bpacnz
PRIMARY CARE
UPDATE SERIES

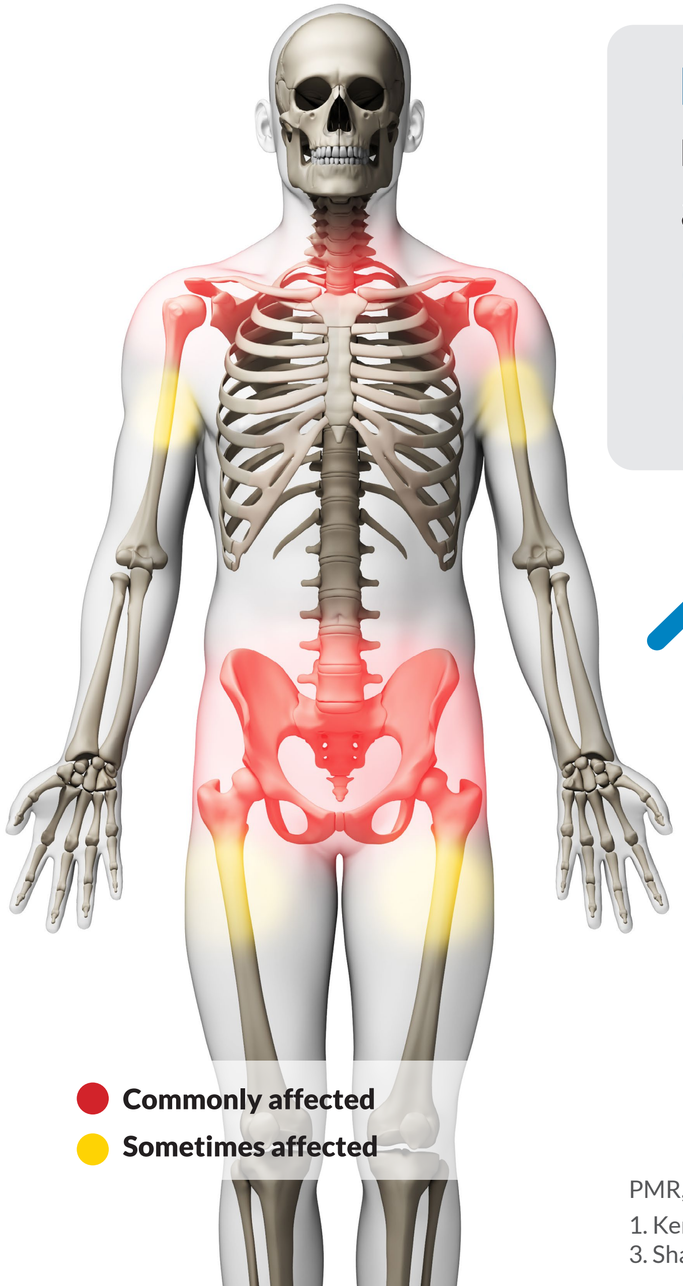
04

POLYMYALGIA RHEUMATICA

PROCEED WITH CAUTION

JULY 2021
VER 1.1

Polymyalgia rheumatica (PMR) – an overview



PMR is an inflammatory rheumatic condition characterised by **aching pain** and **morning stiffness**, predominantly at the **shoulders, neck and hip girdle**, but also sometimes in the upper arms and thighs

- Symptoms are **usually bilateral and symmetrical**
- **Onset is rapid**, usually within a day and up to two weeks
- **Systemic symptoms may be present**, e.g. fever, malaise and weight loss

Almost all people affected are **aged >50 years and of European ethnicity**

- The risk of PMR increases progressively with age until approximately 80 years
- More common in **females** compared with males (approximately 2:1)

Incidence estimates vary (unknown in NZ/Australia):

Northern Europe:
33.6–112.6 per 100,000 people
e.g. Norway, Sweden, Denmark, UK

Southern Europe:
3.2–27.4 per 100,000 people
e.g. Italy, Spain, Turkey

PMR, polymyalgia rheumatica.

1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Sharma A, Mohammad, Turesson C. Sem Arthritis Rheum. 2020;50:1040–8;
3. Sharma A, Mohammad, Turesson C. Sem Arthritis Rheum. 2020;50:1040–8.

Polymyalgia rheumatica (PMR) – an overview

Cause: poorly understood

Muscle: histopathologically normal

Bone/joint: various proximal articular and periarticular structures (bursae and tendons) are affected by inflammatory processes

Current theory: inflammation is potentially triggered by environmental factors (e.g. viral infection) in genetically/immunologically susceptible people

- Autoantibodies are <u>not</u> a feature in patients with PMR (as they are in patients with SLE)

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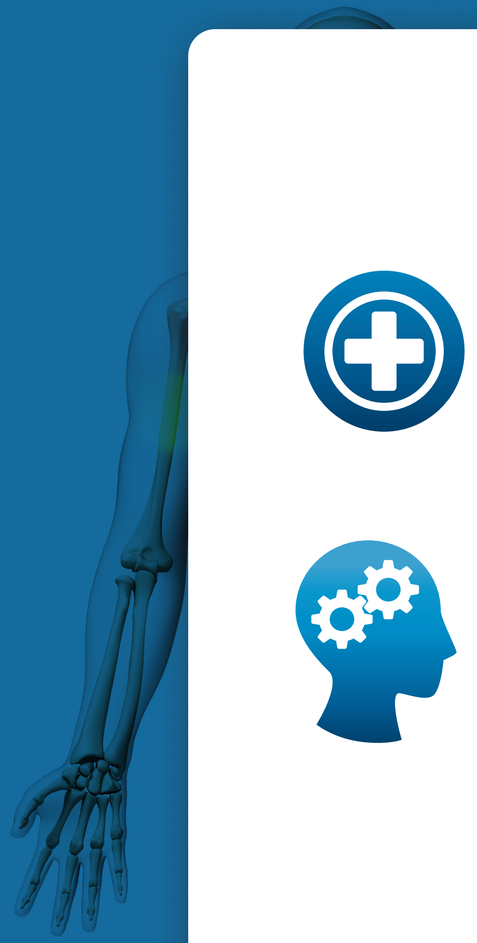

Commonly affected

Sometimes affected

PMR, polymyalgia rheumatica.

1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Sharma A, Mohammad, Turesson C. Sem Arthritis Rheum. 2020;50:1040–8;
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A diagnosis of PMR in primary care is made clinically, supported by laboratory findings

Patient with all of the following features:

- Aged ≥50 years at onset*
- Bilateral shoulder or hip girdle pain; may be unilateral in early stages (however this should increase suspicion of an alternative diagnosis)
- Morning stiffness lasting >30 minutes
- Symptoms are worst with inactivity (often present at night)
- Symptom duration lasting >2 weeks
- Elevated CRP and/or ESR

Exclude other possible causes of symptoms, such as:

- Active infection
- Malignancy
- Active polyarthritis associated with other musculoskeletal conditions, e.g. RA
- Spondyloarthropathy
- Endocrine disorders, e.g. hyperthyroidism
- Inflammatory myopathy (polymyositis)
- Drug-induced myalgia
- Hypercalcaemia
- Vitamin D deficiency

Check for evidence of **giant cell arteritis (GCA)** – see next slide

Still unsure?

Refer to secondary care and **cautiously initiate treatment** while awaiting the appointment

Confident it's PMR?

Initiate treatment with corticosteroids (see later slide)

No response to treatment?

Reconsider alternative diagnoses; refer if needed

Response to treatment?

Diagnosis of PMR is likely; continue treatment/monitoring

Key laboratory investigations:

- CRP (and ESR if CRP is negative)
- FBC
- Creatinine and electrolytes
- Urinalysis (dipstick)
- Liver function tests

Investigations as needed, such as:

- Thyroid stimulating hormone (TSH) level – if thyroid abnormality is suspected
- Rheumatoid factor/anti-CCP antibodies – if RA is suspected
- Serum creatinine kinase – if polymyositis is suspected
- Chest X-ray – if malignancy is suspected
- Ultrasound/MRI – if synovitis suspected

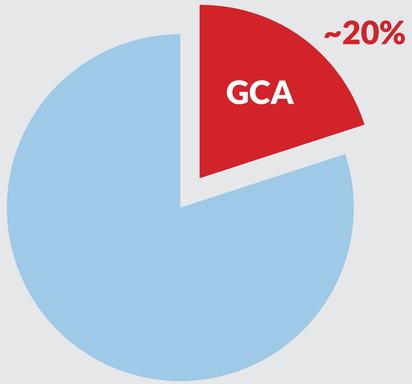
* If the patient is aged less than 50 years, yet has features that strongly suggest PMR is the cause, then refer to secondary care for further assessment.

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FBC, full blood count; PMR, polymyalgia rheumatica; RA, rheumatoid arthritis.

1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Ameer F, McNeil J. AFP. 2014;43:373–6.

Are cranial symptoms also present? **The patient may have giant cell arteritis (GCA)**

People with PMR



- PMR is more prevalent than GCA overall
- GCA can occur in the absence of PMR (approximately half of patients with GCA never develop PMR)
- GCA is more common in females than in males (3:1)

GCA involves inflammation of blood vessels in the head, neck and chest

- It is closely linked to PMR – they are considered to be "*different manifestations of the same disease process*" – however, **the relationship is not completely understood**

Possible acute clinical features:

- New-onset temporal headache
- Temporal artery tenderness
- Jaw/tongue pain when chewing
- Visual impairment, e.g. diplopia, reduced visual acuity, acute visual loss
- Systemic symptoms, e.g. fever

Possible longer-term complications:

- Permanent visual impairment due to ischaemic optic neuropathy (highest risk during the first 3 months)
- Aortic dissection
- Aortic aneurysm
- TIA/stroke

If GCA is suspected, or if the patient has suspected PMR with a CRP >100 mg/L, then **immediately initiate corticosteroid treatment** and **refer the patient for urgent temporal artery biopsy**

- The starting dose of corticosteroids is much higher if the patient has GCA
- If the biopsy indicates that GCA is unlikely, then reduce the corticosteroid dose over a few days to a level more appropriate for managing PMR alone (see next slide)

Low dose aspirin (100 mg daily) can also be considered in some patients, e.g. those with a high arteriosclerotic risk, to reduce cranial ischaemic complications

- This is not firmly established across all international guidelines; if in doubt, consult with a rheumatologist
- A PPI may also be required if aspirin is prescribed due to the risk of gastrointestinal bleeding

CRP, C-reactive protein; PMR, polymyalgia rheumatica; PPI, proton pump inhibitor; TIA, transient ischaemic attack.

1. Sharma A, Mohammad, Turesson C. Sem Arthritis Rheum. 2020;50:1040–8; 2. Bienvenu B, Ly KH, Lambert M, *et al*. Rev Med Interne. 2016;37:154–65; 3. Sharma A, Mohammad AJ, Turesson C. Semin Arthritis Rheum. 2020;50:1040–8.

Corticosteroids are used to treat patients with PMR

The goals of treatment:

- Relieve muscle pain and stiffness
- Resolve any systemic symptoms

Prednisone is generally the corticosteroid of choice

- Wait until laboratory results are available before starting treatment, e.g. CRP (or ESR) results, unless you suspect GCA

	Initial prednisone dose	Tapering protocol once there is a treatment response *(see next slide)*	Possible duration of treatment
PMR alone	**In general: 15 mg/day for 2–4 weeks** • Mild symptoms, relevant co-morbidities or other risk factors for corticosteroid-related adverse effects, or frail patient: 7.5–10 mg/day • Severe initial symptoms: 20 mg/day • Refractory symptoms after one week: consider increasing dose from 15 → 20 mg/day (see next slide)	Reduce by 2.5 mg every 2–4 weeks until at 10 mg/daily, then reduce dose by 1 mg every month; refer patient if dose cannot be decreased below 10 mg/daily	Patients often need to stay on 5 mg prednisone to remain symptom free, with the average duration of use being 18 months. Some patients may need 2–3 years of prednisone use in total (sometimes longer).
PMR + GCA	**In general: 60 mg/day for 2–4 weeks** (+ refer the patient for temporal artery biopsy) • or 1 mg/kg for patients with a low BMI (<18.5 kg/m^2)	Most patients should be able to taper from 60 mg to 20 mg daily over 2–3 months, then from 20 mg to 10 mg daily over 2–3 months, then a more gradual tapering from 10 mg (e.g. in 1 mg increments every 4–8 weeks provided there are no relapses)	Patients may need a longer duration of prednisone use than for PMR alone (see above).

BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

1. Dejaco C, Singh YP, Perel P, *et al*. Ann Rheum Dis. 2015;74:1799–1807; 2. Buttgereit F, Dejaco C, Matteson EL, *et al*. JAMA. 2016;315:2442–58; 3. NZ Formulary (NZF). v107. Available at https://nzf.org.nz/ (Accessed July, 2021)

Assessing the patient's response to corticosteroid treatment

Primary aspect to consider

Monitor the patient's clinical response: expect a prompt improvement in symptoms within 24–48 hours of treatment initiation

E.g. an improvement in morning stiffness and pain, improved ability to raise the arms above shoulder height (or other movements affected) consistent with the patient's baseline mobility before the onset of symptoms

If symptoms do not improve substantially within a week, then re-consider alternative diagnoses

- If PMR is still the most likely cause of symptoms, then consider increasing corticosteroid dose (up to a maximum of 20 mg daily)

Additional aspect to consider

Monitor CRP (or ESR) **levels if they were initially raised**

- These should decrease within a few days and normalise within 2–3 weeks

If the patient responds and symptoms are under control, then **taper the corticosteroid dose progressively and slowly** (as per information on previous slide), with the aim of stopping use as soon as possible
(this process depends on the patient's symptoms and their risk of experiencing corticosteroid-related adverse effects – see later slide)

Relapses are common when tapering the prednisone dose; if this occurs, **increase the dose back to pre-relapse levels**

- Relapses are most likely during the first 18 months and within one year of treatment withdrawal
- Clinical signs and symptoms are the primary marker for relapse (do not increase the dose of prednisone based on a single elevated CRP measurement if the patient remains asymptomatic)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

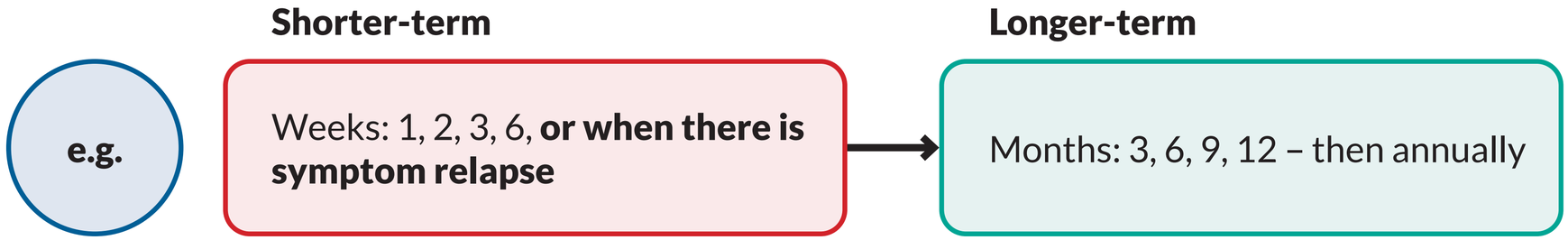
1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Ameer F, McNeil J. AFP. 2014;43:373–6.

Assessing the patient's response to corticosteroid treatment

The longer-term outlook

Monitor the patients clinical status regularly at first then dial-back once symptom control improves

- Laboratory monitoring may include assessment of CRP or ESR (if initially raised), FBC, creatinine, electrolytes and HbA_{1c} (if there are risk factors for diabetes – see later slide)



PMR is usually self-limiting* (average duration is approximately 18 months); however, relapses of symptoms occur in approximately half of patients in the long-term

* In some cases, patients may continue to require low doses of corticosteroids for very long durations, e.g. >5 years. For more information, see the final slide.

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FBC, full blood count.

1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Ameer F, McNeil J. AFP. 2014;43:373–6.

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What are the alternatives to corticosteroids?

In rare cases, patients with mild PMR may be able to manage symptoms with **NSAIDs** alone – however, this should ***not*** be considered as a standard treatment choice

- Short-term NSAID use may be useful (alongside prednisone) in some patients with pain related to other co-morbidities (e.g. osteoarthritis)

For most patients with PMR who require an alternative to corticosteroids – either because they are contraindicated or ineffective – treatment decisions are usually guided by a Rheumatologist

Methotrexate is recommended in some international guidelines and may be considered on a case-by-case basis

- There is currently insufficient evidence to support the routine use of biologics

NSAIDs, non-steroidal anti-inflammatories; PMR, polymyalgia rheumatica.

1. Dejaco C, Singh YP, Perel P, *et al.* Ann Rheum Dis. 2015;74:1799–1807; 2. Liew DF, Owen CE, Buchanan RR. Aust Prescr. 2018;41:14–9

The prognosis is generally very good with prompt treatment

Although pain and functional limitations can impact the patients quality of life, they can usually be reduced (or eliminated) with treatment, and **there is no evidence that PMR alone increases mortality or causes structural damage**

- If the patient has co-morbid GCA, then this is associated with a worse prognosis if it is not treated promptly

Morbidity in patients with PMR more often relates to the **long-term adverse effects of medicines used to treat it**, i.e. corticosteroids

- Management decisions should weigh the benefits of preventing relapses against the risk of these adverse effects

GCA, giant cell arteritis; DEXA, dual energy X-ray absorption; PMR, polymyalgia rheumatica; PPI, proton pump inhibitor.

1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Charlton R. Ther Clin Risk Manag. 2012;8:173–9

The prognosis is generally very good with prompt treatment

Final question: ***"What about those patients that struggle to make that final corticosteroid dose reduction, and continue to require treatment?"***

E.g. 5+ years

Consider adding methotrexate to their regimen. Once tolerance has been established, then trial stopping the corticosteroid, and if they remain symptom free then attempt to taper off methotrexate

Consider whether any other co-morbidities have since developed, such as rheumatoid arthritis, which may require a different approach to treatment

If in doubt, **refer the patient to a rheumatologist**

* Bon
available or the cost of a scan is a barrier for the patient, initiation of treatment can be made on the basis of a fracture risk calculation alone, e.g. with FRAX or Garvan hip fracture risk scores.
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1. Kermani TA, Warrington KJ. Lancet. 2013;381:63–72; 2. Charlton R. Ther Clin Risk Manag. 2012;8:173–9