# Polymyalgia Rheumatica and Giant Cell Arteritis

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## Learning Objectives

1. Evaluate risk factors for the development of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA).
2. Assess common signs and symptoms consistent with a diagnosis of PMR and/or GCA.
3. Interpret laboratory and other diagnostic tests used to assist in the diagnosis of PMR and GCA.
4. Evaluate the role and expected outcomes of pharmacotherapy in the management of PMR and GCA.
5. Design, implement, monitor, and modify a pharmacotherapeutic plan for a patient with PMR, GCA, or both.

## Introduction

Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA; sometimes referred to as temporal arteritis) are common and interrelated inflammatory conditions that almost exclusively affect adults older than 50 years. Polymyalgia rheumatica and GCA are often considered manifestations of the same disease because of their overlapping clinical presentations and pathophysiology. Although related, a specific diagnosis is essential because of differences in pharmacologic management and in the risk of vascular complications (including blindness) associated with GCA. About one-half of patients affected by GCA also meet diagnostic criteria for PMR; however, only about 10% of patients with PMR also have GCA. Corticosteroids remain the cornerstone of pharmacotherapeutic management of both PMR and GCA. Because of the complications associated with corticosteroids, the search continues for alternative agents and steroid-sparing therapies for the management of PMR and GCA.

### Epidemiology and Risk Factors

Polymyalgia rheumatica affects about 1 in 133 adults older than 50 years. Women are affected by PMR 2–3 times more often than men. Giant cell arteritis is less common than PMR and has an annual incidence of between 20 and 30 per 100,000 adults older than 50 years. Increased age is the strongest risk factor for both disorders, with the peak incidence occurring between age 70 years and 80 years. In addition, people residing in northern latitudes appear to be at greatest risk of developing PMR or GCA. The increased incidence at higher latitudes and in people residing in Scandinavian countries, or with strong Scandinavian ancestry, lends support to environmental and genetic causes. The incidence of PMR has been fairly stable over time; however, the incidence of GCA appears to have increased slightly. The overall prevalence of PMR and GCA is expected to increase with the rapid increase in the number of people 65 years or older in developed countries.

### Pathophysiology

The exact cause of PMR and GCA is unknown; they are thought to be polygenic inflammatory disorders, with several genetic and environmental factors likely influencing patient susceptibility and disease severity. In addition to the latitude gradient, there is evidence of cyclic patterns and clustering with GCA, which suggests a possible infectious etiology. A relationship between PMR and GCA with parainfluenza virus type 1, and cyclic peaks during epidemics of *Mycoplasma pneumoniae, Chlamydia pneumonia*, and parvovirus B19 has been suggested, but this has not been found in all studies. There is evidence of immunogenetic differences between PMR and GCA and that certain genes may contribute separately to the susceptibility of one or the other. In both PMR and GCA, the systemic manifestations are a result of the production of pro-inflammatory cytokines derived from macrophages, including tumor necrosis factor, interleukin (IL)-1, and IL-6. Interferon-γ expression can be identified in temporal artery biopsy samples from patients with GCA (but not with isolated PMR) and has been associated with the formation of giant cells, vasculitis, and ischemia.

### Clinical Manifestations and Complications

The clinical signs and symptoms of PMR and GCA overlap to some degree, but important subtle differences exist. More commonly in PMR than in GCA, patients may present with aching, stiffness, and pain in the more proximal joints of the neck, shoulders, and pelvic girdle.

## Abbreviations in This Chapter

| | |
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| CRP | C-reactive protein |
| ESR | Erythrocyte sedimentation rate |
| GCA | Giant cell arteritis |
| IL | Interleukin |
| PMR | Polymyalgia rheumatica |
| PMR-AS | Polymyalgia rheumatic activity score |

Stiffness in the morning typically lasts for more than 30 minutes and usually interferes with daily functioning. Pain is generally more severe with movement and can also affect sleep at night. Other nonspecific symptoms that may be seen in either PMR or GCA include fever, fatigue, anorexia, weight loss, anemia, and depression. With GCA, new-onset headache is one of the more common symptoms and is seen in up to 80% of patients. Also with GCA, examination may reveal thickened, tender, and red temporal arteries. Scalp tenderness can also occur and is commonly revealed in the context of combing or brushing hair. Partial or complete loss of vision can be an early manifestation of GCA and can progress to total blindness if not addressed. Amaurosis fugax is an important visual symptom that can precede permanent visual symptoms. Patients often describe this symptom as being like a shade drawn over part or all of their vision, and this may include one or both eyes. Unfortunately, established visual impairment is not usually reversible.

Although the mortality rate for people who develop PMR or GCA is not significantly different for their sex and age, morbidity is higher (particularly with GCA). With GCA, in addition to vision loss, other less-common vascular and neurologic complications occur including transient ischemic attacks, cerebral infarction, ischemic neuropathies, thoracic aortic aneurysms, and aortic dissection.

# Diagnosis

There are two sets of similar diagnostic criteria for PMR, with one set including response to corticosteroids as a diagnostic feature (Table 1-1). The American College of Rheumatology has developed criteria for the classification of GCA, although these criteria are not considered useful for diagnosing GCA. Temporal artery biopsy is necessary if GCA is suspected or if a patient thought to have isolated PMR does not respond adequately to low doses of steroids.

### Laboratory Evaluation

Laboratory studies of PMR and GCA are not specific to the disease states but reflect the underlying inflammatory aspects of both disorders. The erythrocyte sedimentation rate (ESR) is included in the diagnostic criteria for PMR, with levels of 40 mm/hour or greater consistent with the diagnosis. The American College of Rheumatology classification of GCA includes an elevated ESR of 50 mm/hour or greater as a primary feature. However, not all patients with PMR or GCA will present with an elevated ESR, and up to 20% of trial subjects with PMR or GCA have not presented with elevated ESR levels. An elevated C-reactive protein (CRP) concentration may be a more specific marker of disease activity and inflammation in both disease states, but currently, neither the diagnostic criteria for PMR nor the American College of Rheumatology classification of GCA includes elevated CRP as part of the assessment criteria. Reports of the use of CRP in assessing these disorders began to appear in the literature several years after publication of the diagnostic criteria for PMR and classification of GCA. There is emerging evidence that IL-6 is a more sensitive indicator of disease activity than either ESR or CRP; however, this test is not routinely available from most laboratories. Test results for rheumatoid factor and antinuclear antibodies are usually negative. About one-half of patients have findings of anemia, commonly normochromic and normocytic.

### Role of Imaging Studies

Imaging studies are of little use and have no real role in the diagnosis of PMR when there is no suspicion of GCA. Temporal artery biopsy continues to be the gold standard test for confirming the diagnosis of GCA. However, imaging studies using ultrasonography, magnetic resonance imaging (MRI), and positron emission tomography (PET) have been investigated as less-invasive means of evaluating the temporal artery, as well as other large vessel inflammations seen with GCA. Ultrasonography may be useful to help identify the optimal site for surgical biopsy. Findings with ultrasonography of the temporal artery include edema, which may be described as a halo that is visible around the lumen of the temporal artery. This halo will normally disappear after about 2 weeks of steroid therapy. Magnetic resonance imaging and PET can be useful for determining large artery involvement in GCA; however, use of PET for smaller arteries (i.e., the size of the temporal artery) is limited. High-resolution contrast-enhanced MRI can be supportive in identifying temporal artery inflammation. None of these studies is as valuable as temporal artery biopsy, however, so it remains the standard of care for the diagnosis of GCA.

# Therapy for PMR and GCA

The primary goals of PMR therapy are to reduce the systemic manifestations (including pain and stiffness) and to improve overall patient functioning. Additional goals of PMR therapy include minimizing the risk of clinical relapse and adverse events related to corticosteroid treatment. The goals of GCA therapy are similar to those of PMR therapy but with important differences. Visual impairment is a common complication of GCA. Vision loss that is present before starting treatment is most often irreversible; therefore, initiating therapy as soon as the diagnosis of GCA is suspected is critical. Preventing other vascular complications related to GCA (e.g., aortic dissection, stroke) are important goals when treating patients with GCA. It is important to reiterate that patients can receive diagnoses of concurrent GCA and PMR. In this circumstance, treatment goals for both diagnoses should be considered.

Nonpharmacologic management plays a limited role in PMR and GCA. Initial pharmacologic therapy for PMR

and GCA consists solely of the use of corticosteroids. After an initial course of treatment, steroids are tapered and are usually continued for up to 1–2 years. However, in some instances, clinical relapse during steroid taper may necessitate the use of steroids for several years. The adverse effects associated with long-term steroid use can complicate the treatment of both PMR and GCA.

## Corticosteroids

### Empiric Dosing, Tapering, and Withdrawal

Initial prednisone doses for treating PMR in the absence of GCA are recommended at between 10 mg and 20 mg orally daily. Most patients will have a significant clinical response (i.e., improvement in pain, stiffness, and functioning) within several days to 1 week. Inflammatory markers such as ESR or CRP can normalize within 2–4 weeks. If patient symptoms do not respond initially to this dose, the prednisone dose should be increased to 30 mg/day. If an adequate response is not observed with higher doses of prednisone, the diagnosis of PMR may be incorrect. If the ESR is highly elevated (80 mm/hour or greater) after the use of higher doses of steroids, a temporal artery biopsy should be strongly considered to rule out the possibility of concurrent GCA. If an adequate response is seen after initial steroid use, then the dose should be continued for 2–4 weeks and then tapered at a rate of 2.5 mg every 2 weeks to a daily dose of 10 mg. Subsequent tapering can continue at a rate of 1–2 mg each month, or alternatively at a rate of 2.5 mg/day every 2–3 months, until the prednisone is discontinued.

Clinical symptoms and ESR or CRP concentration can be used to help guide steroid dose changes and the prednisone taper rate. Isolated increases in ESR or CRP concentration without corresponding changes in clinical symptoms should not be used to guide prednisone dose changes. A disease activity scale, the PMR activity score (PMR-AS), has been developed to help objectively evaluate clinical symptoms and monitor disease activity over time. The components of the PMR-AS include a subjective physician-rated visual analog disease activity score of 1–10; a visual analog pain score of 1–10; CRP in milligrams per deciliter; morning stiffness time in minutes (multiplied × 0.1); and ability to elevate upper limbs (0–3). Component scores are added to obtain a total score. Scores less than 7 indicate low disease activity, scores of 7–17 indicate moderate disease activity, and scores greater than 17 indicate high PMR activity. Absolute scores on the PMR-AS may have some use in helping guide decisions regarding prednisone dose changes; however, the change in PMR-AS from previous evaluations may be a better guide in making such decisions. The total duration of steroid therapy is typically within 1–2 years, but some patients may need therapy for longer periods. Relapses that involve a return of clinical symptoms and an increase in ESR or CRP concentration may require reinitiation or an increased dose of prednisone. Relapses most often occur when the daily prednisone dose drops below 7.5 mg/day or has been discontinued. The rate with which prednisone is tapered can also affect the risk of relapse.

The initial dose of prednisone in patients with confirmed or suspected GCA is higher than with PMR and should be between 40 mg and 60 mg daily, or 1 mg/kg/day up to a maximum of 60 mg/day. If GCA is suspected but a temporal artery biopsy has not yet confirmed the diagnosis, higher doses of prednisone should not be delayed until the confirmation of biopsy results, particularly if visual or ischemic symptoms are noted. Intravenous pulse therapy with 1 g/day of methylprednisolone for the first 3 days is advocated in patients with GCA and evidence of severe ischemic changes or recent visual loss. However, there is no evidence to suggest this approach improves outcomes. One small randomized trial using intravenous methylprednisolone 15 mg/kg for 3 days suggested that this approach allows more rapid tapering of steroids and a higher rate of discontinuation of steroids compared with oral prednisone. A larger trial of pulse methylprednisolone, but at a lower dose, did not show any advantage of this route of administration compared with oral prednisone. In a retrospective study of patients with GCA and ischemic visual changes, orally administered high-dose prednisone

**Table 1-1. Diagnostic Criteria for Polymyalgia Rheumatica and the American College of Rheumatology Classification Criteria of Giant Cell Arteritis[a]**

| Polymyalgia Rheumatica | Giant Cell Arteritis |
|---|---|
| Age at onset ≥ 50 years | Age at onset ≥ 50 years |
| ESR > 40 mm/hour | ESR ≥ 50 mm/hour |
| Morning stiffness lasting > 1 hour | New headache |
| Exclusion of all other diagnoses except giant cell arteritis<br>or | Temporal artery abnormality, including tenderness or decreased pulsation unrelated to arteriosclerosis |
| Pain persisting for at least 1 month and involving two of the following areas: neck, shoulders, and/or pelvic girdle | |
| Rapid response to prednisone ≤ 20 mg/day | |

[a]Abnormal findings on biopsy of temporal artery.
ESR = erythrocyte sedimentation rate.
Information from Chuang T-Y, Hunder GG, Ilstrup DM, Kurland LT. Polymyalgia rheumatica: a 10-year epidemiologic and clinical study. Ann Intern Med 1982;97:672–80; Hunder GG, Bloch DA, Michel BA. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990;33:1122–8; and Healey LA. Long-term follow-up of polymyalgia rheumatica: evidence for synovitis. Semin Arthritis Rheum 1984;13:322–8.

was comparable with intravenous pulse methylprednisolone. Larger prospective studies are required to determine whether intravenous pulse therapy is superior to oral prednisone in patients with GCA and visual ischemic changes.

Other than vision loss, which is rarely reversible, clinical symptoms of GCA will see rapid improvement similar to that observed with PMR. The ESR and CRP values will also begin to normalize within 2–4 weeks, after which prednisone doses can be tapered. The daily dose of prednisone can be reduced by 5 mg every 2–4 weeks to about 25 mg/day. The taper should then be slowed to about 2.5 mg/day every 2–4 weeks until a dose of 10 mg/day is achieved. Tapering below 10 mg should be done at intervals of 1–2 months by 2.5 mg/day. Relapses are also seen with GCA, and as a result, prednisone therapy may have to be continued for up to 2–4 years or longer. Alternate-day dosing of prednisone in GCA was evaluated in one study. The clinical relapse rate was 70% for alternate-day dosing compared with 20% in patients with daily dosing. For both PMR and GCA, some patients require continuous therapy to prevent frequent relapses, and as such, steroid-sparing therapies to reduce long-term steroid complications have been used, unfortunately with limited success.

### Management of Steroid Complications

Complications of long-term steroid therapy include osteoporosis, osteoporosis-related fractures, diabetes mellitus, avascular necrosis of the hip, infections, gastrointestinal bleeding, hypertension, and cataracts. More than 60% of patients with PMR and more than 80% of patients with GCA will experience at least one adverse event related to long-term steroid use. The risk of adverse events is increased with increasing age, female sex, and increasing cumulative doses of prednisone. All patients should receive calcium (at least 1500 mg elemental daily) and vitamin D (at least 800 IU/day) supplementation to reduce the risk of osteoporosis. Several recent studies and expert recommendations advocate daily vitamin D supplementation between 1000 IU and 2000 IU daily in general adult and senior populations. It is not clear if this level of supplementation should be promoted for patients with or at risk of glucocorticoid-related osteoporosis.

Patient bone mineral density studies should be performed at baseline for monitoring purposes. Bisphosphonates are recommended for patients who will be taking at least 5 mg of prednisone daily for 3 months or longer, those with bone mineral density studies that demonstrate T-scores less than −1.0 standard deviation, and those with a history of low-impact fracture. Of the oral bisphosphonates, alendronate and risedronate have U.S. Food and Drug Administration (FDA) labeling to prevent and treat steroid–induced osteoporosis. If patients are intolerant of oral bisphosphonates, intravenous bisphosphonates can be considered. Intravenous zoledronic acid administered once yearly was recently approved by the FDA for the prevention and treatment of steroid-induced osteoporosis in patients taking the equivalent of 7.5 mg of prednisone daily for at least 12 months. A recent study of 833 patients demonstrated that a single yearly intravenous dose of zoledronic acid was noninferior to oral daily risedronate for the prevention and treatment of steroid-induced bone loss measured at the lumbar spine. Teriparatide has also been studied in glucocorticoid-induced osteoporosis. A study of more than 400 patients taking at least 5-mg equivalents of prednisone found that treatment with teriparatide increased bone mineral density and reduced new vertebral fractures compared with treatment with alendronate. Teriparatide, however, is not currently labeled for use in treating or preventing glucocorticoid-induced osteoporosis.

## Steroid-Sparing Agents

### Azathioprine

Several antirheumatic therapies have been studied to reduce the risks of long-term prednisone therapy. Adjunctive treatments that allow more rapid tapering, shorter duration of treatment, or discontinuation of steroids could reduce overall steroid exposure and minimize metabolic or bone-related complications. One small study of azathioprine evaluated treatment with prednisolone in 31 patients with either GCA or PMR. Although a lower corticosteroid requirement was found in the azathioprine-treated patients, no difference in steroid-induced complications was observed. Reports of cholestatic jaundice in some patients, together with the negligible benefits seen, do not support azathioprine as a steroid-sparing agent in GCA or PMR.

### Methotrexate

Three trials of adjuvant methotrexate were conducted in patients with PMR. Two of the studies were small and showed mixed results. The third was a randomized, double-blind, placebo-controlled trial conducted in 72 patients with newly diagnosed PMR. Patients received prednisone 25 mg/day plus either methotrexate 10 mg or placebo once weekly. The proportion of patients taking corticosteroids, the number of patients with one or more disease flares, and the total number of disease flares at 1.5 years of follow-up were all lower in the methotrexate group compared with the placebo group. The rate of adverse events, however, was similar between the two groups. Although methotrexate does not appear to affect adverse effects related to steroid use, this study did suggest improved clinical outcomes with methotrexate in PMR compared with prednisone use alone.

Three randomized, controlled trials that evaluated the efficacy of adding methotrexate to prednisone therapy in patients with GCA showed contradictory results. The smallest study, with 21 patients, administered methotrexate 7.5 mg or placebo weekly together with high-dose prednisone for a total of 48 weeks. No marked differences were noted regarding cumulative steroid dose, weeks to taper prednisone, or bone mineral density in the lumbar spine and hip. The second study, which included 50 patients with recently diagnosed GCA, added weekly doses of methotrexate 10 mg or placebo for 2 years. The rate of relapse and the cumulative steroid dose were substantially reduced in the methotrexate group. No significant difference was noted in the rate or severity of adverse events. The third and largest study included 98 patients with GCA; adjuvant methotrexate was initiated at 0.15 mg/kg/week, increasing to 0.25 mg/kg/week up to a maximum of 15 mg/week. No beneficial effects of adding methotrexate to prednisone were seen on disease relapse rate, cumulative steroid dose, or steroid-related toxicity. One difference with this study was that patients were not required to have a positive temporal artery biopsy to be enrolled, which complicated the interpretation of the results. A meta-analysis of the three

trials in GCA suggests that adjuvant methotrexate reduces the risk of a first relapse by 35% and the risk of a second relapse by 51%. The benefits of methotrexate seem to be most apparent after 24–36 weeks of therapy. The use of methotrexate in GCA may best be reserved for patients who are at highest risk of steroid-related adverse effects from comorbid conditions (e.g., diabetes, osteoporosis) or for those who have already experienced severe corticosteroid-related adverse effects.

### Infliximab

The monoclonal anti–tumor necrosis factor antibody infliximab is effective and safe in treating patients with rheumatoid arthritis and ankylosing spondylitis. Because of the inflammatory nature of PMR and GCA, infliximab has also been investigated in these disorders, albeit to a limited extent. One pilot study evaluated the effects of infliximab, dosed at 3 mg/kg at weeks 0, 2, and 6, in four patients with relapsing PMR and steroid-related adverse effects including several vertebral fractures. These patients had been treated for a mean of 4 years and were unable to have prednisone doses tapered below 7.5–12.5 mg/day. Two patients experienced clinical remission, with normal ESR, CRP, and IL-6 values, within 2 weeks after the first infliximab infusion; remission persisted through 1 year of follow-up. Steroid doses were able to be tapered off completely. A third patient had a similar response and achieved clinical remission; however, IL-6 concentrations remained elevated during the follow-up period. The fourth patient continued to have clinical symptoms of PMR, although IL-6 concentrations declined during follow-up, and the prednisone dose was able to be tapered to 5 mg/day.

In another case series involving seven patients with PMR and either diabetes or osteoporosis, infliximab was useful in inducing clinical remission. One randomized, placebo-controlled trial was reported using infliximab in patients with PMR. This study, which included 51 patients, is the largest published study of infliximab use in patients with either PMR or GCA. In this study, patients newly diagnosed with PMR were randomized to either prednisone plus placebo or prednisone plus infliximab administered at weeks 0, 2, 6, 14, and 22. The primary outcome was the proportion of patients without relapse at the end of the study period. At the end of 52 weeks, the proportion of patients without relapse was not significantly different between the infliximab and placebo groups (30% vs. 37%, respectively).

A case series of infliximab treatment involving four patients with long-standing GCA treated with prednisone for 42–54 months has been reported. All four patients continued to have active disease despite prednisone treatment. Infliximab was administered intravenously at a dose of 3 mg/kg at weeks 0, 2, and 6. Three of the four patients had a complete clinical response and normalization of ESR and CRP concentration after the second infusion.

A randomized, placebo-controlled trial of infliximab in 44 patients with newly diagnosed GCA is the largest study to date of infliximab in GCA. To be included in the study, patients were required to achieve remission with prednisone within 4 weeks of diagnosis. Study patients received infusions of infliximab 5 mg/kg or placebo at weeks 0, 2, and 6 and then every 8 weeks after for 1 year. The study was discontinued early at week 22 after an interim analysis showed no beneficial effects of infliximab treatment over placebo for glucocorticoid dosing or the proportion of patients with relapse. Numerically, more patients in the infliximab group experienced infections (71% vs. 56% with placebo), but this was not statistically significant. Currently, the role of infliximab in treating PMR and GCA is unclear; however, its use in patients who are refractory to steroids, or who have already experienced serious steroid-related complications, could be considered. Additional research with infliximab is required to more clearly establish the role of tumor necrosis factor blockade in treating PMR and GCA.

### Antithrombotic Therapy

Acute vision loss and cerebrovascular accidents are common causes of morbidity and mortality in patients with GCA. Low-dose aspirin has been advocated by some experts to reduce the occurrence of ischemic complications related to GCA. There are no prospective controlled studies evaluating the safety or efficacy of low-dose aspirin for preventing ischemic events in patients with GCA. Two retrospective studies of low-dose aspirin use in patients with GCA found associated lower rates of vision loss and stroke without substantial increases in the risk of bleeding; these studies were small, including 143 and 175 patients, respectively. In the absence of specific contraindications, many experts recommend the use of low-dose aspirin, given the relatively low rate of complications associated with its use. Some experts also recommend the concurrent use of a proton pump inhibitor because of the risk of gastrointestinal bleeding associated with the combined use of corticosteroids and aspirin. No data are available regarding this practice in patients with GCA.

## Role of the Pharmacist

Assisting patients in the recognition of nonspecific symptoms related to PMR and GCA and encouraging patients to be examined by their physician are keys to obtaining an accurate diagnosis and are important roles for pharmacists. In particular, visual symptoms with GCA that may minimally affect patient functioning can progress rapidly and lead to permanent vision loss and blindness if not examined and treated appropriately. In addition, pharmacists should make recommendations to patients and their physicians to help minimize complications related to long-term steroid use. Ensuring that patients have adequate intake of calcium and vitamin D is important in reducing the risk of steroid-induced osteoporosis. Recommending bisphosphonates or other therapies for patients most at risk of osteoporosis may also be necessary. Monitoring serum glucose can be done to evaluate diabetic complications related to steroid use. Similarly, screening for hypertension in patients taking steroids can help identify patients who may require antihypertensive therapy to prevent other cardiovascular complications. Pharmacists should also be involved in helping assess patients and their response to changes in steroid doses. Pharmacists should encourage patients with recurring or increasing symptoms related to steroid tapering to be reexamined by their physician so that appropriate treatment can be instituted.

# Conclusion

Polymyalgia rheumatica and GCA are disorders with overlapping pathophysiology, symptomatology, and treatments. Distinguishing between the two is imperative for appropriate management. Occasionally, PMR and GCA can coexist, and it is important to recognize this possibility for treatment. Corticosteroids remain the standard treatment of both disorders, and many patients may require treatment for several years to prevent a relapsing course of illness. Complications from long-term steroid therapy occur in more than half of patients treated for PMR and GCA; therefore, careful monitoring and preventive measures should be considered. Steroid-sparing therapies such as methotrexate and infliximab have been studied, but at this time, the role of these drugs in the management of PMR and GCA is not clearly defined. Additional research is necessary to establish whether these therapies can improve the clinical outcomes of PMR and GCA, reduce the risk of relapse, and minimize the risks and complications related to long-term steroid use.

# Annotated Bibliography


1. Gonzalez-Gay MA, Garcia-Porrua C, Miranda-Filloy JA, Martin J. Giant cell arteritis and polymyalgia rheumatica: pathophysiology and management. Drugs Aging 2006;23:627–49.

   This article is a comprehensive review of PMR and GCA, including immunologic and laboratory findings and the use of temporal artery biopsy for GCA. There is a thorough discussion of the diagnostic features of both disorders, the differential diagnosis, and the use of imaging studies. This review is well referenced and provides a detailed description of the immunologic findings in both PMR and GCA. The clinical studies included are well described and comprehensive. Sufficient detail is provided to assist the reader in analyzing limitations and weaknesses in individual studies. The brevity of the discussions with nonsteroid treatments highlights the necessity of additional research for effective treatments in PMR and GCA.

2. Salvarani C, Cantini F, Hunder GG. Polymyalgia rheumatica and giant-cell arteritis. Lancet 2008;372:234–45.

   This article is the most up-to-date clinical review of PMR and GCA. The authors of this thorough review are among the leading clinical investigators of both PMR and GCA. The article provides valuable summaries of the evidence base regarding the pharmacotherapeutic management of both PMR and GCA. However, many of the details of some of the smaller studies are not discussed. Because most of the studies with adjunctive therapy (e.g., methotrexate, infliximab) are smaller and less well designed, more details and discussions from clinical experts in the field would be useful.

3. Hutchings A, Hollywood J, Lamping DL, Pease CT, Chakravarty K, Silverman B, et al. Clinical outcomes, quality of life, and diagnostic uncertainty in the first year of polymyalgia rheumatica. Arthritis Rheum 2007;57:803–9.

   Polymyalgia rheumatica is a heterogenous disease with an important effect on quality of life (QOL). Because no reliable diagnostic test is available to definitively confirm the diagnosis, patients most often receive a diagnosis based on diagnostic criteria. Rapid resolution of symptoms with steroid therapy is generally considered an important part of confirming the diagnosis. This study examined patients with PMR for response to steroids, QOL measures, laboratory measures, and diagnostic agreement among rheumatologists. The study was relatively small, including only 129 patients. The primary outcomes were response to steroids at 3 weeks, relapses, QOL measured by SF-36 and Health Assessment Questionnaires, and diagnostic reassessment at 1 year. At 3 weeks, less than half the patients met the definition of complete response to steroid therapy. Quality-of-life measures were lower than the general population norms at baseline and were substantially improved at 1-year follow-up. Pain and stiffness were associated with lower physical QOL during follow-up, whereas ESR was most strongly associated with lower mental QOL during follow-up. There was only moderate agreement among rheumatologists regarding the diagnosis of PMR. This study points out some of the difficulties in managing PMR in patients including diagnostic uncertainty, varying response to steroid therapy, and the disorder's substantial impact on QOL.

4. Binard A, DeBandt M, Berthelot JM, Saraux A; Inflammatory Joint Disease Working Group CRI of the French Society for Rheumatology. Usefulness of the disease activity score for polymyalgia rheumatica for predicting glucocorticoid dose changes: a study of 243 scenarios. Arthritis Rheum 2007;57:481–6.

   A disease activity score, also known as the PMR-AS, was developed to assist with the evaluation and monitoring of disease severity over time. Objective measures such as this are a useful means of minimizing exposure to steroid therapy and of assessing the need for steroid dose increases. The purpose of this study was to see whether the PMR-AS as a whole, or components of the PMR-AS, is useful for predicting steroid dose changes by rheumatologists evaluating various clinical circumstances. Nine clinical cases were evaluated by 35 different rheumatologists, who for each case determined whether a steroid dose increase was indicated. Although the overall PMR-AS was a useful predictor of steroid dose change, the change in PMR-AS from previous levels, as well as changes in morning stiffness, CRP, and physician-rated disease activity score, was more sensitive and specific for predicting recommended steroid dose changes. Additional studies such as this, particularly in real clinical cases, are required to help better delineate appropriate management of steroid therapy so that steroid-related toxicity and PMR relapses can be minimized.

5. Binard A, De Bandt M, Berthelot JM, Saraux A. Performance of the polymyalgia rheumatic activity score for diagnosing disease flares. Arthritis Rheum 2008;59:263–9.

   This is the follow-up study to the one described in annotated bibliography 4. Rheumatologists examined 89 patients with PMR. Overall, 137 visits and 49 visits with two rheumatologists examining the same patient were completed. The rheumatologists assessed disease activity using the visual analog scale, whether a disease flare was diagnosed, and whether steroid dosage changes were made. Diagnosis of a disease flare was most strongly associated with a PMR-AS of 9.35 or more and a change in PMR-AS from the previous visit by 6.6 points or more. The change in PMR-AS appeared to have greater clinical relevance than the absolute score. This study provided useful evidence to suggest that the PMR-AS can be useful in clinical practice to assist with disease management and steroid dose changes.

6. Jover JA, Hernandez-Garcia C, Morado IC, Vargas E, Banares A, Fernandez-Gutierrez B. Combined treatment of giant-cell arteritis with methotrexate and prednisone: a randomized, double-blind, placebo-controlled trial. Ann Intern Med 2001;134:106–14.

   High doses of steroids are required for the treatment of GCA. The tapering of steroid doses and steroid-related adverse effects often complicate the treatment of GCA. This study evaluated the combined treatment of GCA with steroids and methotrexate with steroids plus placebo in 42 patients during a 2-year period. Together with prednisone 60 mg/day, a single weekly dose of 10 mg of methotrexate or placebo was given from initiation of therapy. Steroid doses were gradually tapered to 40 mg/day by the end of the first month and to 20 mg/day by the end of the second month. The tapering continued every 2 weeks by decreasing the daily dose by 2.5 mg until steroids were withdrawn. Relapses, cumulative steroid doses, and adverse events were the primary outcomes. The proportion of patients who experienced at least one relapse (45% methotrexate, 84.2% placebo; p=0.02), as well as several relapses (10% vs. 47.4%; p=0.004), was markedly reduced in the group receiving combined prednisone and methotrexate. Overall, combined treatment including methotrexate resulted in more than a 50% reduction in the number of relapses compared with placebo. The mean cumulative dose of prednisone was also significantly reduced (by almost 25%). The overall rate and severity of adverse events was similar in both groups. Although performed in a relatively small group of patients with GCA, this study demonstrated that combined therapy with steroids and methotrexate is about as safe as steroids alone and may be more effective in controlling disease.

7. Caporali R, Cimmino MA, Ferraccioli G, Gerli R, Klersy C, Salvarani C, et al. Prednisone plus methotrexate for polymyalgia rheumatica. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 2004;141:493–500.

   Before this study, studies to evaluate the combined use of prednisone and methotrexate in PMR had been small with mixed results. This study, involving 72 patients, was the largest study to date to evaluate the use of combination therapy. The study was a multicenter, randomized, double-blind, placebo-controlled trial comparing prednisone 25 mg/day plus methotrexate 10 mg/week with prednisone plus placebo. Both groups also took a weekly folic acid supplement. The outcomes measured were the proportion of patients no longer taking steroids, the number of flares, and the cumulative steroid dose after about 1.5 years. Significantly fewer patients in the methotrexate group were taking prednisone at 76 weeks (12.5% vs. 46.7% in the placebo group, p=0.003). The proportion of patients with at least one flare was significantly lower in the methotrexate group (46.9% vs. 73.3% with placebo, p=0.04). The cumulative prednisone dose was almost 30% lower in the methotrexate group at 76 weeks. Rates of adverse events were similar between the two groups. The use of methotrexate may be considered a steroid-sparing strategy in PMR; however, this study did not attempt to show a beneficial effect of reduced steroid-related complications with the addition of methotrexate. Although a reduction in disease flare-ups is a positive finding with the use of methotrexate in this study, the decrease in steroid exposure without a corresponding decrease in steroid-related complications (e.g., osteoporosis, hyperglycemia) is of limited clinical utility.

8. International Network for the Study of Systemic Vasculitides. A multicenter, randomized, double-blind, placebo-controlled trial of adjuvant methotrexate treatment for giant cell arteritis. Arthritis Rheum 2002;46:1309–18.

   High doses of steroids are required for the treatment of GCA. The tapering of steroid doses and steroid-related adverse effects often complicate the treatment of GCA. This was the first study to evaluate the combination of steroids and methotrexate for the treatment of GCA. This multicenter, randomized, double-blind, placebo-controlled trial enrolled 98 patients at diagnosis to receive prednisone 1 mg/kg/day up to 60 mg and either placebo or methotrexate 0.15 mg/kg/week up to 0.25 mg/kg/week, not to exceed 15 mg/week. Patients were observed for 1 year, and outcomes included disease relapses, treatment failures, total dose and duration of steroid therapy, toxicity, and disease-related morbidity and death. No major benefits were observed with the addition of methotrexate to steroid therapy in this study of GCA patients. The disappointing results of this study may relate to the shorter duration of treatment compared with other studies, specifically the study discussed in annotated bibliography 6, which lasted 2 years. It is not completely clear whether the benefits of adding methotrexate therapy are achieved mainly beyond 1 year of therapy. Additional research is required to test this hypothesis.

9. Cantini F, Niccoi L, Salvarani C, Padula A, Olivieri I. Treatment of long-standing active giant cell arteritis with infliximab: report of four cases. Arthritis Rheum 2001;44:2932–5.

   This trial provided the first published data of infliximab in the treatment of GCA. The report describes the experience of four patients (three women) aged 72–75 years with GCA treated with infliximab after not achieving remission with steroid treatment. All patients had been treated with steroids for between 42 months and 54 months when infliximab was initiated. Each patient received three intravenous infusions of infliximab at 0, 2, and 6 weeks at a dose of 3 mg/kg. Three of the four patients (two women, one man) responded well to the infliximab therapy and achieved remission. No substantial adverse effects were reported. Because this study was a short-term open-label investigation without the use of active or placebo controls, only limited evidence can be obtained from these findings. However, the patients included in the study had not responded optimally to extended steroid treatment, and few options are available to patients who do not respond to steroids.

10. Hoffman GS, Cid MC, Rendt-Zagar KE, Merkel PA, Weyand CM, Stone JH, et al. Infliximab for maintenance of glucocorticoid-induced remission of giant cell arteritis. Ann Intern Med 2007;146:621–30.

    This study investigated the efficacy of infliximab or placebo in 44 patients with steroid-induced remission of GCA. For entry, patients were required to have received at least 1 week of prednisone (40–60 mg/day), have an ESR less than 40 mm/hour, and have no active signs of GCA. Patients were randomized 2:1 to either infliximab 5 mg/kg or placebo at weeks 0, 2, and 6 and every 8 weeks thereafter. The primary end points were the proportion of patients who remained relapse free and the number and type of adverse events at study's end. The planned 1-year study was discontinued early at week 22 after an interim analysis. At week 22, no significant differences were observed for the proportion of patients without relapse (43% in the infliximab

group vs. 50% in the placebo group). The incidence of infection was 71% with infliximab and 56% with placebo, but this was not statistically significant. This was a small study, but no evidence was observed to suggest a beneficial effect of infliximab in patients with steroid-induced remission of GCA. Unlike the small case series reported in annotated bibliography 9, this study included patients who had responded to steroid treatment. Based on the findings of this study, it seems that infliximab may not have a role in the treatment of GCA in patients who respond well to steroid therapy.

11. Salvarani C, Cantini F, Niccoli L, Catanoso MG, Macchioni P, Pulsatelli L, et al. Treatment of refractory polymyalgia rheumatic with infliximab: a pilot study. J Rheumatol 2003;30:760–3.

    This pilot study assessed the effects of infliximab, dosed at 3 mg/kg at weeks 0, 2, and 6, in four patients with relapsing PMR and steroid-related adverse effects, including several vertebral fractures. These patients had been treated for a mean of 4 years and were unable to have prednisone tapered to target doses. Two patients experienced clinical remission, with normal ESR, CRP, and IL-6, within 2 weeks after the first infliximab infusion; this remission lasted through 1 year of follow-up. Steroid doses were able to be tapered off completely. A third patient had a similar response and achieved clinical remission; however, IL-6 concentrations remained elevated during the follow-up period. The fourth patient continued to have clinical symptoms of PMR, although IL-6 concentrations declined during follow-up, and the prednisone dose was able to be tapered to 5 mg/day. This was an open-label pilot study of only four patients with no active or placebo controls. Furthermore, these patients with PMR were refractory to steroid treatment and had developed steroid-related complications. Extrapolation of the benefits of infliximab based on these findings, particularly in nonrefractory patients, should be scrutinized.

12. Salvarani C, Macchioni P, Manzini C, Paolazzi G, Trotta A, Manganelli P, et al. Infliximab plus prednisone or placebo plus prednisone for the initial treatment of polymyalgia rheumatica: a randomized trial. Ann Intern Med 2007;146:631–9.

    Infliximab has been used successfully to treat rheumatologic disorders. A previous report of four patients demonstrated a steroid-sparing effect with infliximab in PMR patients who had developed adverse effects from steroids. This was a 1-year randomized, placebo-controlled study conducted in 51 patients with newly diagnosed PMR. Patients received prednisone 15 mg/day, which was tapered and then discontinued at 16 weeks, and placebo or infliximab infusions 3 mg/kg at weeks 0, 2, 6, 14, and 22. The primary outcome was the proportion of patients without relapses and recurrences through 52 weeks. No important benefits were seen with infliximab treatment for the primary outcome or with secondary outcomes. The proportion of patients who were relapse free at 52 weeks was 30% in the infliximab group and 37% in the placebo group (p=0.8). Although this study was small, the use of infliximab combined with prednisone in newly diagnosed PMR appears to be of little if any benefit. The population included in this study was quite different from the population described in the pilot study in annotated bibliography 11. The use of infliximab as adjunctive therapy in newly diagnosed PMR has no beneficial role.

13. Lee MS, Smith SD, Galor A, Hoffman GS. Antiplatelet and anticoagulant therapy in patients with giant cell arteritis. Arthritis Rheum 2006;54:3306–9.

    Ischemic complications produce much of the morbidity and mortality in patients with GCA. Low-dose aspirin therapy has been advocated by many experts to prevent ischemic and visual complications in these patients. This was a retrospective study of 143 patients with a diagnosis of GCA, 73% with biopsy-proven disease. Sixty percent of subjects received either aspirin or warfarin during the mean follow-up of 4 years. The rate of ischemic events in patients receiving antithrombotic or anticoagulant therapy was 16%, versus 48% in patients who did not receive antithrombotic or anticoagulant therapy. Bleeding events were not markedly different between groups (two patients receiving aspirin, one patient receiving warfarin, and five patients receiving neither aspirin nor warfarin). Although this was a retrospective study, the magnitude of the difference between groups was large, and prospective studies are required to confirm whether antithrombotic or anticoagulant therapy should be considered for patients with ischemic symptoms in GCA.

# Self-Assessment Questions

**Questions 1–3 pertain to the following case.**
J.D. is a 72-year-old woman weighing 65 kg who presents to your clinic with a 6-week history of aching pain and stiffness in her shoulders and upper arms. She also complains of pain and stiffness in her hips, stating that she is having difficulty bathing and dressing, and complains of generalized fatigue. J.D. has lost 6.8 kg (15 lb) since her last clinic visit 4 months ago. On physical examination, it is noted that she has a limited range of motion in her neck, shoulders, and hips because of pain. Laboratory testing detects an elevated erythrocyte sedimentation rate (ESR; 44 mm/hour) and C-reactive protein (CRP) concentration (4.0 mg/dL). She also has a normochromic normocytic anemia. She reports no visual changes or headache, and an ocular examination detects no notable findings.

1. Which one of the following is the most important risk factor for a diagnosis of polymyalgia rheumatica (PMR) or giant cell arteritis (GCA) in J.D.?
   A. Female sex.
   B. Age.
   C. Recent weight loss.
   D. ESR.

2. A bilateral temporal artery biopsy is performed on J.D., the results of which are negative. She is given a diagnosis of PMR. Which one of the following best describes the primary therapeutic goals for J.D.?
   A. Normalize ESR and CRP concentration.
   B. Improve function and prevent the development of visual symptoms.
   C. Improve function; reverse weight loss, fatigue, and anemia.
   D. Decrease symptoms, improve function, and prevent relapse.

3. Which one of the following is the best recommendation for initial therapy for J.D.'s PMR?
   A. Prednisone 7.5 mg/day orally.
   B. Prednisone 15 mg/day orally.
   C. Prednisone 1 mg/kg/day orally.
   D. Methylprednisolone 15 mg/kg/day intravenously.

**Questions 4 and 5 pertain to the following case.**
A 68-year-old man is examined for symptoms consistent with GCA. He had a temporal artery biopsy today, but the results are not expected for 48 hours. He has no vision changes or ischemic symptoms on physical examination.

4. Which one of the following is the best recommendation for this patient?
   A. Prednisone 20 mg/day orally.
   B. Prednisone 30 mg/day orally.
   C. Prednisone 60 mg/day orally.
   D. Methylprednisolone 15 mg/kg/day intravenously.

5. Which one of the following imaging studies would be most useful to evaluate temporal artery inflammation for supporting a diagnosis of GCA in this patient?
   A. Positron emission tomography.
   B. Magnetic resonance imaging (MRI).
   C. Contrast-enhanced MRI.
   D. Ultrasonography.

6. A 66-year-old woman with a history of PMR has been taking prednisone for about 6 months. Her initial dose of prednisone was 20 mg/day, but it has been tapered to her current dose of 5 mg/day, which she has been taking for about 2 weeks. Before that, she was taking 7.5 mg/day, and her symptoms were well controlled. She presents today with complaints of increasing morning proximal joint stiffness lasting more than 60 minutes, weakness, and pain. Laboratory tests show an ESR of 42 mm/hour (compared with 16 mm/hour 1 month ago). Which one of the following is the best recommendation for this patient?
   A. Continue prednisone 5 mg/day.
   B. Increase prednisone to 7.5 mg/day.
   C. Increase prednisone to 20 mg/day.
   D. Increase prednisone to 60 mg/day.

7. A 65-year-old woman with a history of PMR has been taking prednisone for about 5 months. Her initial dose of prednisone was 15 mg/day, but it has been tapered to her current dose of 7.5 mg/day, which she has been taking for about 1 month. Before that, she was taking 10 mg/day, and her symptoms were well controlled. She presents today for a routine follow-up and has no symptomatic complaints. She does not have substantial pain and has only minimal morning stiffness lasting less than 30 minutes, which is unchanged. Laboratory tests reveal an ESR of 40 mm/hour (compared with 20 mm/hour 1 month ago). Which one of the following recommendations is best for this patient?
   A. Continue prednisone 7.5 mg/day.
   B. Increase prednisone to 10 mg/day.
   C. Increase prednisone to 15 mg/day.
   D. Increase prednisone to 20 mg/day.

8. A 57-year-old woman given a diagnosis of GCA 1 year ago is seen in the clinic for a routine follow-up. Her symptoms have been well controlled on prednisone 10 mg/day orally for the past 2 months. She is leaving tomorrow for a month-long trip outside the country. Her physician would like to check her blood chemistry to see whether it is feasible to decrease the dose of her prednisone before she leaves. Which one of the following blood tests is best to perform to help make this decision?
   A. ESR.
   B. CRP.

C. Interleukin (IL)-6.
D. Interferon-γ.

9. A 70-year-old man has been taking prednisone for about 10 months for the treatment of GCA. His prednisone dose is currently 10 mg/day; he had one episode of disease relapse when his daily dose dropped below 10 mg. The patient's physician is concerned about prednisone-related complications and wants to know the best course of action for this patient. Which one of the following recommendations is the best response to the physician?
   A. Alternate-day dosing of prednisone.
   B. Adjuvant treatment with methotrexate.
   C. Adjuvant treatment with infliximab.
   D. Continue prednisone as prescribed.

10. A 74-year-old woman is seen for complaints of new-onset proximal joint pain of the shoulders, neck, and hips and morning stiffness that lasts more than 1 hour. These symptoms have been occurring for 1 month. She also complains of fatigue and a headache that makes her unable to brush her hair. Laboratory evaluation shows an ESR of 54 mm/hour and a CRP of 5.1 mg/dL. On physical examination, it is noted that she has tenderness and erythema of the temporal area bilaterally. She reports no changes in vision or visual symptoms. A temporal artery biopsy is performed, which shows granulomatous inflammation. Which one of the following is the most likely diagnosis for this woman?
   A. PMR.
   B. GCA.
   C. PMR and GCA.
   D. Temporal arteritis.

11. A 61-year-old woman is given a diagnosis of PMR (initial ESR of 60 mm/hour), and prednisone 20 mg/day is initiated. After 2 weeks, she returns to the clinic with a slight improvement in pain; however, her stiffness remains, and her functional status is unchanged. Her ESR at this visit is 71 mm/hour. Which one of the following is the best recommendation for this patient at this time?
   A. Continue prednisone 20 mg/day orally for 2 additional weeks.
   B. Increase to prednisone 30 mg/day orally; reevaluate in 2 weeks.
   C. Increase to prednisone 60 mg/day orally; reevaluate in 2 weeks.
   D. Switch to methylprednisolone 15 mg/kg/day intravenously until response documented; switch to oral prednisone 60 mg/day.

12. A 64-year-old woman is beginning prednisone therapy 15 mg/day for the treatment of PMR. Her physician is concerned about this patient developing steroid-related osteoporosis with long-term use of prednisone. Dual-energy x-ray absorptiometry (DEXA) is performed at the lumbar spine and hip for baseline measures. Her T-score of the lumbar spine is 0.4 and of the hip, 0.6. Which of the following is the best recommendation at this time for this patient?
   A. Calcium and vitamin D supplementation.
   B. Alendronate.
   C. Calcium, vitamin D, and alendronate.
   D. Repeat DEXA in 6 months.

13. A 71-year-old man has been given a diagnosis of GCA. On presentation, he complained of visual symptoms consisting of transient monocular vision loss (amaurosis fugax). He also had complaints of jaw claudication and headache. He presented to the emergency department with these symptoms and was given methylprednisolone 15 mg/kg intravenously. A DEXA scan was performed while he was at the hospital, and his T-scores were 0.1 at the lumbar spine and 0.2 at the hip. He has a history of hypertension, osteoarthritis, and benign prostatic hyperplasia. His current drugs include hydrochlorothiazide 25 mg/day, lisinopril 10 mg/day, acetaminophen 1000 mg three times/day, and tamsulosin 0.4 mg/day. In addition to prednisone, which one of the following is the best adjunctive therapy to recommend for this patient?
   A. Infliximab.
   B. Methotrexate.
   C. Aspirin.
   D. Alendronate.

14. A 67-year-old woman came to the clinic 2 weeks ago with symptoms of generalized fatigue, pain, and stiffness in the shoulder, neck, and hips. She had no visual symptoms. Her ESR was 36 mm/hour. She was given a diagnosis of PMR and initiated on prednisone 20 mg/day. After 1 week of therapy, she returned to the clinic with only minor improvement in her symptoms. Her ESR at that time was 38 mm/hour. Her prednisone dose was increased to 30 mg/day. One week after taking prednisone 30 mg/day, she returns to the clinic with no notable improvement in her symptoms. Her ESR today is 36 mm/hour. Which one of the following is the best recommendation for this patient?
   A. Check CRP.
   B. Check IL-6.
   C. Check interferon-γ.
   D. Perform a temporal artery biopsy.

15. A 70-year-old man is initiated on prednisone 60 mg/day for treatment of GCA, confirmed by temporal artery biopsy. After 8 weeks on this dose, he has minimal physical symptoms and has experienced no visual symptoms. His ESR and CRP concentration at baseline were 54 mm/hour and 5.2 mg/dL, respectively. Today, his ESR and CRP concentration are 19 mm/hour and 0.5 mg/dL, respectively. Which one of the following is the best recommendation regarding prednisone in this patient?
   A. Continue at 60 mg/day for 4 more weeks before tapering.

B. Decrease to 55 mg/day, then by 5 mg every 2–4 weeks.
C. Decrease to 25 mg/day, then by 2.5 mg every 1–2 weeks.
D. Increase to 80 mg/day for 4 more weeks before tapering.

16. A 65-year-old woman's PMR is newly diagnosed. She has a history of diabetes and a fall-related fracture. The physician is initiating her on oral prednisone today, but he is concerned about using steroids because of this patient's history. He would like for her to discontinue prednisone as quickly as possible to minimize steroid-related adverse effects, as well as reduce the risk of relapse. Which one of the following is the best recommendation for this patient?
    A. Initiate prednisone at 60 mg/day orally.
    B. Initiate methylprednisolone 1 g/day intravenously for 3 days before oral prednisone.
    C. Add methotrexate 10 mg/week orally to prednisone.
    D. Add infliximab 3 mg/kg intravenously at weeks 0, 2, and 6 to prednisone.

17. Which of the following is the most clinically useful information for recommending a dose decrease of prednisone in a patient with PMR?
    A. ESR of 15 mm/hour.
    B. Total polymyalgia rheumatic activity score (PMR-AS) of 8.
    C. CRP of 0.5 mg/dL.
    D. PMR-AS decrease of 8.

18. A 56-year-old woman comes to her regular pharmacy to pick up her prescriptions for prednisone, methotrexate, alendronate, metformin, and hydrochlorothiazide. In speaking with the patient, the pharmacist notes that she has been given diagnoses of PMR, osteoporosis, diabetes, and hypertension. The pharmacy is offering free blood glucose testing and blood pressure screening, so she has these tests. Her blood glucose is 76 mg/dL (she has not eaten today), and her blood pressure is 152/90 mm Hg. The patient states that she has recently been experiencing headaches and reports changes in her vision, but no other symptoms. Which one of the following is the best recommendation for this patient?
    A. Wait 15 minutes and recheck her glucose and blood pressure.
    B. Send her to the emergency department.
    C. Advise her to make an appointment to see her physician in the next 1 or 2 days.
    D. Advise her to make an appointment to see her physician within the next week.

19. A 68-year-old man has been taking prednisone for 4 months for a diagnosis of GCA confirmed by biopsy. His symptoms have not resolved, and he has developed partial vision loss. His ESR and CRP concentrations have not declined substantially since beginning prednisone. He was initiated on infliximab 3 mg/kg intravenously 3 weeks ago (week 0), and he received his second dose 1 week ago (week 2). He is in the clinic for examination today; his symptoms have markedly improved, and his vision is stable. His ESR and CRP have normalized. Which one of the following is the best recommendation for this patient?
    A. Discontinue infliximab and taper prednisone.
    B. Reduce infliximab dose to 1.5 mg/kg every 2 weeks and taper prednisone.
    C. Continue infliximab at current dose every 2 weeks and taper prednisone.
    D. Continue infliximab at current dose at week 6 and every 8 weeks thereafter; taper prednisone.

20. A 64-year-old woman who was given a diagnosis of PMR 6 months ago is seen for a routine follow-up. She was initially administered prednisone 20 mg/day orally but is currently taking 7.5 mg/day orally. She had two episodes of clinical relapse when her prednisone dose was reduced below 7.5 mg/day. At diagnosis, she was initiated on calcium and vitamin D supplements as well as risedronate 35 mg orally once weekly. Her baseline T-scores were −1.2 at the lumbar spine and −1.3 at the hip. She states that she has been taking the risedronate routinely but complains of adverse gastrointestinal effects. She is following appropriate administration recommendations. A repeat DEXA is performed, and her T-scores are −1.6 at the lumbar spine and −1.8 at the hip. The risedronate is discontinued. Which one of the following is the best recommendation for this patient?
    A. Alendronate 70 mg/week orally.
    B. Ibandronate 150 mg/month orally.
    C. Zoledronic acid 5 mg/year intravenously.
    D. Teriparatide 20 mcg/day subcutaneously.