EXTENDED REPORTS

Can methotrexate be used as a steroid sparing agent in the treatment of polymyalgia rheumatica and giant cell arteritis?

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Abstract

Objective—To investigate whether methotrexate (MTX) has a steroid sparing effect in the treatment of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA).

Methods—We carried out a randomised double blind, placebo controlled study in 40 patients with PMR, six of whom also had clinical symptoms of GCA. A temporal artery biopsy specimen was available from 37 patients; GCA was found in six of the specimens. Among the six patients with clinical signs of GCA, three had a positive biopsy specimen. All patients were started on prednisone 20 mg/day, irrespective of clinical signs and biopsy result, supplemented with a weekly, blinded capsule containing either MTX 7.5 mg or placebo. The prednisone dose was decreased as soon as clinical symptoms disappeared and erythrocyte sedimentation rate, C reactive protein level, or both, had normalised.

Results—Twenty one patients were followed for two years, or at least one year after discontinuing medication. No differences were found between the MTX group and the placebo group concerning time to achieve remission, duration of remission, number of relapses, or cumulative prednisone doses. After 21 weeks the mean daily prednisone dose was reduced by 50%. Forty percent of all patients were able to discontinue prednisone within two years. Median duration of steroid treatment was 47.5 weeks (range 3–104). No serious complications from GCA were encountered.

Conclusions—With a (rapid) steroid tapering regimen, it was possible to reduce the mean daily prednisone dose by 50% in 21 weeks and to cease prednisone in 40% of the patients within two years. With this regimen, no steroid sparing effect of MTX in a dosage of 7.5 mg/week was found.

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onset of disease usually is abrupt, but may be preceded for months by malaise, depression and loss of weight. The erythrocyte sedimentation rate (ESR) is almost always strongly increased and symptoms usually respond very well to a small dose of prednisone (10–20 mg/day). PMR can occur in combination with giant cell arteritis (GCA). Manifestations of GCA are headache, tenderness of the scalp, especially over the temporal arteries, jaw claudication, and visual loss. PMR and GCA frequently coexist, but the percentages of concurrence vary in different populations.^{1 2} Some authors consider PMR and GCA as different manifestations of the same underlying process.³

Corticosteroid treatment usually induces prompt relief of symptoms, and some authors consider this dramatic response to be one of the diagnostic criteria for both diseases.^{2 4 5} The ideal initial prednisone dose, tapering scheme, and duration of treatment are much debated.^{6–10} Current opinion is that alteration in steroid dose should be based predominantly on clinical signs and symptoms as an increase in ESR or C reactive protein (CRP) does not always predict relapse; that treatment usually lasts at least two years; and that relapses are most frequent within the first one or two months (related to attempted reduction of steroid dose) and within one year of withdrawal of steroids.^{3 4 11 12} Usually, GCA is treated with high doses of prednisone (1 mg/kg/day) for fear of ocular complications. However, corticosteroid treatment does not always prevent blindness and, furthermore, a clear relation has been found between initial and cumulative prednisone doses and side effects.¹³ Methotrexate (MTX) has been suggested as a steroid sparing agent in the treatment of chronic steroid dependent asthma.¹⁴ Several preliminary reports suggest that MTX may be steroid sparing in patients with GCA and Takayasu's arteritis.^{15 16} We conducted a double blind, placebo controlled study on the possible steroid sparing effect of MTX in the treatment of PMR and GCA, and present the results after two years of follow up.

Patients and methods

Between November 1989 and November 1991, 40 patients with active untreated PMR, GCA, or both, were included in a randomised double

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Polymyalgia rheumatica (PMR) is a clinical syndrome of older patients, characterised by pain and stiffness in the neck, shoulders, or hips that persists for at least a month. The

blind, placebo controlled study that was carried out in four outpatient clinics for rheumatology (University Hospital Utrecht, St Antonius Hospital Nieuwegein, Diaconessen Hospital Utrecht, and Eemland Hospital Amersfoort) cooperating in the Arthritis Research Foundation Utrecht. Randomisation was performed separately for each clinic. Criteria for diagnosis of PMR were pain and stiffness in shoulders, hips, or both, existing for more than one month in patients older than 50 years of age, and ESR ≥ 40 mm/1st h. Criteria for a clinical diagnosis of GCA were new onset temporal headache, jaw claudication, temporal artery tenderness on palpation or decreased pulsation, abnormal temporal artery biopsy specimen, and ESR ≥ 50 mm/1st h, beginning at age 50 or older.¹⁷ Patients with signs or laboratory findings suggestive of polyarthritis, polymyositis, malignancy, thyroid dysfunction, Parkinson's disease, or severe infections were not included in the study. Patients with abnormal liver tests (aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than twice the normal value), renal insufficiency (serum creatinine ≥ 150 $\mu\text{mol/l}$), or abuse of alcohol were not included.

At initial presentation the following were investigated in all patients: haemoglobin, leucocyte count, platelet count, ESR (Westergren), CRP (nephelometric), serum creatinine, alkaline phosphatase, AST, ALT, lactate dehydrogenase, plasma proteins, serum protein electrophoresis, creatine phosphokinase, glucose, thyroid stimulating hormone, Latex fixation, and Waaler-Rose test. Radiographs of the chest, cervical spine, and pelvis and, if possible, lung function tests were performed. To avoid bias and negative selection in one of the treatment groups we took temporal artery biopsy specimens from all patients except three who did not give their consent.

All patients started taking prednisone 20 mg/day, irrespective of the presenting symptoms (PMR only, or PMR and GCA) and outcome of temporal artery biopsy. In addition, they received once a week a blinded capsule containing either MTX 7.5 mg or placebo. All non-steroidal anti-inflammatory drugs were stopped. A rapid steroid tapering regimen was designed in order to stress potential differences between the two treatment groups. As soon as, and as long as, clinical symptoms had disappeared **and** ESR was ≤ 15 mm/1st h or CRP was ≤ 0.6 mg%, the daily dose of prednisone was reduced by 2.5 mg every three weeks until it reached 7.5 mg; it was then tapered by 2.5 mg every six weeks (minimal cumulative dose 2126.25 mg in 33 weeks). After discontinuation of prednisone, the blinded capsule was taken once every two weeks for three administrations and then stopped. To prevent steroid induced osteoporosis, oral calcium supplements were prescribed.

Remission was defined as the time of discontinuing both prednisone and trial medication. *Relapse* was defined as recurrence of the original symptoms **and** an increase of 100% in ESR or CRP in patients still receiving corticosteroids. *Recurrence* was defined as recur-

rence of the original symptoms **and** an increase of 100% in ESR or CRP after stopping prednisone and trial medication. An increase in ESR without symptoms was not considered sufficient evidence of relapse or recurrence. In the event of relapse, the current prednisone dose was doubled (to a maximum of 20 mg/day) until symptoms disappeared **and** ESR or CRP normalised. The tapering scheme described above was then resumed.

Follow up was every three to six weeks until the patient achieved remission, after which the patient's visits were scheduled every three months up to two years or at least one year after withdrawal from medication. On each visit, the patient was asked about muscle pain or stiffness, morning stiffness, malaise, headache, visual disturbances, and jaw claudication. Body weight and blood pressure were recorded. ESR, CRP, full blood count, creatinine, AST, ALT, glucose and albumen were measured. The number of adverse effects was noted: gastrointestinal complaints, oral ulceration, hair loss, rash, osteoporosis, and infections.

STATISTICS

Differences in continuous variables between groups were analysed with the two tailed Student's *t* test. Statistical significance of differences in binomial or categorised variables was assessed with χ^2 tests with the Yates' correction; in the event of small numbers, Fisher's exact test was used. Significance was accepted for $p \leq 0.05$. Medians and range are given for variables that did not show a normal distribution. All analyses were performed with the statistical package SPSS-PC + 4.0.

Results

PATIENTS

Forty patients (30 women, 10 men) were included in the study: 20 in the MTX group and 20 in the placebo group. Mean age was 70.9 years (range 53–84). All patients presented with symptoms of PMR and six also had signs of GCA. Twenty one patients were followed up to two years, or at least one year after discontinuing medication. Fourteen patients withdrew from the study during the first year: four in the MTX group and 10 in the placebo group (table 1). In the second year, another five patients from the MTX group withdrew, but none from the control group did so. Data of all patients were included in the study results until the time of their withdrawal, reasons for which are shown in table 1. One patient died during the study period, two weeks after reaching remission. Five patients died after withdrawal. Causes of death were malignancy (three cases), multiorgan failure (possibly as a result of amyloidosis: one case) and cardiac death (two cases). There was no evidence that arteritis or trial medication was related to cause of death. In three patients, the steroid scheme was violated so that evaluation was no longer possible: one patient needed intravenous administration of steroids because

Table 1 Details of patients who withdrew during the study

Study drug	Sex	Age (yr)	Time of withdrawal (week No)	Reason for withdrawal
MTX	F	78	5	Oral ulceration and psychosis*
	M	56	35	Cardiac death two weeks after remission
	F	53	41	Abnormal liver tests
	F	56	42	Psychological reasons
	F	81	55	Depression
	F	60	69	Withdrawal after third relapse
	M	62	71	Stopped capsules before total hip surgery
	F	78	74	Violation of steroid regimen
	F	84	88	Developed RF-ve polyarthritis
Placebo	F	59	3	Multiorgan failure*
	F	69	5	Psychological reasons
	F	77	10	Liver carcinoma*
	F	74	23	Developed RF-ve polyarthritis
	F	83	25	Violation of steroid regimen
	M	78	25	Psychological reasons
	F	78	35	Bladder carcinoma*
	F	72	36	Non-Hodgkin lymphoma*
	M	83	39	Lost to follow up
	F	79	41	Violation of steroid regimen

*Patient died shortly after withdrawal.
MTX = Methotrexate; RF = rheumatoid factor.

Table 2 Numbers of patients experiencing adverse effects

	MTX group	Placebo group
Gastrointestinal complaints	5	5
Hair loss	1	0
Oral ulceration	3	3
Rash	0	1
Increase in blood pressure	11	8
Hypertension	9	5
Increase in body weight	14	11
Cardiac insufficiency	2	1
Osteoporosis (fractures)	1	2
Infections	5	2
Thrombocytopenia	0	1
Increase in AST/ALT	15	8
Increase in serum creatinine	7	10
Hyperglycaemia	5	7

MTX = Methotrexate; AST = serum aspartate aminotransferase; ALT = serum alanine aminotransferase.

of an exacerbation of chronic bronchitis, one patient was suspected of suffering adrenal insufficiency during a hospital stay for cardiac failure and received high dose corticosteroids, and one patient refused oral prednisone after 25 weeks and was prescribed an alternative intramuscular regimen. Three patients withdrew for psychological reasons. Two patients developed rheumatoid factor negative polyarthritis. Two other patients stopped the capsules: one awaiting surgery (total hip replacement for osteoarthritis), and one because of lack of efficacy (third relapse in week 69). Three patients experienced adverse effects, most probably attributable to trial medication: one patient had oral ulceration and psychosis, recurring after rechallenge with the blinded capsule; one patient had liver abnormalities for

which the medication was interrupted and, in error, not restarted after normalisation; one patient was depressed and refused to continue taking the capsules.

In both groups, many side effects were encountered that did not lead to withdrawal (table 2). All patients experienced at least one adverse effect; the number of effects experienced varied from one (six patients) to eight (two patients). Twenty five patients (63%) experienced an increase in body weight (≥ 1 kg) and 19 patients (48%) had an increase in blood pressure (≥ 5 mm Hg diastolic or systolic); overt hypertension (diastolic pressure ≥ 100 mm Hg or systolic pressure ≥ 200 mm Hg) occurred in 14 patients (35%).

The total number of patient-weeks of follow up was 2906 (1624 for the MTX group and 1282 for the placebo group) and the mean duration of follow up in the two groups was 81.2 and 64.1 weeks, respectively. Because of these differences between the two groups, data on cumulative prednisone dosages, duration of prednisone treatment, and number of relapses were corrected for the number of patient-weeks per group.

TEMPORAL ARTERY BIOPSY

Thirty seven patients gave their permission for the removal of a temporal artery biopsy specimen before starting treatment. Six patients had at least two clinical signs of GCA (table 3); in only three of them was histological proof of arteritis found in the biopsy specimen. In three other patients without clinical evidence of GCA, biopsy revealed arteritis. Positive biopsy results were distributed equally between the groups ($n = 3$ in each group). No correlation was found between clinical signs and biopsy results (table 3). The one patient who had four signs of GCA (headache, visual symptoms, jaw claudication, and tender temporal arteries on palpation) and a positive biopsy result had to be withdrawn from the study after 10 weeks, because she appeared to have carcinoma of the liver.

RELAPSE RATE

While still taking prednisone, 10 patients in the MTX group had a total of 18 relapses and nine patients in the placebo group had a total of 15 relapses, requiring an increase in their dose of prednisone. The most common symptoms during relapses (as a percentage of all symptoms) were muscle pain and stiffness (about 45%) (table 4). Visual complaints and headache occurred only in small percentages of the patients, with no difference between the two groups or between patients with positive and negative biopsy results. Relapses occurred in seven patients receiving prednisone doses of 10–15 mg/day and in 26 receiving doses ≤ 7.5 mg/day.

REMISSION

The median time to achieve remission and stop prednisone in the MTX group was 48 weeks

Table 3 Clinical signs of giant cell arteritis* related to biopsy results

Sex	Group	Headache	Visual symptoms	Jaw claudication	Tender temporal artery	Absent temporal artery pulse	Positive biopsy
F	P	+	–	–	–	–	–
F	P	+	+	+	+	–	+
F	P	–	–	+	–	–	–
F	MTX	+	–	–	–	–	–
F	P	+	+	+	–	–	–
F	P	–	–	–	–	–	+
F	MTX	+	+	–	+	–	+
F	MTX	–	–	+	+	–	–
M	P	–	–	–	–	–	+
F	MTX	+	+	+	+	+	–
F	P	+	–	–	–	–	–
F	MTX	+	–	–	+	–	+
F	MTX	–	–	–	–	–	+

*All patients reporting a clinical sign are shown.
MTX = methotrexate; P = placebo.

Table 4 Frequency of symptoms during relapses

	Symptom occurrence (%)				
	Muscle pain/ stiffness	Morning stiffness	Malaise	Visual symptoms	Headache
MTX group	48	19	19	4	10
Placebo group	44	22	18	7	9
Biopsy positive	42	19	15	6	19
Biopsy negative	47	21	20	5	7

MTX = Methotrexate.

(range 30–100); that in the placebo group was 45 weeks (range 22–104). Median duration of remission was 7 weeks (range 1–74) and 35 weeks (range 0–71), respectively. These differences were not statistically significant. Duration of remission varied widely and did not seem to be correlated with the time to achieve remission (table 5). Eleven patients were able to stop all medication (six within one year, five in the second year) without any recurrence in the two years of follow up. Nine patients had a recurrence: two of them did not want to restart prednisone, two needed an additional limited course (of 19 and 37 weeks, respectively), and five were still taking prednisone at week 104. One patient who completed follow up had not been able to withdraw from steroids.

TREATMENT WITH CORTICOSTEROIDS

In all patients, prednisone 20 mg/day was sufficient to control symptoms of PMR/GCA. No significant differences were found in the course of changes in ESR and CRP between the two groups (table 6): after three weeks of treatment, ESR and CRP were more reduced

in the MTX group than in the placebo group, but this difference was not statistically significant. Table 6 shows that prednisone dosages and the tapering regimen did not differ significantly between the two groups during the first year of the study. After 21 weeks, the mean daily dose of prednisone was reduced by 50%, and after one year it was 3.5 mg. To achieve remission, the MTX group needed a median total dose of 2756 mg prednisone (range 2100–7087) and the placebo group 2747 mg (range 1452–5294). The median cumulative prednisone dose after the first year was 2052 mg (range 1293–3825) in the MTX group and 2286 mg (range 1515–4047) in the placebo group. After two years the values were 2400 mg (1293–4364) and 2947 mg (1515–4641), respectively. Patients in the MTX group had a median steroid treatment period of 41 weeks (range 3–63); for those in the placebo group it was 29 weeks (range 2.5–81) (values are corrected for patient-weeks of follow up). None of these differences between the two groups was statistically significant.

After two years of follow up, six of 21 patients (28.5%) were still taking corticosteroids, and 15 of 21 patients (71.5%) had ceased taking prednisone. Among the patients who withdrew from the study (n = 19), six had died, seven were still taking prednisone after two years, one was no longer taking steroids; no information on prednisone use was available for five patients. Thus at least 16 of the initial 40 patients (40%) were no longer taking corticosteroids after two years.

COMPLICATIONS OF THE DISEASE

At the start of the study there were no patients with irreversible visual disturbances. During follow up no other ocular or vascular complications occurred.

Discussion

Complete follow up was available for 21 patients; unfortunately, 19 of the initial 40 patients withdrew from the study. Only three of those withdrew because of adverse effects of MTX; in all other cases, withdrawal most probably was not related to PMR/GCA or the trial medication. Data were included in the analysis up to the time of withdrawal from the trial, for every patient.

Table 5 Time to achieve remission, and duration of remission

MTX group (n = 11)		Placebo group (n = 9)	
Time to remission (weeks)	Duration of remission (weeks)	Time to remission (weeks)	Duration of remission (weeks)
30	—	33	—
31	—	33	2
33	3	36	—
43	—	41	8
43	21	45	—
48	7	59	—
50	32	66	—
55	7	69	—
69	—	70	—
94	3		
100	2		

— = Still in remission at week 104.

Table 6 Mean and range of daily prednisone dose, erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) during the first year of the study

Week No	MTX group				Placebo group			
	Prednisone dose (mg)	ESR (mm/1st h)	CRP (mg%)	No of patients	Prednisone dose (mg)	ESR (mm/1st h)	CRP (mg%)	No of patients
Start		82	7.1	20		91	9.0	20
3	20.0	19	0.5	20	19.5 (15–20)	28	2.4	20
6	18.4 (17.5–20)	24	1.0	19	17.6 (12.5–20)	25	2.2	18
9	16.8 (15–20)	28	1.3	19	16.0 (10–20)	24	0.8	18
12	14.7 (12.5–20)	20	0.4	19	14.3 (7.5–20)	23	1.4	17
15	13.2 (10–20)	15	0.6	19	12.4 (7.5–17.5)	30	0.8	17
18	11.5 (6.25–20)	20	0.2	19	11.0 (7.5–20)	23	1.8	17
21	10.9 (6.25–20)	20	0.8	19	9.5 (2.5–20)	27	1.3	17
30	7.0 (1.25–15)	22	1.4	19	6.3 (2.5–15)	21	0.5	14
42	4.6 (0–12.5)	18	1.0	17	4.5 (0–10)	17	2.4	10
52	3.5 (0–15)	25	0.6	16	3.6 (0–10)	23	0.6	10

MTX = Methotrexate.

Eleven patients achieved remission in 30–70 weeks (median 45) and maintained remission throughout the study. Nine patients had a recurrence of symptoms after discontinuing medication; five of them were still taking steroids after two years of follow up. One patient was never able to withdraw completely from prednisone. Many relapses were seen, most frequently with prednisone doses ≤ 7.5 mg/day, requiring dose adjustment. Although, at the start of the study, we defined relapse as a combination of clinical symptoms **and** increase in ESR or CRP, it was not always possible to put these criteria strictly into practice. Sometimes patients increased their dose between visits to the outpatient clinic, without ESR or CRP being measured. Therefore, from a pragmatic point of view, all increases in prednisone dose were considered as relapse.

No differences were found between the MTX group and the placebo group concerning the time to achieve remission, duration of remission, or number of relapses. Duration of remission was shorter in the MTX group, in which seven of 11 patients had a recurrence, than in the placebo group, in which two of nine patients had a recurrence. However, this clinically relevant difference did not reach statistical significance. An explanation for a more rapid recurrence in the MTX group could be the rather quick discontinuation of MTX, six weeks after stopping prednisone. It is possible that, as in rheumatoid arthritis, a flare of disease activity occurs after stopping MTX. No differences were found between the two groups in the prednisone tapering regimen, median prednisone dose needed to achieve remission, cumulative doses after one and two years, or duration of steroid treatment. Furthermore, by combining the most relevant outcome variables (time to achieve remission, duration of remission, number of relapses, cumulative prednisone doses) into a pooled index,¹⁸ we were still not able to demonstrate a difference between the groups. The conclusion from our data is that MTX in a dosage of 7.5 mg/week does not have a steroid sparing effect in the treatment of PMR/GCA. However, the high recurrence rate in the MTX group, possibly as a result of a flare of disease activity induced by discontinuation of MTX, might suggest at least some effect of MTX. It could be possible that the MTX dose that we used was not large enough; Hernández *et al*¹⁶ used a dose of 10 mg/week in their pilot study on GCA, Krall *et al* found a steroid sparing effect of MTX for corticosteroid resistant PMR and GCA at a dose of 12.5 mg/week (three case histories),¹⁹ and for the treatment of steroid resistant or relapsing Takayasu arteritis, a mean MTX dose of 17.1 mg/week was used.¹⁵ Another explanation for our failure to demonstrate a steroid sparing effect of MTX might be that the low cumulative dose of corticosteroids that we used prevented the demonstration of an additional steroid sparing effect of MTX.

No correlation was found between the time to achieve remission and the time of recurrence

(table 4). No variables were found to be indicative for rapid response to treatment, relapse rate, or chance of recurrence. In contrast with other studies, we found that many patients were able to stop corticosteroid treatment within two years: 15 (71.5%) of the 21 patients who completed the study and at least 16 (40%) of the initial group of 40 patients. In common with other authors, we seemed to find two populations of patients: one group with a self limiting disease, and another with a more persistent process.⁸

Despite the relatively low cumulative dose of steroid, many adverse effects were seen, most of which were probably attributable to prednisone. Adverse effects were reported in 65% of the follow up visits of the MTX group and in 70% for the placebo group. All patients experienced at least one side effect: increase in body weight (63%, ≥ 1 kg) and blood pressure (48%) were noted most frequently. Our data are consistent with those from an earlier prospective study which found an incidence of 36% of steroid associated side effects or, if weight gain was included, 76%.¹³ It should be pointed out, however, that weight loss before entry to the study, as a result of the disease, was not accounted for.

No differences in the clinical course were found between patients presenting with symptoms of PMR only or PMR and GCA, with or without a positive temporal artery biopsy result. We did not find a correlation between biopsy result and clinical presentation (table 3). This corroborates the findings of Bengtsson *et al*, who reported 46% negative biopsy results in patients with clinical signs of GCA and 31% positive results in patients with signs of PMR only.²⁰ Temporal artery biopsy does not seem to be of prognostic value in PMR.^{5, 21} Retrospectively, one of our patients was shown to have concurrent biopsy proven GCA and liver carcinoma. At the start of the study, no patient presented with severe visual disturbances, and during follow up no ocular or vascular complications were encountered. We treated all patients with the same low dose of prednisone (20 mg/day), without problems. These findings corroborate those of Myles *et al*,²¹ who found that prednisolone 20 mg/day was an adequate starting dose for the treatment of GCA, providing a very high degree of protection from serious ocular complications, and those of Delecoeuillerie *et al*,²² who found that low doses of corticosteroids seemed an adequate treatment for most cases of temporal arteritis. Furthermore, larger doses of steroids have been shown not to offer complete protection from ocular complications.²¹ However, the number of patients in our study was too limited to permit definite conclusions to be drawn concerning the relation between biopsy findings and clinical symptoms, or the optimal steroid dose to treat GCA.

We conclude from our results, that, with frequent and careful monitoring, rapid tapering of corticosteroids to the minimum effective dose can be carried out on the basis of clinical symptoms **in combination with** measurement of ESR or CRP, as late serious

complications seem to be rare. A considerable percentage of patients can be withdrawn from steroids within one or two years. Others will require a low daily dose of a few milligrams for a longer period of time. In a treatment schedule of that kind, there is no steroid sparing effect of MTX in a dosage of 7.5 mg/week.

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Case reports of coexistent gout and rheumatoid arthritis

Source	Sex/ Age (yr)	Age at diagnosis (yr)		RF titre	Rheuma- toid nodules	Tophi	MSU		Uric acid	Response to colchicine	Histopathology
		Gout	RA				Synovial	Tophi			
McCarty 1964 ³	M:75	63	75	2560	+	+		+	↑		Rheumatoid nodule
Owen <i>et al</i> , 1964 ⁴	M:64	49	63	320	+	+		+	13.2	Yes	Synovium, pannus
Bloch-Michelle <i>et al</i> , 1968 ⁵	F:38	26	31	320			+		11.0		Synovium, pannus and MSU crystals
Schwartzberg <i>et al</i> , 1978 ⁶	M:39	39	23	5120	+	+	+		10.0	Yes	Synovium, pannus and nodule with MSU crystals
Wallace <i>et al</i> , 1979 ⁷	F:73	72	38	5120	+	+	+		16.2	Yes	NA
Rizzoli <i>et al</i> , 1979 ⁸	M:58	58	70	1280	+	+		+	12.6	Yes	Meniscectomy MSU crystals
Jessee <i>et al</i> , 1980 ⁹	M:71	61	64	640	+	+	+		7.2	Yes	Rheumatoid nodule
Atdjian <i>et al</i> , 1981 ¹⁰	M:56	50	55	5120	+	+	+	+	6.4		Rheumatoid nodule and MSU crystals; synovium, pannus
Raman <i>et al</i> , 1981 ¹¹	F:67	63	50	256		+		+	↑		Rheumatoid nodule
Waterworth 1981 ¹²	M:61	61	64	320	+		+		↑		Rheumatoid nodule
Gordon <i>et al</i> , 1985 ¹³	M:60	54	56	2048	+	+		+	↑	Yes	Rheumatoid nodule; synovium, pannus
Martinez-Cordero <i>et al</i> , 1988 ¹⁴	M:37	27	30	1280		+		+	8.9		Rheumatoid nodule
Spector <i>et al</i> , 1989 ¹⁵	M:39	41	57	640	+			+	4.5		Rheumatoid nodule
Wendling <i>et al</i> , 1991 ¹⁶	F:45	45	45	2560			+		↑	Yes	NA
Present study	F:61	58	42	2560	+	+		+	13.2		NA

NA = Not available.

appear sooner than in men,²⁴ and interphalangeal joints are involved frequently.²⁵

Although the coexistence of RA and gout is extremely rare, the latter should be sought in patients with inflammatory arthropathies and otherwise asymptomatic hyperuricaemia if acute or chronic gout, or both, are to receive the correct treatment in these patients.

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Correction

Can methotrexate be used as a steroid sparing agent in the treatment of polymyalgia rheumatica and giant cell arteritis?

van der Veen *et al* (*Ann Rheum Dis* 1996; **55**: 218-223)

It is regretted that an incorrect affiliation was given for Dr H J Dinant, who is now rheumatologist at the Jan van Breemen Instituut, Amsterdam.

the patient relapsed, developing oral and genital ulcers, again requiring treatment in hospital. However, the seric concentration of liver enzymes remained normal and the titre of antibodies did not increase. She received topical treatment and the dose of steroids was increased to 12 mg/day. Three weeks later she was discharged from hospital and, at present, remains clinically stable.

In the present report a correlation between the titre of antibodies to ribosomal P proteins and the development of hepatic disease was seen. The levels of liver enzymes increased and decreased in parallel with the titres of ribosomal antibodies. Correlation between the titres of autoantibodies and other clinical manifestations was not found as the titres remained unchanged despite two acute episodes with important articular and dermatological complications. We do not have a definitive explanation of the relation between hepatic disease and the presence of ribosomal antibodies. However, it has recently been shown that these antibodies may bind to liver membranes in cell cultures.⁸ It may be, therefore, that these autoantibodies cause hepatopathy by binding in vivo to certain proteins in the hepatocyte membrane. Further studies will help to confirm this suggestion.

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