

---

---

# Polymyalgia rheumatica can recur years after discontinuation of corticosteroid therapy

---

---

W.P. Docken

---

---

Brigham and Women's Hospital, Boston, Massachusetts, USA.

William P. Docken, MD.

Please address correspondence to:  
William P. Docken, MD, Brigham and Women's Hospital, Boston, MA 02118, USA.

E-mail: wdocken@partners.org

Received on June 18, 2008; accepted in revised form on September 16, 2008.

Clin Exp Rheumatol 2009; 27 (Suppl. 52): S25-S27.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2009.

**Key words:** Polymyalgia rheumatica, adrenal cortex hormones.

## ABSTRACT

**Objective.** To describe disease recurrence in polymyalgia rheumatica.

**Methods.** I present 12 patients with recurring PMR from a single clinical practice with long-term clinical follow-up (mean 14.3 years).

**Results.** Despite a disease-free interval off corticosteroids of 2 years or longer, these patients experienced 1 overt recurrence (or more) of PMR.

**Conclusion.** The course of PMR is not uniformly monophasic, and patient and physician should remain alert to the possibility of recurring disease.

## Introduction

Although relapses of polymyalgia rheumatica (PMR) are well recognized (1-3), overt recurrences of this disease have been but rarely acknowledged. (*Relapse* is herewith defined as increased disease activity, including worsened symptoms and rises in the acute phase reactants, occurring the face of ongoing treatment; *recurrence* is defined as renewed disease activity after complete cessation of treatment.) This report describes 12 patients who experienced recurrences of PMR 2 years or more after discontinuation of corticosteroid (CS) therapy.

## Patients and methods

Twelve patients with recurrences of PMR are reported from my clinical practice of 30 years, all of whom had been off treatment for this disease for at least 2 years. Eight patients were female, 4 were male, extending in age from 53 to 78 years (mean 64.1 years) at the time of initial diagnosis. Formal criteria for the diagnosis of PMR have not yet been codified (4); in this report the diagnosis of PMR is based on the Healey criteria (5). Nine patients had PMR per the classic Healey criteria at the time both of initial diagnosis and of subsequent recurrence; 3 patients who fulfilled these criteria but who presented with erythrocyte sedimentation rates

(ESRs) less than 40 mm/h are also included (6). The ESRs of the 9 patients presenting with ESRs >40 mm/h ranged from 43 to 150 (mean 85 mm/h). The ESRs of the 3 patients with initial values <40 mm/hour ranged from 21 and 32. The period of follow-up covered 7.3 to 25.1 years (mean 14.3 years).

## Results

The CS dose to achieve remission – defined as the absence of morning stiffness, painless range of motion at the shoulders and hips, and normalization of the ESR – was 10 to 15 mg of prednisone per day (mean 12.5 mg). Once remission was achieved, CS therapy was slowly tapered, usually by monthly decrements of 1 mg. The duration of initial CS therapy lasted 1.0 to 11.2 years (mean 3.4 years). At the time of discontinuation of CS all patients were asymptomatic, with a range of ESRs from 4 to 29 (mean 19).

The duration between cessation of CS therapy and its resumption for recurrence of disease was 2.0 to 14.7 years (mean 6.1 years). ESRs at the time of recurrence ranged from 6 to 82 (mean 52 mm/h). The mean CS dose to achieve remission for recurrences was 10 to 15 mg per day (mean 12.5 mg).

During the period of follow-up, no patient was positive for rheumatoid factor, and none evolved erosive disease. One patient developed biopsy-proved giant cell arteritis. One patient had peripheral arthritis with pitting edema (so-called “RS3PE syndrome”) at the time of disease recurrence. Four of 12 patients had 1 or 2 additional instances of recurring PMR.

At present, 7/12 patients remain off treatment, 4/12 are still on low dose CS therapy, and 1 has been lost to follow-up.

## Discussion

An early study of PMR found a median duration of disease of but 11 months (7), thus requiring the relatively brief

Competing interests: none declared.

deployment of CS for management. Subsequent studies, however, suggested a more heterogeneous course, necessitating longer term CS use. The Geisinger Clinic in central Pennsylvania, for example, described a median duration of some CS therapy in the treatment of PMR of 37 months (8). Kyle and Hazelman in England (9) and Myklebust and Gran in Norway (10) found that a quarter of patients with PMR were still taking steroids after 2 years. Cimmino recently reported that a third of patients required CS treatment for more than 6 years (11).

The need for continued steroid use in a sizeable portion of patients with PMR has generated further studies aimed at identifying factors that could predict the occurrence of *relapse* – *i.e.* increased disease activity during treatment in turn prompting higher and more protracted steroid doses. Such clinical factors have included female sex (12), the co-existence of giant cell arteritis (13), the speed of CS taper (3), persisting elevations of such acute phase reactants as C-reactive protein and interleukin (IL)-6 (14), and increased levels of soluble IL-6 receptor at disease onset (15). Proposed pathophysiologic mechanisms contributing to an increased frequency of relapse have included the presence of the HLA-DRB1\*04 allele (2) and genetic polymorphisms of IL-6 promoter (16) and of intercellular adhesion molecule-1 (17).

These studies all focused on the issue of relapse of PMR, with only passing allusions to the issue of overt disease *recurrence* – *i.e.* explicit recrudescence of disease activity after termination of treatment. The current report describes such recurrences of PMR in a dozen patients who had been off CS for a median of 6.1 years. Their demographics, clinical presentations, and responses to steroids were typical for PMR, both at initial evaluation and at subsequent recurrence(s). The singular strength of this presentation is its long duration of follow-up (spanning 7.3 to 25 years, mean 14.3 years) – the longest reported period of follow-up of patients with PMR – which has allowed for an extended observation of the course of this disease and its treatment, and thus

appreciation of the potential for disease recurrence. Indeed, during this prolonged follow-up, 4 of the 12 patients described in fact had *more* than 1 recurrence (3 patients with 2 recurrences and 1 with 3 recurrences). No patients manifested stigmata of other systemic rheumatic disease during follow-up, especially rheumatoid arthritis, either serologically or radiographically.

Was the PMR in true remission during this time, or could there instead have been smoldering, subclinical disease activity? Levels IL-6 (known to remain elevated in some patients in the face of long-term treatment with CS) and of CRP have been suggested as more accurate indices of disease activity in PMR (3, 14, 18), but were not measured, so smoldering disease cannot be ruled out. But these patients were solidly in clinical remission – asymptomatic, off steroids, with normal ESRs – and by insisting on a steroid-free hiatus of 2 years in the definition of “recurrence”, I have tried to insure separation from PMR patients with mere relapsing disease.

Why PMR is polyphasic in some patients is unclear. There were no unusual clinical features in the patients described here in terms of their demographics, presentation, and response to treatment. The doses of CS were normative, and the subsequent taper was gradual. The phenomenon of recurrence was seen in patients whose initial presentations involved both elevated and normal ESRs. Laboratory features that could potentially identify risk factors for recurrence and help differentiate patients with a polyphasic course – such as pro-inflammatory cytokine levels (14, 15), genetic background (2), and gene-gene interactions (16, 17) – were not investigated.

I do not have specific figures for the incidence of disease recurrence in PMR, but it is uncommonly referenced in the literature. In an older series from 1983, Behn reported recurrence in 19 of 36 patients with PMR, most within 12 months of cessation of CS, and recommended that patients be “followed up for at least 2 years after corticosteroid withdrawal” (19). In Gonzalez-Gay’s more recent 1999 series of 185 patients with PMR, 7 patients (6.4%) were said to have “had a flare of PMR

after at least 12 months” off CS therapy, though these patients were not further characterized clinically (2).

Clinical experience with PMR has suggested 2 subsets of patients, one with generally mild disease, for which 1-2 years of CS treatment suffices, and another with more protracted, often relapsing disease, for which several years of such treatment is required (20). This report suggests that there is another clinical subset of patients with PMR – that of disease recurring years after CS have been discontinued. Awareness of this possibility should be maintained by both patient and physician.

## References

1. BENGTSSON BA, MALMVALL BE: Prognosis of giant cell arteritis including temporal arteritis and polymyalgia rheumatica. A follow-up study on ninety patients treated with corticosteroids. *Acta Med Scand* 1981; 209: 337-45.
2. GONZALEZ-GAY MA, GARCIA-PORRUA C, VAZQUEZ-CARUNCHO M, DABABNEH A, HAJEER A, OLLIER WER: The spectrum of polymyalgia rheumatica in northwestern Spain: incidence and analysis of variables associated with relapse in a 10 year study. *J Rheumatol* 1999; 26: 1326-32.
3. MARADIT KREMERS H, REINALDA MS, CROWSON CS, ZINSMEISTER AR, HUNDER GG, GABRIEL SE: Relapse in a population based cohort of patients with polymyalgia rheumatica. *J Rheumatol* 2005; 32: 65-73.
4. DASGUPTA B, MATTESON EL, MARADIT-KREMERS H: Management guidelines and outcome measures in polymyalgia rheumatica (PMR). *Clin Exp Rheumatol* 2007; 25 (Suppl. 47): S130-S136.
5. HEALEY LA: Long-term follow-up of polymyalgia rheumatica evidence for synovitis. *Semin Arthritis Rheum* 1984; 13: 322-8.
6. HELFGOTT SM, KIEVAL RI: Polymyalgia rheumatica in patients with a normal erythrocyte sedimentation rate. *Arthritis Rheum* 1996; 39: 304-7.
7. CHUANG TY, HUNDER GG, ILSTRUP DM, KURLAND LT: Polymyalgia rheumatica. A 10-year epidemiologic and clinical study. *Ann Intern Med* 1982; 97: 672-80.
8. AYOUB WT, FRANKLIN CM, TORRETTI D: Polymyalgia rheumatica. Duration of therapy and long-term outcome. *Am J Med* 1985; 79: 309-15.
9. MYKLEBUST G, GRAN JT: Prednisolone maintenance dose in relation to starting dose in the treatment of polymyalgia rheumatica and temporal arteritis. A prospective two-year study in 273 patients. *Scand J Rheumatol* 2001; 30: 260-7.
10. KYLE V, HAZELMAN BL: The clinical and laboratory course of polymyalgia rheumatica/giant cell arteritis after the first two months of treatment. *Ann Rheum Dis* 1993; 52: 847-50.

11. CIMMINO MA, SALVARANI C, MACCHIONI P *et al.*: for the Systemic Vasculitis Study Group of the Italian Society for Rheumatology. *Clin Exp Rheumatol* 2008; 26: 396-400.
12. CIMMINO M, PARODI M, CAPORALI R, MONTECUCCO C: Is the course of steroid-treated polymyalgia rheumatica more severe in women? *Ann NY Acad Sci* 2006; 1069: 315-21.
13. NARVAEZ J, NOLLA-SOLE JM, CLAVAGUERA MT, VALVERDE-GARCIA J, ROIG-ESCOFET D: Longterm therapy in polymyalgia rheumatica: effect of coexistent temporal arteritis. *J Rheumatol* 1999; 26: 1945-52.
14. SALVARANI C, CANTINI F, NICCOLI L *et al.*: Acute-phase reactants and the risk of relapse/recurrence in polymyalgia rheumatica: a prospective follow-up study. *Arthritis Rheum* 2005; 53: 33-8.
15. PULSATELLI L, BOIARDI L, PIGNOTTI E *et al.*: Serum interleukin-6 receptor in polymyalgia rheumatica: a potential marker of relapse/recurrence risk. *Arthritis Rheum* 2008; 59: 1147-54.
16. BOIARDI L, CASALI B, FARNETTI E *et al.*: Relationship between interleukin 6 promoter polymorphism at position -174, IL-6 serum levels, and the risk of relapse/recurrence in polymyalgia rheumatica. *J Rheumatol* 2006; 33: 703-8.
17. AMOLI MM, SHELLEY E, MATTEY DL *et al.*: Intercellular adhesion molecule-1 gene polymorphisms in isolated polymyalgia rheumatica. *J Rheumatol* 2002; 29: 502-4.
18. KREMERS HM, REINALDA MS, CROWSON CS, ZINSMEISTER AR, HUNDER GG, GABRIEL SE: Relapse in a population based cohort of patients with polymyalgia rheumatica. *Arch Int Med* 1999; 159: 577-84.
19. BEHN AR, PERERA, MYLES AB: Polymyalgia rheumatica and corticosteroids: how much for how long? *Ann Rheum Dis* 1983; 42: 374-8.
20. SALVARANI C, CANTINI F, BOIARDI L, HUNDER GG: Polymyalgia rheumatica. *Best Pract Res Clin Rheumatol* 2004; 18: 705-22.