



# POLYMYALGIA RHEUMATICA:

Look before you leap

*Polymyalgia rheumatica is an inflammatory condition that causes a particular pattern of joint pain and stiffness, most commonly in older people. It is a rheumatic disorder closely associated, and often co-existing, with giant cell arteritis. Diagnosis is based on the patient's clinical features, supported by laboratory investigations. Before making a diagnosis, other conditions which can mimic polymyalgia rheumatica should be ruled out, and most importantly, the patient should be assessed for co-existing giant cell arteritis. Treatment of polymyalgia rheumatica, with long-term oral prednisone, can usually be managed in primary care, but referral to a Rheumatologist may be necessary if the diagnosis is unclear, the response to treatment is poor or multiple relapses of symptoms occur during tapering.*

## What is polymyalgia rheumatica?

Polymyalgia rheumatica is an inflammatory rheumatological syndrome that causes pain and stiffness, most commonly in the neck, shoulders and pelvic girdle. The pain and stiffness is worse in the morning, usually lasts for one hour or more and may be accompanied by systemic features, such as fever, fatigue and anorexia.<sup>1</sup> The onset of symptoms is typically between two weeks and two months.<sup>2</sup>

The incidence of polymyalgia rheumatica increases with age, with an average age of onset of approximately 70 years, and it rarely occurs in people aged under 50 years.<sup>3</sup> The incidence of polymyalgia rheumatica is highest in people of Scandinavian or Northern-European descent, although it does occur in people of other ethnicities.<sup>3</sup> Polymyalgia rheumatica is twice as common in females.<sup>3</sup> In total, the yearly incidence is approximately 50 per 100 000 people aged over 50 years.<sup>4</sup>

It is not known what causes polymyalgia rheumatica. It is closely associated with giant cell arteritis, although it is two to three times more common.<sup>2</sup> Like giant cell arteritis, both genetic and external factors, e.g. infection, are thought to be involved in the development of the condition.<sup>3</sup>

Polymyalgia rheumatica is managed with corticosteroids and significant remission of symptoms can be expected within one week of starting treatment.<sup>5</sup> The prognosis is usually good and complications, such as recurrent relapse of symptoms, are limited.<sup>3</sup>

## Never trust a diagnosis of polymyalgia rheumatica

As polymyalgia rheumatica has a non-specific clinical presentation and few significant sequelae, it should be diagnosed with caution. Ruling out other illnesses, such as cancers or insidious-onset rheumatoid arthritis, is more important than immediately treating polymyalgia rheumatica, if it is present. Unlike giant cell arteritis, a delay in treatment will not significantly endanger a patient. Conversely, long-term corticosteroid treatment can have significant adverse effects and a daily treatment course of up to three years will be a burden for many people. In addition, an initial or partial response to corticosteroids may be seen in people with other conditions who present with similar features to polymyalgia rheumatica, such as rheumatoid arthritis, and this may provide false reassurance that the correct diagnosis has been identified. Therefore, even if a patient presents with clinical features typical of polymyalgia rheumatica, and a working diagnosis is made, they should be regularly reviewed and other possible causes always considered, particularly if the patient does not respond to treatment.

 For further information, see: "Giant cell arteritis", Page 16.

## Making a diagnosis

The British Society for Rheumatology has developed a set of inclusion and exclusion criteria for diagnosing polymyalgia rheumatica.<sup>6</sup> These criteria were derived by consensus and represent a clinically typical patient with polymyalgia

rheumatica. They are most useful for “ruling in”, i.e. a patient who meets the criteria is likely to have polymyalgia rheumatica, rather than “ruling out”, as people with polymyalgia rheumatica can present atypically, such as with a shorter duration of symptoms or found to have a normal acute phase response.

The core inclusion criteria are:<sup>6</sup>

- Age > 50 years
- Symptom duration > two weeks
- Bilateral shoulder or pelvic girdle aching, or both
- Morning stiffness duration of > 45 minutes
- Evidence of an acute-phase response, e.g. raised CRP

The core exclusion diagnoses are:<sup>6</sup>

- Infection
- Malignancy
- Giant cell arteritis

## Patient presentation, history and examination

### Shoulder, neck, hip and pelvic pain

Shoulder pain occurs in 70 – 95% of people with polymyalgia rheumatica.<sup>2</sup> Between 50 – 70% of people report hip and neck pain.<sup>2</sup> Upper arm pain is also common. Pain is usually bilateral and symmetrical, although it may be worse on one side early in the course of the condition.<sup>3</sup> Pain will usually worsen with movement of the affected area. Pain may radiate to the elbows and knees.<sup>3</sup> There may be tenderness on examination, most commonly in the upper arms, neck and shoulders, usually related to synovial or bursal inflammation. Muscle weakness is not a feature of polymyalgia rheumatica, although this may be difficult to assess due to muscle pain.<sup>5</sup>

### Stiffness

Marked morning stiffness that persists for at least 45 minutes is typical for people with polymyalgia rheumatica.<sup>6</sup> The patient may describe difficulties with daily activities, such as brushing their hair or getting out of bed. In some patients the stiffness will be so severe that rising from a chair or turning over in bed are difficult. Asking the patient about the severity of stiffness in the morning compared to the evening may be helpful. Stiffness and pain that lessens over the course of the day can be important in differentiating polymyalgia rheumatica from other forms of degenerative arthritis, which usually cause pain or stiffness that is worse with activity and worse later in the day.<sup>1</sup>

### Systemic symptoms and signs

Systemic features may be present in approximately one-third of patients and include low grade fever, malaise, anorexia and weight loss.<sup>2</sup> A brief general examination, including assessment of temperature, pulse and blood pressure, is recommended.

### Peripheral symptoms

Symptoms, such as pain or stiffness in the joints of the hands and feet, are present in approximately half of people with polymyalgia rheumatica, however, peripheral symptoms are also common in other, similar conditions, such as rheumatoid arthritis and other inflammatory arthritides.<sup>2</sup> A predominance of peripheral symptoms may suggest an alternative diagnosis, such as rheumatoid arthritis.<sup>3</sup> It is important to also examine the hands, feet, knees and elbows for signs of joint inflammation.

#### Giant cell arteritis symptoms

Always specifically enquire about symptoms that may suggest giant cell arteritis, such as unilateral temporal headaches, scalp tenderness, jaw claudication or visual symptoms.<sup>3</sup>



For further information, see: “Giant cell arteritis”, Page 16.

## Differential diagnosis

The differential diagnosis of polymyalgia rheumatica is critically important, particularly for atypical cases, or where inflammatory markers are normal. Incorrectly diagnosing polymyalgia rheumatica and missing a diagnosis such as cancer or an occult infection can have significant consequences. Conversely, a patient with polymyalgia rheumatica who remains untreated in the short term is unlikely to have any significant adverse effects. The aim should be to rigorously exclude all other possibilities rather than quickly diagnosing polymyalgia rheumatica. Atypical clinical features such as age < 60 years, chronic onset (longer than two months), lack of shoulder involvement, muscle weakness, peripheral joint disease, predominance of pain with little or no stiffness, prominent systemic features, a very high or normal CRP (see “Laboratory investigations”) or lack of response to a trial dose of prednisone (see “Treatment of polymyalgia rheumatica”) should lead to consideration of alternative diagnoses and consultation with a Rheumatologist where necessary.

Conditions that should be considered include:<sup>3,6</sup>

- Giant cell arteritis
- Malignancy

- Rheumatoid arthritis and other arthritides
- Endocrine and iatrogenic causes of proximal myopathy, e.g. hypothyroidism, Cushing's disease, statin-induced myopathy/myalgia
- Osteoarthritis and other degenerative musculoskeletal conditions, e.g. rotator cuff tendinopathy
- Systemic lupus erythematosus or polymyositis
- Fibromyalgia and localised causes of pain
- Occult infection, e.g. sub-acute bacterial endocarditis

### Laboratory investigations

If the patient's presentation suggests polymyalgia rheumatica is likely, the following tests should be requested:<sup>4-6</sup>

- C-reactive protein (CRP)
- Full blood count (FBC)
- Liver function tests (LFTs)
- Creatinine and electrolytes – as a baseline prior to initiation of corticosteroid treatment

An elevated CRP level in a patient with symptoms of polymyalgia rheumatica should increase suspicion of the condition.<sup>6</sup> However, a normal acute phase response does not rule out polymyalgia rheumatica. ESR is sometimes recommended in the literature, however, CRP alone is likely to be sufficient to aid the diagnosis of polymyalgia rheumatica in most people. In addition, some laboratories will no longer accept requests for ESR outside of a limited range of conditions. If the initial CRP is normal, and the patient's symptoms strongly suggest polymyalgia rheumatica, it may be appropriate to then request an ESR at follow-up.

Most patients with polymyalgia rheumatica have mild-to-moderate anaemia, and may have elevated white blood cell and platelet levels.<sup>2</sup> Approximately one-third of patients will have mildly abnormal liver function tests, particularly alkaline phosphatase.<sup>2</sup>

Depending on the patient's symptoms and signs, additional tests may need to be added to rule out other potential diagnoses, including:<sup>6</sup>

- Thyroid stimulating hormone (TSH)
- Rheumatoid factor and, potentially, anticyclic citrullinated peptide (anti-CCP) antibodies
- Serum protein electrophoresis (consider serum free light chain assay if electrophoresis is negative)
- Creatine kinase
- Antinuclear antibodies

### Distinguishing polymyalgia rheumatica from rheumatoid arthritis

Rheumatoid arthritis can be a challenging condition to differentiate from polymyalgia rheumatica, particularly in patients who are subsequently found to have seronegative or late-onset rheumatoid arthritis.<sup>3</sup> Although the initial clinical presentation can be very similar with many overlapping symptoms and signs, the following features may help distinguish between the two conditions:

- Polymyalgia rheumatica is rare in people aged < 50 years, therefore rheumatoid arthritis is a much more likely diagnosis in this age group<sup>5</sup>
- The onset of symptoms tends to be more gradual in people with rheumatoid arthritis
- Typically, symptoms of pain and swelling in the smaller distal joints are more common in people with rheumatoid arthritis, however, approximately half of people with polymyalgia rheumatica will also have involvement of the peripheral joints<sup>3</sup>
- Characteristically the wrist and metacarpophalangeal (MCP) joints are affected in people with rheumatoid arthritis, therefore a patient presenting with myalgia and clinical evidence of symmetric synovitis in the wrists or MCP joints is more likely to have a diagnosis of rheumatoid arthritis than polymyalgia rheumatica<sup>3</sup>
- A family history may increase the individual risk of rheumatoid arthritis, and should be considered<sup>7</sup>

If the clinical diagnosis remains uncertain:

- Rheumatoid factor should be requested, however, a negative test does not rule out the condition as some patients will have seronegative rheumatoid arthritis. If there is still doubt about the diagnosis, anti-CCP antibodies may be useful.<sup>2</sup>
- X-rays of affected joints may show erosive changes consistent with rheumatoid arthritis

A trial of treatment with corticosteroids can be considered in patients who are seronegative for rheumatoid factor and have symptoms and signs that could be indicative of either condition. In a patient with polymyalgia rheumatica there is likely to be a rapid, strong clinical response to low dose prednisone (15 mg). If the patient has rheumatoid arthritis, the response to low dose prednisone is likely to be less pronounced.<sup>3,8</sup> In some patients, clinical features more characteristic of rheumatoid arthritis may evolve during the trial of corticosteroid.

## Imaging is not essential for diagnosis

If ultrasound is accessible, assessment of the shoulder and hip joints can be considered.<sup>6</sup> Bursitis and synovitis are common manifestations of polymyalgia rheumatica.<sup>2</sup> Plain x-rays of affected joints will usually be normal and therefore are not required for investigating polymyalgia rheumatica.

Additional investigations such as CT scanning, and MRI imaging may be used in a secondary care setting to help identify bursitis, synovitis or tenosynovitis in the shoulders and hips in atypical cases, and for ruling out other potential diagnoses.

## Treatment of polymyalgia rheumatica

Corticosteroids are the first-line treatment for polymyalgia rheumatica. Corticosteroid treatment is predominantly for symptom control, and there is no clear evidence that it will alter the natural history of the condition, which is largely self-limiting.

Once all other differential diagnoses have been considered, the patient should be assessed for response to an initial dose of prednisone, 15 mg, daily.<sup>6</sup> The dose should be taken in the morning, with food.

If the patient reports a significant improvement in their symptoms within one week, this is consistent with polymyalgia rheumatica, and treatment can continue.<sup>6</sup> Alternative diagnoses should be considered if there is a minimal response to corticosteroid treatment.

The patient's acute phase response, measured with CRP, should normalise within four weeks.<sup>6</sup>

The British Society for Rheumatology guidelines suggests the following method for titrating the dose of prednisone in people with polymyalgia rheumatica:<sup>6</sup>

- Initial dose – 15 mg, once daily, for three weeks, followed by;
- 12.5 mg, once daily, for three weeks, followed by;
- 10 mg, once daily, for four to six weeks, followed by;
- A reduction of 1 mg from the daily dose, every four to eight weeks

In practice, Rheumatologists may use a faster tapering regimen to lessen exposure to prednisone, such as reducing the dose every two weeks, down to 10 mg, followed by reductions of 1 mg per month, depending on the patient's symptoms. If

the patient is at higher risk of adverse effects from long-term steroid use, e.g. is elderly or has co-morbidities, discuss an appropriate dosing regimen with a Rheumatologist.

If symptoms of polymyalgia rheumatica reoccur during the dose tapering period, return the patient to their previous steroid dose and then re-start the taper again from that point. The low dose "tail" of the taper will need to be very gradual in some people to prevent symptom recurrence. Some patients will require treatment with low-dose corticosteroids for two to three years due to recurrent relapses.

Vitamin D supplements should be prescribed alongside long-term corticosteroid treatment for all people with polymyalgia rheumatica. Adequate dietary calcium, or supplementation if this is not possible, is also necessary.

Bisphosphonates should be considered in patients with a previous history of fragility fractures or reduced bone-mineral density.<sup>6</sup>

A proton pump inhibitor (PPI), such as omeprazole may be considered for people who experience adverse gastrointestinal effects when taking prednisone.<sup>6</sup>

 For further information, see "Practical consideration when prescribing long-term corticosteroids".

## Follow-up of people with polymyalgia rheumatica

Early follow-up to assess the response to treatment is recommended. A follow-up consultation should be scheduled within a few days after starting corticosteroid treatment, and then further follow up appointments scheduled one, two, three and six weeks later, where possible. Follow-up should then occur once every three months for the duration of corticosteroid treatment.

A history and clinical examination including an assessment for symptoms and signs of giant cell arteritis, such as scalp tenderness, temporal artery tenderness and new-onset or new type of headache, should be included in each follow-up. If symptoms of giant cell arteritis arise, the patient should be presumed to have the condition, and referred to secondary care for temporal artery biopsy.<sup>6</sup> Also assess for symptoms and signs of corticosteroid adverse effects (see: "Practical considerations when prescribing long-term corticosteroids" for further information).

Clinical signs and symptoms are the primary marker for relapse,

with laboratory tests providing supporting information only.<sup>1</sup> CRP, FBC, creatinine, electrolytes and HbA<sub>1c</sub> tests\* (due to the increased risk of diabetes in people taking long-term steroids) are recommended at each follow-up consultation,<sup>6</sup> however, in practice, not all tests would be necessary in each follow up appointment and this is based on clinical judgement.

Relapses of polymyalgia rheumatica symptoms should be treated with a return to the higher, previous dose of prednisone.<sup>6</sup> After two relapses, consideration should be given to a trial of disease-modifying anti-rheumatic drugs (DMARDs), usually methotrexate.<sup>6</sup> This will require consultation with a Rheumatologist, and if a DMARD is prescribed,

regular monitoring is necessary. The dosing and monitoring regimen should be decided upon in consultation with the Rheumatologist. Methotrexate is usually continued until the corticosteroids can be tapered without the recurrence of polymyalgia rheumatica symptoms.<sup>4</sup> Once the steroids have been successfully tapered, methotrexate can usually be tapered over approximately three months.<sup>4</sup>

\* A fasting glucose test should be used for monitoring in the first two months of steroid treatment, as serum glucose will rise too rapidly to be accurately captured by HbA<sub>1c</sub>. After two months, an HbA<sub>1c</sub> test can be used.

## Practical considerations when prescribing long-term corticosteroids

Corticosteroids are associated with significant adverse effects and they must be slowly tapered rather than stopped abruptly. The lowest effective dose should be used, then tapered and stopped as soon as possible.

The following practice points should be considered whenever a patient is prescribed corticosteroids long-term:<sup>9</sup>

- The patient's co-morbidities and risk factors for adverse effects should be evaluated and managed where indicated, these include; hypertension, diabetes, peptic ulcer, recent fractures, cataract/glaucoma, chronic infection, dyslipidaemia and concurrent NSAID use
- During the course of treatment, monitor body weight and blood pressure, assess for peripheral oedema and heart failure and test serum lipids, HbA<sub>1c</sub> (or fasting glucose in the first two months) depending on the individual patient's risk of adverse effects, dose and duration
- If the patient's dose is  $\geq 7.5$  mg, daily, for more than three months, vitamin D supplementation is necessary, along with adequate dietary calcium
- Bisphosphonates should be prescribed to patients with risk-factors for osteoporosis
- Patients treated with corticosteroids and NSAIDs should be given appropriate gastro-protective medicines, usually a proton pump inhibitor

- Patients taking corticosteroid treatment for longer than one month, who need to undergo surgery, will require perioperative management with adequate glucocorticoid replacement to overcome potential adrenal insufficiency

### Tapering the dose

Tapering must be done carefully to avoid relapses of the condition and potential adrenal deficiency resulting from hypothalamic-pituitary-adrenal axis (HPA) suppression. Higher doses of corticosteroid, e.g. 20 mg daily, for more than three weeks, or bedtime dosing increase the likelihood of HPA axis suppression. Higher doses also increase the likelihood of adverse effects. The taper is usually started as soon as symptoms are under control. The dose is reduced by 10% every two to four weeks depending on the severity of symptoms, response to prednisone and the starting dose. The individual condition being treated will alter the length of the taper, e.g. in a person with polymyalgia rheumatica, the course of treatment is usually two to three years, with a gradual taper period. The dose of prednisone should be titrated against the patient's symptoms, not their acute phase response, i.e. the dose may not need to be increased when the CRP rises if the patient remains asymptomatic.

## The adverse effects of corticosteroid treatment

Adverse effects of corticosteroids include:<sup>10</sup>

- Skin changes and disorders, e.g. thinning and bruising, striae, acne, alopecia and hirsutism
- Body composition changes, e.g. weight gain, Cushingoid features
- Ocular disorders, e.g. glaucoma and cataracts
- Cardiovascular disease
- Gastrointestinal disorders, e.g. dyspepsia, oesophagitis, gastritis, ulcers, bleeding
- Osteoporosis
- Central nervous system changes, e.g. mood changes, restlessness, depression, psychosis
- Diabetes
- Renal changes, e.g. hypertension and fluid retention

Older age, higher cumulative doses of corticosteroids and female sex increase the risk of adverse effects occurring.<sup>11</sup>

## Preventing the adverse effects of corticosteroids

Vitamin D supplements should be prescribed alongside long-term corticosteroid treatment, in patients taking doses of  $\geq 7.5$  mg, daily, for more than three months.<sup>9</sup> Colecalciferol\* 1.25 mg, once monthly, is recommended for vitamin D supplementation.<sup>10</sup> Patients do not need their vitamin D levels to be tested, but if they have been, and severe deficiency has been detected, a loading dose of one 1.25 mg tablet, daily for ten days is recommended.<sup>10</sup> Calcitriol, 500 – 750 nanograms, daily, can be used instead of colecalciferol for patients with severe renal impairment.<sup>10</sup>

\* Recommended International Non-proprietary Names (RINN or INN) spelling

Calcium supplementation is also recommended, but there have been concerns that calcium supplementation may increase cardiovascular risk, particularly in older people.<sup>12,13</sup> General dietary advice may be more appropriate for most people, and supplementation reserved for people in whom dietary calcium intake alone is insufficient. If calcium supplementation is required, oral calcium carbonate 1.5 g, daily, can be considered.<sup>10</sup>

Ideally a bone-mineral density (BMD) scan of the lumbar spine and hip should be requested for patients when starting long-term corticosteroids, however, this depends on the availability and funding of the local service, e.g. some services require that patients have been taking corticosteroid treatment for three months before a scan is prioritised.<sup>2</sup>

Bisphosphonates should be considered in patients with a previous history of fragility fractures or reduced bone-mineral density.<sup>6</sup> Alendronate or zoledronic acid are recommended for most people who require a bisphosphonate for corticosteroid-related osteoporosis prevention, based on patient preference and the expected length of corticosteroid treatment.

Alendronate, 70 mg, once weekly, should be taken first thing in the morning, on an empty stomach, with a full glass of water to ensure adequate absorption.<sup>10</sup> The patient should then refrain from eating or taking other medicines and remain upright (i.e. sitting or standing) for thirty minutes to minimise the risk of oesophageal irritation or erosion.

Zoledronic acid, 5 mg IV infusion over 15 minutes, once per year is an alternative.<sup>10</sup> The patient should be well hydrated prior to starting the infusion. The patient should have their renal function assessed prior to starting, and be informed that dizziness and influenza-like symptoms are common after infusion.

The Special Authority requirements for the initial application for either alendronate or zoledronic acid require that:

- The patient is receiving systemic glucocorticosteroid treatment ( $\geq 5$  mg per day prednisone equivalent) and has already received or is expected to receive treatment for at least three months, and;
  - The patient has documented BMD  $\geq 1.5$  standard deviations below the mean normal values in young adults (i.e. T-Score  $\leq 1.5$ ), or;
  - The patient has a history of one significant osteoporotic fracture demonstrated radiologically, or;
  - The patient has had a Special Authority approval for alendronic or zoledronic acid\* (underlying cause – glucocorticosteroid therapy) or raloxifene

\* If either alendronate or zoledronic acid has been approved, and the other bisphosphonate is to be trialled, then the patient is considered to have already meet the requirements for the new medicine.

If a funded bisphosphonate is required, but the patient does not meet the Special Authority requirements of alendronate or zoledronic acid, etidronate disodium may be used, however, etidronate is significantly weaker than either alendronate or zoledronic acid.

Etidronate disodium is prescribed at 400 mg, daily on and empty stomach, for 14 days, repeated every three months.

 Risedronate, an alternative to alendronate, is to be listed on the Pharmaceutical Schedule, without restrictions, from 1 September, 2013.

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