Corticosteroid Requirements in Polymyalgia Rheumatica

Cornelia M. Weyand, MD; James W. Fulbright, MS; Jonathan M. Evans, MD; Gene G. Hunder, MD; Jörg J. Goronzy, MD, PhD

Background: Polymyalgia rheumatica (PMR) is a systemic inflammatory disease of unknown cause that affects older individuals. Clinical symptoms respond promptly to corticosteroids, but treatment is often required for several years, frequently resulting in adverse drug effects. Guidelines for the optimal use of corticosteroids that maximize relief of symptoms but minimize adverse effects of the therapy are needed.

Objective: To determine whether clinical or laboratory parameters in PMR could be identified that allow for stratifying patients into subsets with differences in corticosteroid requirements.

Patients and Methods: We studied 27 patients with PMR treated with a standardized schedule of prednisone. Patients were reevaluated at monthly intervals for pain scores and physician and patient assessments. Plasma interleukin 6 level and the erythrocyte sedimentation rate were measured at each visit. The duration of steroid therapy and the cumulative steroid dose were calculated.

Results: Based on the initial response to therapy and the duration of disease, the 27 patients could be subdivided into 3 distinct groups. Eight with low erythrocyte sedimentation rates responded rapidly and required corticosteroids for less than 1 year with rare disease flares on tapering of prednisone. Twelve others responded well initially but did not tolerate reduction to lower doses and had remitting disease of more than 1 year. Seven patients had only a partial response to the initial steroid regimen. After 4 weeks of therapy, the erythrocyte sedimentation rates improved, but levels of interleukin 6 remained elevated. Pretreatment pain scores were also higher in these partial responder patients ($P = .05$).

Conclusions: Polymyalgia rheumatica is a heterogeneous disease with variations in the treatment duration and dose of corticosteroids required for suppression of symptoms. Pretreatment erythrocyte sedimentation rate and nonresponsiveness of interleukin 6 to steroid therapy are helpful in dividing patients into subsets with different treatment requirements.

Arch Intern Med. 1999;159:577-584
PATIENTS AND METHODS

This study was approved by the institutional review board.

PATIENTS

Thirty consecutive patients who were newly diagnosed as having PMR between October 1993 and April 1996 participated. The diagnosis of PMR was based on the presence of: (1) morning stiffness of 30 minutes or longer; (2) pain in the shoulders and/or arms, hips and/or thighs, neck, and/or torso for 1 month or more, and (3) an ESR of 40 mm/h or more. Patients with an ESR of 40 mm/h or less and a typical presentation for PMR were enrolled if the diagnosis was independently confirmed by a second rheumatologist. A temporal artery biopsy specimen was obtained in all patients who had clinical features suggestive for GCA such as headaches, jaw claudication, scalp tenderness, or abnormal temporal arteries. Patients with histological evidence of GCA and patients with other diseases were excluded.

TREATMENT

Patients were started on a regimen of 20 mg of prednisone daily as a single morning dose. If the patient did not respond to the initial dose with a reduction of symptoms, it was increased by 10 mg/d before the tapering schedule was started. The dose was then tapered by 2.5 mg every 2 weeks for as long as the symptoms remained improved. This schedule resulted in a minimal treatment duration of 18 weeks. Prednisone doses were increased by 5 mg/d if the patient experienced a return of active disease. Active PMR was defined as the presence of 3 of the following 5 criteria in the absence of another medical condition explaining the symptoms: (1) patient global assessment 2 or higher; (2) physician global assessment 2 or higher; (3) patient pain assessment 3 or higher; (4) morning stiffness 60 minutes or more, and (5) elevated ESR. Adjustments after the third flare of active disease were left to the discretion of the treating physician. All were followed up for a minimum of 6 months after discontinuation of prednisone therapy to identify possible disease relapses.

MEASUREMENTS

All patients had a complete physical examination at the initial evaluation and were then followed up at 4-week intervals. At each return visit the patient was examined. Duration of morning stiffness was averaged from a log the patient kept each day for the third week of the treatment interval. Severity of pain and stiffness was assessed on a visual analog scale ranging from no symptoms (0 cm) to as bad as could be (10 cm). Patient and physician global assessments regarding status were obtained on a scale of 1 to 5.

Laboratory tests were performed in the morning before the intake of the steroid dose and included ESR, plasma IL-6, hemoglobin, hematocrit, and platelets. Interleukin 6 was determined by using a commercially available kit (R&D Systems, Minneapolis, Minn). Normal serum level of IL-6 is less than 2 pg/mL.

STATISTICAL ANALYSIS

Patients were subsetted according to their initial response to steroid treatment and the length of treatment. The 3 resulting subsets were compared for pain scores, ESR, and plasma IL-6 at the initial presentation and after 4 weeks of steroid treatment using the rank sum test (SigmaStat 2.0; Jandel Scientific, San Rafael, Calif).

RESULTS

PROSPECTIVE TREATMENT STUDY OF PMR

Thirty untreated patients who fulfilled the diagnostic criteria for PMR were enrolled into the study. The 27-

hisotomorphology. Interleukin 2, IL-1, IL-6, and transforming growth factor β1 genes are transcribed in temporal artery tissue, a pattern resembling that in fully developed GCA. From these studies, it appears that vascular involvement in most PMR cases remains subclinical but that similar pathogenic mechanisms may apply to both PMR and GCA. It is not understood why some patients with PMR develop frank vasculitis and why the disease process remains limited in others. It is possible that yet another variant of PMR exists that is strictly limited to musculoskeletal manifestations. Identification of patient subsets differing in disease course and prognosis would enhance our understanding of PMR and would be important in developing a differential therapeutic approach.

Typically, in patients with PMR marked improvement in symptoms occurs within 24 to 48 hours after initiating low- or moderate-dose corticosteroid therapy. This prompt relief following introduction of corticosteroid is sometimes considered a diagnostic criterion to differentiate PMR from other inflammatory arthropathies and myopathies. Because PMR is considered a chronic, yet self-limited condition, the goal of therapy is to relieve stiffness and pain, to suppress the systemic symptoms, and to prevent vascular complications should GCA develop later. Although corticosteroids are universally accepted as the treatment of choice, no guidelines on the optimal dose and duration of treatment have been developed based on clinical findings.

It was the purpose of this study to prospectively evaluate a cohort of patients with PMR who received a defined regimen of corticosteroids. We wanted to explore whether differences exist in the clinical and laboratory responses to initial steroid therapy that might be used to guide treatment. Prednisone was tapered rapidly to minimize cumulative steroid doses. The patients displayed marked heterogeneity in their early and late treatment responses, suggesting that the diagnostic category of PMR includes several distinct variants of the disease. During the chronic phase of the disease, flares could usually be treated with low doses of prednisone. Pretreatment ESR and the response of plasma IL-6 concentrations to corticosteroid were identified as parameters that helped separate patients with PMR into categories with different prognoses and steroid requirements.
The response to corticosteroids and the duration of therapy varied within the patient cohort. In 4 patients, clinical improvement permitted discontinuation of corticosteroid treatment as early as 18 weeks without a relapse. The remaining patients required more prolonged therapy. As shown in Figure 1, 50% of the patients were still receiving treatment after 15 months. The study cohort also included 1 individual who had a long-term course with ongoing corticosteroid therapy more than 2 years following enrollment.

 PATIENT SUBSETS BASED ON THE RESPONSE TO INITIAL ORAL CORTICOSTEROIDS AND THE DURATION OF THERAPY

Analysis of the clinical and laboratory responses to initial corticosteroid therapy and the time that elapsed before corticosteroids could be discontinued showed that the patients could be classified into 3 distinct subsets. One subgroup of 8 patients (30%) was characterized by a short disease course, during which the response to initial therapy with 20 mg of prednisone daily was rapid and tapering was unassociated with significant relapses. In these 8, the treatment period was less than 1 year. Four patients were able to follow the scheduled steroid withdrawal without alterations and received treatment for only 4.5 months. Four additional patients transiently required an increase in the prednisone dose of 5 mg but could then discontinue the medication in less than 12 months. On long-term follow-up, these patients remained in remission. Overall, their clinical outcome indicated a benign course. Prednisone doses and recorded pain scores from a patient in that category are shown in Figure 2, A.

The remaining 19 patients needed treatment for more than 12 months. Twelve (44%) of these patients had resolution of symptoms with the initial dose of 20 mg of prednisone daily. When prednisone was reduced to 10 mg daily, the disease remained inactive. However, tapering below that level resulted in recurrence of pain and stiffness. The number of disease flares increased as the dose of prednisone was further decreased to 5 mg and 2.5 mg daily. All these 12 patients needed to be treated for longer than 1 year because their prednisone therapy had to be repeatedly adjusted upward temporarily to control recurrent disease flares. Corticosteroid doses in relation to pain scores from a representative patient are shown in Figure 2, B.

Seven patients (26%) required corticosteroid therapy beyond 12 months and had early evidence of more resistant disease. These 7 patients responded incompletely to the starting dose of 20 mg of prednisone daily. Most of the patients in this category had clinical improvement on initiation of treatment, but none of them had a complete resolution of aching within 4 weeks. Prednisone doses were increased to 30 mg daily or the treatment period with 20 mg daily was extended to more than 4 weeks to control symptoms. These dose adjustments resulted in a reduction in pain scores in all 7 patients. Eventually, acceptable control of clinical disease activity was reached in all 7 initial poor responder patients and corticosteroid doses could then be decreased. A typical course of pain indexes and steroid treatment for a patient from this subset is shown in Figure 2, C.

In summary, 3 distinct subsets of patients could be distinguished by response to corticosteroids and the clinical course. One subset (subset A) had an excellent response to initial therapy and corticosteroid requirements of less than 1 year. Another subset (subset B) had a satisfactory response to initial therapy but a long-term relapsing course that required corticosteroids for more than 1 year. The third subset (subset C) consisted of patients who responded only partially to the initial corticosteroid dose and also required corticosteroids for longer than 1 year.

CLINICAL DISEASE ACTIVITY PARAMETERS IN THE 3 SUBSETS OF PATIENTS WITH PMR

The resulting treatment-based subsets were compared using the patient and physician global assessment and the visual analog scale (0-10) measuring pain and stiffness. Table 1 lists the median pain indexes for the first 16 weeks of the study in the 27 patients and is stratified according to the 3 subsets. Pretreatment levels of pain were
the lowest in subset A (median, 6.7) and the highest in subset C (median, 8.4). This difference was significant at the \( P = .05 \) level. On initiation of therapy, patients in subsets A and B demonstrated excellent improvement. Their median pain indexes dropped below 1.0, indicating complete or nearly complete resolution of myalgia and stiffness within the first month of treatment. In subset B patients, the treatment response was maintained until week 12. At that time in the reduction schedule, the dose of prednisone was dropped from 7.5 to 5 mg daily. In parallel with this dose reduction, median pain indexes rose again, reflecting the remittent course of the disease in subset B \( (P = .01, \text{A vs B, week 16}) \). A different picture emerged for patients in subset C. At no time in the first 4 months of therapy did the median pain/stiffness index drop below 1.0, indicating only a partial response to steroids. Because they had insufficient pain relief with the initial dose of 20 mg of prednisone, corticosteroid doses were increased to 30 mg or the treatment period with 20 mg was extended. Despite this increase in the dose of corticosteroids, median pain indexes remained elevated. The incomplete clinical response persisted and was not only a feature of the early phase of the disease. Pain indexes were higher in subset C patients essentially for the first year of treatment. The duration of morning stiffness and global assessment measurements did not yield significant results (data not shown).

Another measure of disease duration and severity in PMR is the occurrence and number of disease flares, either spontaneous or related to reduction in corticosteroid treatment. In the case of a flare, the study protocol

---

**Table 1. Median Pain Scores in Polymyalgia Rheumatica Subsets**

<table>
<thead>
<tr>
<th>No. of Weeks Elapsed</th>
<th>Subset A ((n=8))</th>
<th>Subset B ((n=12))</th>
<th>Subset C ((n=7))</th>
<th>Difference from A vs B</th>
<th>Difference from A vs C</th>
<th>Difference from B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.7</td>
<td>7.1</td>
<td>8.4</td>
<td>.46</td>
<td>.05</td>
<td>.16</td>
</tr>
<tr>
<td>4</td>
<td>0.4</td>
<td>0.9</td>
<td>2.9</td>
<td>.45</td>
<td>.10</td>
<td>.03</td>
</tr>
<tr>
<td>8</td>
<td>0.5</td>
<td>1.0</td>
<td>2.8</td>
<td>.49</td>
<td>.12</td>
<td>.31</td>
</tr>
<tr>
<td>12</td>
<td>0.5</td>
<td>1.5</td>
<td>2.5</td>
<td>.22</td>
<td>.09</td>
<td>.38</td>
</tr>
<tr>
<td>16</td>
<td>0.7</td>
<td>3.8</td>
<td>2.6</td>
<td>.01</td>
<td>.31</td>
<td>.40</td>
</tr>
</tbody>
</table>

**Figure 2. Disease heterogeneity in polymyalgia rheumatica. Longitudinal prednisone doses and pain scores of 3 patients representative of the 3 clinically defined subsets are shown: A, subset A; B, subset B; and C, subset C.**
required an increase of the daily corticosteroid dose by 5 mg to suppress recurrent pain and stiffness. After pain relief had been achieved, tapering was again attempted. As seen in Table 2, disease flares were a typical feature of patients in subsets B and C. Disease flares were infrequent in subset A patients with a median number of 1 recurrence per patient. Half of the patients in subset A tolerated the withdrawal of corticosteroids without any recurrence of clinical symptoms. The infrequent flares occurred after a median of 4 months of treatment when the patients had reached a median dose of 1 mg of prednisone daily. Patients in subset B experienced a median number of 7 flares and were indistinguishable from patients in subset C. Subset B patients returned with complaints about pain and stiffness when the steroid dose was reduced below 7.5 mg daily. Flares were diagnosed in subset B patients after a median of 3.4 months of treatment. At this time, the patients were taking a median dose of 5 mg of prednisone daily. Thus, subset C patients did not have a higher number of clinically recognized disease relapses but had them early in the course of treatment at higher doses of prednisone during tapering.

LONG-TERM STEROID REQUIREMENTS IN THE 3 SUBSETS OF PATIENTS WITH PMR

The cumulative dose of prednisone in the 3 subsets was determined for 6, 12, and 18 months. Results of this analysis are shown in Figure 3. After 6 months, patients in subset A had taken a median cumulative dose of 1326 mg of prednisone. Patients in subset B had received a significantly higher dose of 1795 mg of prednisone (P = .002). Patients in subset C took the largest amounts of corticosteroid, a median cumulative dose of 3148 mg (P<.001, A vs C; P = .001, B vs C). Differences in steroid requirements continued for the second 6-month period of treatment. Patients in subset A were given a median cumulative dose of 114 mg of prednisone from months 7 to 12. Many of these patients discontinued treatment before month 12 of the study. Patients in subset B were given a median of 888 mg of prednisone (P<.001, A vs B) to control disease activity, which was less than the 1627 mg given to subset C patients during the same period (P = .06, B vs C). Thus, differences in steroid requirements between subsets B and C in the early phase of the disease continued in the second half of treatment year 1, suggesting that disease activity of both the early and chronic phases of the disease were distinct in these 2 patient subpopulations. However, this trend did not continue over the subsequent third 6-month period. Cumulative steroid doses used in subset B patients between months 13 and 18 were not different from those given to subset C patients (P = .77). During the second year, patients in subset C were taken off of therapy in a pattern similar to patients in subset B.

Table 2. Disease Flares in Polymyalgia Rheumatica Subsets

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subset A (n = 8)</th>
<th>Subset B (n = 12)</th>
<th>Subset C (n = 7)</th>
<th>A vs B</th>
<th>A vs C</th>
<th>B vs C</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of flares per patient</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>1.00</td>
</tr>
<tr>
<td>Days elapsed at first flare</td>
<td>125</td>
<td>103</td>
<td>9</td>
<td>.008</td>
<td>.006</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prednisone at first flare, mg</td>
<td>1.3</td>
<td>5.0</td>
<td>20.0</td>
<td>.11</td>
<td>.006</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Days elapsed at second flare</td>
<td>179</td>
<td>148</td>
<td>106</td>
<td>.07</td>
<td>.12</td>
<td>.01</td>
</tr>
<tr>
<td>Prednisone at second flare, mg</td>
<td>5.0</td>
<td>5.0</td>
<td>10.0</td>
<td>.89</td>
<td>.18</td>
<td>.02</td>
</tr>
</tbody>
</table>

Figure 3. Steroid requirements in the clinically defined patient subsets. Cumulative steroid doses for the first (top), the second (middle), and third (bottom) 6-month periods of steroid treatment were determined for the 3 patient subsets. Results are shown as box plots displaying medians, 25th and 75th percentiles as boxes, and 10th and 90th percentiles as whiskers.
sponded with a prompt normalization of the ESR. As nign course of the disease. and IL-6 levels in untreated patients correlate with a be-

tients (measured before prednisone was the lowest at 39 mm/h. positively (allel, IL-6 concentrations were lower in subset A pa-
sets are shown in and IL-6 levels for the 3 clinically defined patient sub-
levels were greater than 5 pg/mL. Nine patients had more IL-6 was less than 5 pg/mL and in 22 patients, the IL-6 values in the 27 patients were as follows: 2 patients, less than 20 mm/h; 15 patients, 20 to 50 mm/h; and 10 pa-
tients, more than 50 mm/h. Similar measurements were obtained for pretreatment plasma IL-6. In 5 patients, the IL-6 was less than 5 pg/mL and in 22 patients, the IL-6 levels were greater than 5 pg/mL. Nine patients had more than 20 pg/mL IL-6 in the plasma. Median ESR values and IL-6 levels for the 3 clinically defined patient sub-
sets are shown in Figure 4. In subset A, the median ESR measured before prednisone was the lowest at 39 mm/h. This distinguished subset A patients from all other pa-
tients (P = .02). Pretreatment ESR results in subset A and subset C patients were clearly different (P = .01). In parallel, IL-6 concentrations were lower in subset A pa-
tients, although they could not be statistically differenti-
tiated from the other patients (P = .11). Erythrocyte sedimentation rate and IL-6 concentrations correlated positively (R² = 0.32). These data suggest that low ESRs and IL-6 levels in untreated patients correlate with a be-

On initiation of prednisone therapy, patients responded with a prompt normalization of the ESR. As shown in Figure 4, the median ESR of all patient subsets returned to the normal range after 4 weeks of treatment. Even in subset C patients, whose clinical response was incomplete and required increased doses of prednisone in the early phase of the disease, the ESR improved with a reduction of median ESR from 49 to 22 mm/h. A dif-

rence in the IL-6 concentrations. Treatment with prednisone reduced levels of circulating IL-6 in many but not all patients. Median IL-6 values dropped below 10 pg/mL in the patients in subsets A and B. In subset B, the pretreatment to posttreatment change was statistically signifi-
cant (P = .005). In contrast, IL-6 produc-
duction remained elevated in the subset C patients, who clinically were categorized as partial responders. In that patient subset, median IL-6 levels determined before and after prednisone therapy were unchanged with median levels of 28.2 pg/mL and 21.9 pg/mL (P = .99).

In summary, pretreatment ESRs were helpful in identifying patients who required low doses of corticoste-
roid therapy for less than 1 year (subset A), and the re-

isease at the start of treatment and later. Pountain and Hazleman also noted that a high pretreatment ESR correlated with duration of treatment.

While most physicians agree that corticosteroids are the treatment of choice in patients with PMR, controversy exists as to how much corticosteroid should be given ini-

tially and how it should be tapered. The aim of this pro-
spective treatment study was to determine whether clinical or laboratory findings or response to a fixed schedule of prednisone with rapid dose reductions could be used to differentiate patients with mild and severe disease and to develop a rationale for therapeutic guidelines in PMR. The results indicated that patients varied clinically and in their initial response to treatment, which predicted their course and the ability to reduce steroid intake during the chronic phase of the disease.

While it has been observed that patients with PMR differ in their steroid requirements, information from con-

rolled studies is limited. This partially relates to the dif-
ficulties in unequivocally diagnosing PMR, difficulties in quantitating the clinical symptoms, and in excluding ac-
tive GCA in some of the patients who have no vascular symptoms or findings. It has been proposed that on follow-
up, the diagnosis has to be revised in up to 25% of pa-
tients initially diagnosed as having PMR. In the cur-

ent study cohort, the diagnosis changed in 10% of the patients. We found no clinical or laboratory features that distinguished these patients.

In previous studies on the treatment of PMR, dif-

ferences in clinical course, outcome, and response to therapy have been commonly noted, but factors deter-
m

ing these differences have not been well defined. Dolan and coworkers noted that high pretreatment ESRs indi-
cated more severe disease in their patients as evidenced by a longer course and reduced spine bone density at the start of treatment and later. Pountain and Hazleman also noted that a high pretreatment ESR corre-

lated with duration of treatment.
In 20 patients with PMR, Schreiber and Buyse measured the C-reactive protein, ESR, and fibrinogen before therapy with 15 mg of prednisone per day and again after 1 week of treatment. In 11 patients, they found the C-reactive protein had returned to normal after 1 week of therapy, whereas it remained elevated in the other 9. The former patients, the patients with PMR, had a shorter treatment course and required lower amounts of corticosteroids. They concluded that the C-reactive protein initial response to corticosteroid therapy may be a prognostic factor in patients with PMR. These results are consistent with our findings.

In this study, we were able to demonstrate considerable diversity among patients when treated with a fixed corticosteroid regimen, allowing us to group the patients into 3 subsets. One subset of patients was characterized by excellent early and continued corticosteroid response. The short duration of disease was the most important feature of these patients. Therapy was discontinued for all within 1 year. Their clinical presentation, including pretreatment pain levels and prompt clinical improvement with corticosteroid treatments, were typical of PMR. It is likely that these patients could be treated with lower initial doses than we used. However, this question needs to be approached prospectively. It is possible, though, that the abbreviated course of their disease was a consequence of effective suppression during early management. Laboratory parameters indicated that these patients had lower pretreatment ESRs and a trend for lower plasma IL-6 levels as well. The long-term prognosis of these patients was excellent and none developed frank GCA nor returned with recurrent disease.

Twelve patients (subset B) (44%) in the study cohort fell into a category of satisfactory early treatment responses but frequent disease relapses on steroid tapering. Interestingly, these patients were able to rapidly reduce the daily steroid dose to 7.5 mg but then required chronic treatment with low doses of prednisone to control pain and stiffness. Overall these patients had a good long-term prognosis. One of the 12 patients later developed arteritis. A temporal artery biopsy was performed when she presented with clinical signs of cranial arteritis after several months of corticosteroid treatment. Most (89%) of these patients were able to discontinue corticosteroid treatments in less than 2 years.

The most unexpected finding was the high proportion of patients (26%) who did not respond adequately to the initial dose of prednisone, ie, 20 mg/d. Patient selection and referral bias may explain this. The study protocol allowed for continuing the initial dose of 20 mg/d of prednisone or increasing to 30 mg/d if there was little response to 20 mg/d. Despite increased doses of prednisone, these patients had continued symptoms and seldom had pain scores below 1.0, which essentially correlated with clinical remission. In concordance with the continuous clinical activity, these patients had elevated IL-6 levels even after 4 weeks of corticosteroid therapy. Interestingly, their ESRs had normalized, pointing out that this laboratory parameter is not always able to measure persistent acute phase responses. Rather, the normalization of the ESR was probably mistaken by the treating physician as a sign of successful therapy. Pretreatment ESRs and IL-6 values were not helpful in distinguishing patients in subsets B and C, but nonresponder patients could easily be detected by the persistent elevation of IL-6 production after initiation of prednisone therapy. We have preliminary evidence that responses of IL-6 concentrations 24 hours following a single 20-mg dose of prednisone might be useful to identify patients in whom IL-6 production cannot be suppressed within the first 4 weeks of treatment. This parameter could thus be used in selecting the patient subset with higher corticosteroid requirements early in the management of PMR. Over the chronic course of the disease, subset C patients were characterized by continuously elevated pain scores, which indicated continued active disease. It is possible that the insufficient suppression of inflammation affects the long-term outcome of these patients. Two of the 7 patients in this subset developed GCA. Our study cohort was too small to estimate whether the overall risk of this subset to progress to GCA is increased. Because patients with uncontrolled GCA are at risk to develop vascular complications such as aortic aneurysms, it would be important to identify and sufficiently treat them with the goal to eliminate the inflammatory process in the arterial wall. The current data indicate that a significant proportion of our patients with PMR were undertreated with an initial dose of prednisone 20 mg/d.

As a basis for further discussion and study, the data lend themselves to the beginning of guidelines for therapy and expectations of outcome in PMR (Table 3). Be-

### Table 3. Preliminary Treatment Guidelines for Polymyalgia Rheumatica*

<table>
<thead>
<tr>
<th>Critical Criteria</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subset A</td>
<td></td>
</tr>
<tr>
<td>Initial ESR &lt; 50 mm/h</td>
<td>Initial dose, 10 mg/d of prednisone; reduce by 1 mg every month; expect short course of disease uncomplicated by exacerbations</td>
</tr>
<tr>
<td>Initial IL-6 &lt; 10 pg/mL</td>
<td></td>
</tr>
<tr>
<td>Pain level after 2 wk of treatment &lt; 2</td>
<td></td>
</tr>
<tr>
<td>IL-6 after 1 mo of treatment &lt; 10 pg/mL</td>
<td></td>
</tr>
<tr>
<td>Subset B</td>
<td></td>
</tr>
<tr>
<td>Initial ESR &gt; 50 mm/h</td>
<td>Initial dose, 20 mg/d of prednisone; reduce by 2.5 mg every month to 10 mg/d, then 1-mg reductions every month; expect intermediate course with exacerbations if prednisone reduced too quickly</td>
</tr>
<tr>
<td>Initial serum IL-6 &gt; 10 pg/mL</td>
<td></td>
</tr>
<tr>
<td>Pain level after 2 wk of treatment &lt; 2</td>
<td></td>
</tr>
<tr>
<td>IL-6 after 1 mo of treatment &lt; 10 pg/mL</td>
<td></td>
</tr>
<tr>
<td>Subset C</td>
<td></td>
</tr>
<tr>
<td>Initial ESR &gt; 50 mm/h</td>
<td>Initial dose, 20 mg/d of prednisone for 2-4 wk; then adjust dose to control symptoms and normalize IL-6 levels; expect prolonged course with need for increased prednisone doses; consider temporal artery biopsy; measurement of temporal artery cytokines may help direct future therapy</td>
</tr>
<tr>
<td>Initial IL-6 &gt; 10 pg/mL</td>
<td></td>
</tr>
<tr>
<td>Pain level after 2 wk of treatment &gt; 2</td>
<td></td>
</tr>
<tr>
<td>IL-6 after 1 mo of treatment &gt; 10 pg/mL</td>
<td></td>
</tr>
</tbody>
</table>

*ESR indicates erythrocyte sedimentation rate; IL-6, interleukin 6.
at lower doses, we have included our more commonly used method of dose reduction. Further testing of these guidelines is needed to determine their usefulness. In addition, therapy for osteoporosis needs to be considered in all patients being started on a regimen of long-term corticosteroid treatment.

Understanding the unique effects of corticosteroids in PMR holds promise to provide clues to the pathogenesis of this disease. Unraveling the molecular basis of the therapeutic action of corticosteroids may also permit the development of alternative treatment strategies. As opposed to other rheumatic diseases in which steroid-sparing agents such as cytotoxic medications have a role, corticosteroid and possibly nonsteroidal anti-inflammatory agents appear to be the only effective treatments for PMR. Recognizing that PMR might indeed be a heterogeneous disorder, including several variants of disease, will be essential in guiding the necessary clinical and pathogenic studies.

Accepted for publication June 22, 1998.

This study was supported in part by the Mayo Foundation, R&D Systems, Minneapolis, Minn, and grant EY11916 from the National Institutes of Health, Bethesda, Md.

We thank Jane Jaquith for her time and effort spent with the patients, Toni L. Higgins and Staci Thesing for secretarial support, and our colleagues in the Division of Rheumatology, Mayo Clinic Foundation, Rochester, Minn, for referring patients for this study.

Reprints: Cornelia M. Weyand, MD, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (e-mail: weyand.cornelia@mayo.edu).

REFERENCES