muscle disease (pyomyositis, muscle infarction).

- Neurophysiology studies – Electromyogram (EMG) with nerve conduction studies (NCS) may be helpful to support the diagnosis of inflammatory or metabolic myopathy, as well as a neuropathic process. (See "Overview of electromyography", section on 'Diagnostic electromyography' and "Overview of and approach to the idiopathic inflammatory myopathies", section on 'Electromyography'.)

- Tissue sampling (eg, aspiration or biopsy) – Most patients with myalgia will not require tissue sampling. However, it may be diagnostic for patients with suspected abscess, inflammatory myopathy, vasculitis, or systemic lupus erythematosus.

MANAGEMENT

There are no established guidelines or expert consensus regarding how best to treat myalgia. Features of the history, physical examination, and selective testing may prove particularly useful to identify the etiology that will guide management.

If medication-induced myalgia is suspected, a trial off the medication is warranted, though only after balancing the clinical improvement gained from such a trial with the risks of stopping the drug. It may take weeks or even months, however, to get a clear sense of whether myalgia was related to a medication [39]. A notable exception is polymyalgia rheumatica (PMR), a condition in which a rapid and dramatic improvement within a few days of low-dose corticosteroid treatment is typical. In fact, this prompt response to treatment can help confirm the diagnosis. (See "Treatment of polymyalgia rheumatica", section on 'Initial dose'.)

When the cause of myalgia cannot be readily identified, patients should be closely observed and treated symptomatically if needed. In the absence of specific contraindications, treatment may include heat, rest, acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), and/or
muscle relaxants.

Indications for referral include suspicion of a particular condition for which specialty care is warranted (such as referral to a rheumatologist for suspected PMR) or severe, functionally limiting symptoms, especially if they are worsening or persistent.

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Nocturnal (nighttime) leg cramps (The Basics)"

SUMMARY AND RECOMMENDATIONS

- Etiologies: Diffuse versus localized myalgia – The etiology of myalgia can be divided into conditions causing diffuse or localized symptoms (table 1 and table 2). Conditions leading to diffuse myalgias include systemic rheumatic disease, fibromyalgia, infection, medication use, metabolic derangements, hypothyroidism, and psychiatric causes. Conditions leading to localized myalgia include strenuous activity, soft tissue disease, pyomyositis, myofascial pain syndrome, muscle infarction, and compartment syndrome. (See 'Etiology' above.)

- Evaluate for potentially life-threatening conditions – Prompt diagnosis and treatment are required for bacterial infections, especially endocarditis and impending sepsis, which may present with diffuse myalgia as well as fever, chills, and arthralgia. Rhabdomyolysis can present with diffuse myalgias, as well as renal failure and/or compartment syndrome in severe cases. (See 'Serious conditions' above.)
• **Assessment** – The clinical history should include mode of onset, location of pain, muscle weakness, associated symptoms, medication use, and any previous trauma. The physical examination should include an assessment of focal muscle pain or inflammation, muscle weakness, and examination of findings associated with other medical conditions. (See 'History' above and 'Physical examination' above.)

• **Laboratory evaluation** – For mild symptoms, watchful waiting without laboratory evaluation may be appropriate, as symptoms often resolve on their own. However, for more significant symptoms including severe pain or muscle weakness, selected laboratory studies may be quite helpful in ruling in or ruling out disease. As an initial assessment, a complete blood count, urinalysis, and measures of renal and liver function are appropriate for most patients with significant myalgia. Other specific testing will depend on the history and physical examination findings. (See 'Laboratory studies' above.)

• **Management** – Management of myalgia usually depends on the underlying cause. When the cause cannot be readily identified, patients should be closely observed and treated symptomatically. In the absence of specific contraindications, empiric treatment may include heat, rest, acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), and/or muscle relaxants. (See 'Management' above.)

**REFERENCES**


This generalized information is a limited summary of diagnosis, treatment, and/or medication information. It is not meant to be comprehensive and should be used as a tool to help the user understand and/or assess potential diagnostic and treatment options. It does NOT include all information about conditions, treatments, medications, side effects, or risks that may apply to a specific patient. It is not intended to be medical advice or a substitute for the medical advice, diagnosis, or treatment of a health care provider based on the health care provider's examination and assessment of a patient's specific and unique circumstances. Patients must speak with a health care provider for complete information about their health, medical questions, and treatment options, including any risks or benefits regarding use of medications. This information does not endorse any treatments or medications as safe, effective, or approved for treating a specific patient. UpToDate, Inc. and its affiliates disclaim any warranty or liability relating to this information or the use thereof. The use of this information is governed by the Terms of Use, available at https://www.wolterskluwer.com/en/know/clinical-effectiveness-terms ©2023 UpToDate, Inc. and its affiliates and/or licensors. All rights reserved.

Topic 2751 Version 37.0

Contributor Disclosures

Robert H Shmerling, MD Consultant/Advisory Boards: Creda Health [Advise on matters relating to the company's business, technology and products]. All of the relevant financial relationships listed have been mitigated. Mark D Aronson, MD No relevant financial relationship(s) with ineligible companies to disclose. Karen Law, MD No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy