INSTRUCTIONS FOR LETTERS TO THE EDITOR

Editorial comment in the form of a Letter to the Editor is invited; however, it should not exceed 800 words, with a maximum of 10 references and no more than 2 figures (submitted as camera ready hard copy per Journal Guidelines) or tables and no subdivision for an Abstract, Methods, or Results. Letters should have no more than 4 authors. Full name(s) and address of the author(s) should accompany the letter as well as the telephone number, fax number, or E-mail address.

Contact. **The Managing Editor, The Journal of Rheumatology, 365 Bloor Street East, Suite 901, Toronto, ON CANADA M4W 3L4. Tel: 416-967-5155; Fax: 416-967-7556; E-mail:jrheum@jrheum.com Financial associations or other possible conflicts of interest should always be disclosed.**

Rheumatoid Arthritis: Radiographic Progression Is Getting Milder

To the Editor:

Dr. Sokka and colleagues[1] have made an important contribution to the growing evidence that outcomes in rheumatoid arthritis (RA) have been improving over time. We believe, however, that Sokka, *et al* are too even-handed in their discussion of the 3 explanations for their data: (1) self-selection, (2) milder disease, and (3) improvement in treatment. While these potential explanations are not mutually exclusive, we believe that the overwhelmingly dominant cause must be the great increase in use of disease modifying antirheumatic drugs (DMARD) proven to retard functional decline and radiographic progression.

Self-selection of milder patients is effectively precluded by the entry criteria Sokka, *et a*l have used. They present compelling graphic evidence of individual patient trends across cohorts showing nearly identical baseline values but a profound reduction in the number of patients with high radiographic progression slopes; this reduction is even more striking in the seropositive patients. The differences over time are due to an almost complete absence of rapid radiographic deterioration in the later cohorts, consistent with more aggressive tratment.

To address the question whether RA is becoming a milder disease, one needs to examine data from successive incidence cohorts where baseline health status measurements have been performed consistently over the years. We analyzed baseline functional disability in a large (n = 3035) prospective muticenter study, and found no substantial changes over a 20 year period in baseline values of early RA cases. On the other hand, we found a 2% annual decline in functional disability in our cohorts over the past 2 decades[2,3]. Sokka, *et al* report the same thing with radiographic endpoints; no difference in median Larsen scores at baseline over time, but large differences after 5 years.

In contrast to the stability of baseline severity over time, there have been dramatic changes toward DMARD based treatment strategies[4], with reduction in duration of disease at first DMARD, and increases in the number of DMARD per patient, relative effectiveness of available DMARD, numbers of patients taking DMARD and DMARD combinations, and percentage of courses on DMARD over time[2,5]. For a strongly positive effect from these well documented trends *not* to have occurred would have to mean that all of our clinical trials and observational studies have been wrong. We now have better treatments and better treatment strategies and better functional outcomes and better radiographic outcomes. We should not be afraid to connect the dots.

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Dr. Sokka, *et al* reply

To the Editor:

We are delighted that Dr. Krishnan and Dr. Fries make a point we wanted to make in our report, but a long and tedious review process (including previous journals) tempted us not to emphasize the effects of DMARD, especially those of methotrexate, as the most important basis of reduction of radiographic damage.

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Steroids and Myocardial Infarction in Rheumatoid Arthritis

To the Editor:

Dessein, *et al*[1] have put forward evidence to support the thesis that the use of systemic steroids may in large part be responsible for premature myocardial infarction in patients with rheumatoid arthritis (RA). I was particularly pleased to see this data as I often feel we have been crying out in the wilderness for the last 30 years based, admittedly, on less impressive clinical data[2,3]. They modify their conclusion with the sentence, "The use of glucocorticoids in RA may merely reflect more aggressive disease". I suspect it was put in to appease some reviewers, but while it is often accepted as "common sense," there really is no evidence to support it.

Quite apart from the fact that we are still discussing how exactly to predict who will actually have severe disease, Crisswell, *et al*[4] pointed out some years ago that the training and views of the prescribing physician are often more relevant than the characteristics of the patient in making a decision regarding steroid use. I think more rheumatologists have a growing intuition that steroids are harmful. Thus, with the biologics, a reduction or discontinuation of steroids is already considered as a measure of success. I think the current data will certainly add weight to that impression.

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Dr. Dessein and Dr. Stanwix reply

To the Editor:

The encouraging comments made by Dr. Russell regarding our investigation on the adverse effects of glucocorticoids on insulin sensitivity in rheumatoid arthritis (RA) are welcome[1]. More evidence that glucocorticoids may be responsible for a substantial proportion of cardiovascular events in RA was recently reported by Wolfe, *et al*[2,3]. Thus, in 12,142 patients, prednisone use was complicated by a significant 70% increased incidence of acute myocardial infarction (AMI)[2]. Further, in another large cohort study by the same investigators, the use of corticosteroids was an independent predictor for the development of diabetes mellitus, while diabetic patients with RA experienced a 3-fold increased incidence of AMI[3]. These results support our findings, since insulin resistance is a pathogenetic mechanism of diabetes. Suissa, *et al* also found a 70% increased occurrence of AMI with selective cyclooxygenase-2 inhibitors, while traditional nonsteroidal antiinflammatory agents had no effect on cardiovascular event rates, and disease modifying agents including leflunomide, methotrexate, and anti-tumor necrosis factor-α agents were protective[4].

Dr. Russell raises the discussion that the extensive use of glucocorticoids in RA is driven by the training and views of the prescribing physician rather than disease severity, and that the availability of biologicals may improve the situation. Recent reports reveal that oral predniso(lo)ne may still often be "routinely" prescribed in RA. In a recent investigation on adalimumab, concomitant standard antirheumatic therapy included the use of oral glucocorticoids in 52.7% of patients[5]. Even more convincing, Nell, *et al* reported that 60% of patients with very early RA (median disease duration of 3 months) and 55% of patients with late early RA (median disease duration 12 months) were receiving corticosteroids before DMARD initiation[6].

Many RA patients cannot afford biologicals, and safety issues may first need to be more thoroughly addressed in areas where tuberculosis is highly prevalent, for example in South Africa. Hence, glucocorticoids are still bound to constitute an important part of RA treatment for a considerable time in the future, at least in the form of bridge therapy upon initiation of traditional disease modifying agents and/or leflunomide, since the latter agents typically take months to alleviate RA symptoms and signs.

Based on reported clinical trials, we have previously suggested that pulsed (intraarticular, intramuscular, or intravenous) glucocorticoids are more beneficial and better tolerated than chronic oral pharmacological dose (e.g., > 4 mg prednisone per day) of glucocorticoids in RA[7]. This and more recent evidence is summarized in Table 1[7-11]. In our latest report, high doses of pulsed glucocorticoids were also associated with decreased insulin sensitivity. However, several patients had received intravenous doses as high as 3 g methylprednisolone administered over 3–5 days. Encouragingly, low dose intraarticular pulses do not seem to have longterm adverse effects on insulin sensitivity when used as bridge therapy[10].

Maybe the time has come to reconsider the route of administration of glucocorticoids in RA[11].

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Table 1. Effects of oral pharmacological and pulsed glucocorticoids in RA[7-11].

Effect	Oral Glucocorticoids	Pulsed Glucocorticoids
Side effects		
Overall	Numerous	Minimal
Cushing's	Common	Not reported
Psychological	Depression	Improved psychological status
Cardiovascular risk		
Lipid metabolism	Adverse	Not adversely affected
Glucose metabolism	Adverse	Not adversely affected
Blood pressure	Adverse	Not adversely affected
Disability	Increased	Decreased
Mortality	Increased	Unaffected
Rebound flaring	Common	Not reported
Disease abortion	None	50% in early disease
Adrenocortical function	Suppression	Not adversely affected
Nuclear factor-κB inhibition	None	Profound
Nongenomic physiochemical effects	None	Profound
TNF-α blockade-like effects	Dissimilar	Similar

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Sensitivity and Specificity of Anti-α-Fodrin Antibodies in Primary Sjögren's Syndrome

To the Editor:

We read with interest the report by Ruffatti, *et al*[1], whose results correspond to our recent findings suggesting a low sensitivity and a high specificity of IgA and IgG-type anti-α-fodrin antibodies.

In 1998, at the Department of Clinical Immunology, University of Debrecen, we investigated anti-α-fodrin antibodies in 67 patients with primary Sjögren's syndrome (SS), 20 with rheumatoid arthritis (RA), 21 with systemic lupus erythematosus (SLE), 20 with secondary SS associated with RA, and 17 with secondary SS associated with SLE, and in 30 healthy blood donors. Autoantibodies against class IgA and IgG-type α-fodrin were detected by the same commercial ELISA kit used by Ruffatti, *et al*. In the year 1998, European Community Study Group criteria[2] were used to diagnose SS. The sensitivity for IgA and IgG anti-α-fodrin for SS was 37.3% and 38.8%, respectively. The specificity was 93.3% for both isotypes[3].

In 2003, we repeated the measurement of anti-α-fodrin in the sera of 46 patients with SS and healthy blood donors, using the American-European Consensus criteria[4] for SS and using the same ELISA kit for detection of antibodies. The sensitivity for IgA and IgG anti-α-fodrin was 17.3% and 28.2%, the specificity 93.3% and 100%, respectively.

Similarly to Ruffatti, *et al* we also concluded that the antibodies against anti-α-fodrin are not sufficiently sensitive for diagnostic markers for SS, especially after the diagnostic criteria have been made more rigorous. Interestingly, we did find correlation between the presence of anti-SSA and IgG-type anti-α-fodrin autoantibodies, and we suggest using anti-α-fodrin autoantibodies in screening patients followed serologically and clinically for early diagnosis of SS.

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Dr. Ruffatti, *et al* reply

To the Editor:

We thank Dr. Szántó and colleagues for their interest in our article[1]. The results they report[2] confirm low sensitivity of IgA and IgG anti-α-fodrin antibodies for primary Sjögren's syndrome (SS) using ELISA. Indeed, we found a similar low prevalence for both IgA and IgG anti-α-fodrin antibodies in primary SS sera: 32.5% vs 37.3% and 21.1% vs 38.8%, respectively. These findings are in keeping with other recent studies[3,4], which appeared while our report was being evaluated for publication, that reported a low frequency of anti-α-fodrin antibodies in primary SS patients on the basis of various techniques including immunoprecipitation, immunoblotting, and ELISA. On the other hand, we observed specificity of both IgA and IgG anti-α-fodrin antibodies lower than that reported by Szántó, *et al*[2]: 68.1% versus 93.3% and 79% versus 93.3%, respectively. This difference could be due to a variation in the number of control subjects. Moreover, the specificity of anti-α-fodrin antibodies for primary SS presently is debatable, probably because the numbers of patients with connective tissue diseases reported in the control groups were not homogeneous[1-4].

Most studies showing a high prevalence of anti-α-fodrin antibodies in primary SS[5-8] utilized the European Community Study Group criteria[9] for classification. Using the same criteria we observed a low prevalence of anti-α-fodrin antibodies in patients with primary SS, in agreement with Szántó, *et al.* When antibody frequency in primary SS patients classified according to the European criteria was compared with that in patients classified according to the San Diego criteria[10] a higher antibody prevalence was found in the latter group[3,11]. The difference, however, was statistically significant in only one of the 2 studies[11]. According to Szántó, *et al*, a low prevalence of IgA and IgG anti-α-fodrin antibodies was recently reported[4] in primary SS patients meeting the American/European Consensus criteria[12].

Due to the low sensitivity of anti-α-fodrin antibodies confirmed by recent reports[2-4] and by our experience[1], we are doubtful about the use of these antibodies as a diagnostic marker. On the basis of Ulbricht's study[13] describing normalization of anti-α-fodrin antibodies after 3 months of successful therapy and a correlation between antibody concentration and the degree of lymphocytic infiltration in the salivary glands, it remains to be seen if anti-α-fodrin antibodies may be considered an early marker for disease activity of primary SS.

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Usefulness of Bone Ultrasound Techniques in Pediatric Rheumatic Diseases

To the Editor:

We read with interest the article by Hartman, *et al*[1] on the validity of quantitative ultrasound bone sonometry as a screening tool for the diagnosis of osteoporosis in children with chronic rheumatic diseases (CRD), compared to the conventional dual x-ray absorptiometry (DXA).

In this cross-sectional study, using an ultrasound bone sonometer device at distal third of radius and mid-shaft of tibia, reduced values of speed of sound were found in 15 out of 39 children with CRD. Bone mineral density (BMD) at the lumbar spine and speed of sound values at the radius showed a significant correlation. Hartman and colleagues conclude that quantitative ultrasound bone sonometry, giving results largely comparable to those of lumbar DXA, might be used as a screening tool for osteoporosis in pediatric CRD.

We agree: as the authors correctly report, several other studies have highlighted quantitative ultrasound techniques as an appealing alternative to measure bone status in children[2-7]. With its low cost, portability, and short duration of examination, this radiation-free assessment is indicated as a useful measurement tool of bone status in CRD. Indeed, quantitative ultrasound provides evidence not only on bone mineralization, as DXA does, but also on bone structure and elasticity[8].

The authors did not mention the possibility that in children with rheumatic diseases bone status can also be reliably monitored over time by quantitative ultrasound. In a one year longitudinal study, we reported contact ultrasound bone analysis at the calcaneus (CUBA) as a noninvasive and feasible tool for assessment and monitoring of bone status in 67 children with CRD[9]. Our study population included 46 with juvenile idiopathic arthritis, 11 juvenile dermatomyositis, and 10 systemic lupus erythematosus, in an age range of 2.8 to 18.1 years; among these children, in contrast to Hartman's analysis, 7 were younger than 4 years old. Assuming appropriate reference values adjusted for age, and with strategies to obtain their collaboration, the CUBA method seems reliable as well in this age group.

Not surprisingly, we have seen that changes in prospective bone density measures during the course of illness are related to the treatment given: patients who were taking corticosteroids experienced decreased bone mass, while those taking alendronate or having intraarticular steroid injection showed an increase in quantitative ultrasound values after one year.

Although DXA remains the gold standard to measure BMD, we feel the current literature provides supportive evidence to introduce quantitative ultrasound into routine clinical investigations and followup of bone assessment in childhood CRD.

Osteoporosis is one of the major causes of comorbidity in these young patients; to carry out the best available treatment[10], evaluating bone status at disease onset and with periodic measurements should be considered in any child with CRD.

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Drs. Hartman and Brik reply

To the Editor:

We thank Drs. Simonini, Cimaz, and Falcini for their letter and for reporting their own experience, which lends gratifying support to our findings. It was interesting to learn from their data that quantitative ultrasound bone sonometry can be reliably employed also in patients who are younger than 4 years. There is enough evidence now in the literature that quantitative ultrasound bone sonometry is a noninvasive and safe technique that appears to be ideal for repeated use even in very young children.

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Etidronate and Glucocorticoid Induced Osteoporosis

To the Editor:

In their interesting article, Drs. Buckley and Hillner effectively analyze 3 different therapeutic regimes for the prevention of vertebral fractures in women treated with glucocorticoids[1]. They use a decision analysis model based on different clinical assays from the literature, concluding that calcium and vitamin D supplements and low cost bisphosphonate regimens such as cyclic etidronate decrease the lifetime vertebral fracture risk at acceptable costs, and should be considered when initiating glucocorticoid treatment for women who do not have osteoporosis. We offer a few considerations based on a study we recently performed.

A total of 44 asthmatic women undergoing chronic therapy with glucocorticoids (Table 1) were randomized to receive either etidronate or placebo for 14 days every 3 months. Both groups were instructed to take at least 1000 mg of calcium daily and received, furthermore, an extra 500 mg of calcium carbonate daily. We chose etidronate because it has proved its efficacy in the prevention of osteoporosis in postmenopausal women in treatment with glucocorticoids[2] and because of its low cost, in the belief that this could contribute to improving adherence to treatment. In total, 23 women received placebo and 21 etidronate. The patients were reviewed every 3 months to assess their clinical situation and reinforce adherence to treatment. Despite this, there were 7 dropouts at 6 months, 2 in the etidronate group and 5 placebo; and another 7 at 12 months, again 2 in the etidronate group and 5 placebo. Therefore, at the end of the one-year followup, a total of 14 patients had abandoned the study (31.8% of the study population). In only 2 cases was withdrawal due to possible adverse effects (cephalalgia in one patient and urolithiasis in another). In the remaining 12, withdrawal was related to discomfort associated with administration of etidronate, since the manufacturer recommends not taking any food 2 hours before and 2 hours after the drug. Other investigators report withdrawal rates similar to ours, although in studies with longer followup[3]. There were no significant differences among the 2 groups regarding lumbar spine bone mineral density (BMD). At the end of the study, the group receiving etidronate had a gain of 0.74% (95% CI –0.6, 2.1) in BMD, whereas the group receiving only calcium had a gain of 0.92% (95% CI –0.7, 2.5). These findings are lower than in reports in other prevention studies where the difference between both groups was of 3.7% (range 2.6% to 4.7%), although most of the patients included in those studies were postmenopausal women, in contrast to our cohort[4].

Table 1. Characteristics of the study population.

	Placebo Group, n = 23	Etidronate Group, n = 21	p
Age, yrs	33 (8)	35 (6)	NS
Body mass index	26.1 (4.3)	24.3 (3.9)	NS
Years of asthma	10 (7)	13 (7)	NS
Prednisone daily dose, mg	3.8 (4.3)	3.9 (5)	NS
Budesonide daily dose, µg	1248 (501)	952 (384)	NS
Basal T score in lumbar spine	–0.68 (1.05)	–0.38 (1.17)	NS
Change in lumbar spine BMD in 1 year (%)	0.92	0.84	NS

BMD: bone mineral density.

Buckley and Hillner point out some limitations of their study, namely the accuracy of the estimates and assumptions in respect to the bone loss and fracture rates. Nevertheless, when trying to obtain conclusions based on daily clinical activity, other factors must be considered, such as adherence to treatment; although drugs can be very effective, if dosage or administration requirements are too complex, it may cause the patient to abandon treatment. This aspect is especially important in drugs like etidronate because of complicated and uncomfortable administration that can lead to withdrawal.

We agree with the authors that treatment strategies should be considered for women who do not have osteoporosis at the time glucocorticoid treatment is initiated to prevent bone loss and irreversible changes in bone quality; but we think that apart from adequate intake of calcium and vitamin D, use of drugs with easy administration must be considered, such as weekly bisphosphonates, which have proved to have better efficacy and can achieve a better adherence from the patients[5,6].

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Is Polymyalgia Rheumatica Caused by Infectious Agents?

To the Editor:

Many infectious causes have been suggested for polymyalgia rheumatica (PMR) and/or giant cell arteritis (GCA): *Chlamydia pneumoniae*, *Yersinia enterocolitica*, *Borrelia burgdorferi*, hepatitis, parainfluenza and herpes viruses, adenoviruses, enteroviruses, cytomegalovirus, Epstein-Barr virus, and parvovirus B19 are frequently considered as possible triggers in the pathogenesis of these disorders[1-11]. The seroprevalence for each of these infectious agents[2-11] was investigated, as well as *Chlamydia* and parvovirus B19 in temporal artery biopsies from patients with GCA[12-14], but the results are still controversial.

We conducted a case-control study on the seroprevalence of a large series of microorganisms in 51 outpatients with PMR, compared to 51 sex and age matched controls. Between 2001 and 2003, 51 patients (33 women, 18 men; mean age 72 ± SD 6.1 yrs) were recruited from those referred to our Department of Internal Medicine for pain and stiffness in the neck, shoulders, and pelvic girdle. Patients were diagnosed as having PMR[15], of which the mean duration was 2.2 ± 1.6 months. At recruitment, no patient presented signs or symptoms suggesting GCA, and none was undergoing corticosteroid treatment. The controls (33 women, 18 men; mean age 70 ± 3 yrs) were outpatients with osteoarthritis[16].

Sixteen patients and 16 controls were examined in 2001, 20 patients/20 controls in 2002, and 15 patients/15 controls in 2003; seasonally, 12 patients/12 controls were recruited in autumn, 15 patients/15 controls in winter, 13 patients/13 controls in spring, and 11 patients/11 controls in summer. Patients and controls provided written informed consent. Serum samples obtained at the time of diagnosis were stored at –20°C until antibody evaluation was performed (January 2004). Serum antibodies (IgG and IgM together) to *Chlamydia*, adenovirus, poliovirus, rotavirus, coxsackievirus A and B, echovirus N and P, and parainfluenza viruses were dosed using the CFT-Mat hemolytic system kit (Diesse, Siena, Italy); serum IgG and IgM antibodies to *Borrelia* using the Vidas Lyme IgG-IgM kit (bioMérieux, Marcy-Etoile, France); serum IgG and IgM antibodies to cytomegalovirus, herpesvirus simplex, herpesvirus zoster, Epstein-Barr virus, and mumps virus using a commercial kit (Behring-Date Marburg GmbH, Marburg, Germany); serum hepatitis B surface antigen (HBsAg), serum antibodies to hepatitis B surface antigen (anti-HBs Ag), to hepatitis B anticore antigen (anti-HBc Ag), and to hepatitis C virus (anti-HCV) using a commercial kit (Abbot Axsym, Wiesbaden, Germany); and serum IgG and IgM antibodies to parvovirus B19 using a parvovirus B19 ELISA kit (DRG Instruments GmbH, Germany). Statistical analysis was by Fisher's exact test.

As shown in Table 1, high serum IgG and IgM antibody titers for *Chlamydia* were observed in 2 (3.9%) patients and in 2 (3.9%) controls, and high serum IgM antibody titers for parvovirus B19 in 3 patients (5.8%) and 2 (3.9%) controls, with no significant difference between the 2 groups. IgG and IgM serum antibodies against adenovirus, poliovirus, rotavirus, and hepatitis C virus were not found in patients or controls. Serum IgG antibodies were detected, at different percentages, for coxsackie, herpes and parainfluenza viruses, echoviruses, mumps virus, Epstein-Barr virus, cytomegalovirus, and *Borrelia*, with no significant difference between patients and controls. HBsAg result was positive in only one patient and one control, and anti-HBcAg in the same HbsAg-positive patient. Anti-HBcAg and anti-HCV Ab were not observed in patients or controls. Serum IgG and IgM antibodies for *Chlamydia* and IgM parvovirus B19 were found in a small sample, suggesting recent onset of infection; however, there was no significant statistical difference between patients and controls. No evidence of recent or previous infection was found for adenovirus, poliovirus, rotavirus, and hepatitis C virus in patients or controls. Previous infection for coxsackie, herpes and parainfluenza viruses, echoviruses, cytomegalovirus, Epstein-Barr virus, mumps virus, and *Borrelia* was identified in patients as in controls, with no significant difference between the 2 groups. No evidence of recent infection was seen for hepatitis B virus.

We emphasize that in these patients and controls the recent infections

Table 1. Seroprevalence (%) of hepatitis B surface antigen (HBsAg) and antibody titers to different microorganisms in patients with PMR and controls.

	Patients, n = 51	Controls, n = 51
HBsAg	0	0
Anti-HBsAg	1 (1.9)	1 (1.9)
Anti-HBcAg	0	1 (1.9)
Anti-HCV Ab	0	0
Anti-Chlamydia IgG-IgM Ab	2 (3.9)	2 (3.9)
Anti-adenovirus IgG-IgM Ab	0	0
Anti-rotavirus IgG-IgM Ab	0	0
Anti-coxsackievirus A IgG-IgM Ab	1 (1.9)	1 (1.9)
Anti-coxsackievirus B IgG-IgM Ab	3 (5.8)	2 (3.9)
Anti-echovirus N IgG-IgM Ab	1 (1.9)	1 (1.9)
Anti-echovirus P IgG-IgM Ab	2 (3.9)	1 (1.9)
Anti-parainfluenza 1 IgG-IgM Ab	3 (5.8)	3 (5.8)
Anti-parainfluenza 2 IgG-IgM Ab	2 (3.9)	1 (1.9)
Anti-parainfluenza 3 IgG-IgM Ab	1 (1.9)	1 (1.9)
Anti-poliovirus IgG-IgM Ab	0	0
Anti-cytomegalovirus IgG Ab	40 (78.4)	38 (74.5)
Anti-cytomegalovirus IgM Ab	0	0
Anti-herpesvirus simplex IgG AB	26 (50.9)	30 (58.8)
Anti-herpesvirus simplex IgM AB	0	0
Anti-herpesvirus zoster IgG Ab	2 (3.9)	3 (5.8)
Anti-herpesvirus zoster IgM Ab	0	1 (1.9)
Anti-EBV IgG Ab	30 (58.8)	28 (54.9)
Anti-EBV IgM Ab	0	0
Anti-Borrelia IgG Ab	1 (1.9)	2 (3.9)
Anti-Borrelia IgM Ab	0	0
Anti-mumps IgG Ab	16 (31.33)	18 (35.2)
Anti-mumps IgM Ab	0	0
Anti-parvovirus B19 IgG Ab	3 (7.8)	5 (9.9)
Anti-parvovirus B19 IgM Ab	3 (58)	2 (39)

EBV: Epstein-Barr virus.

had shown their typical seasonal pattern[17]. In accord with some previous reports[3,5,9,12,13], but contrary to others[5,7,8,10,11,14], we concluded there is no specific serological evidence that microbiological agents can trigger PMR. Elling and coauthors[18] affirmed that an epidemic pattern can trigger some cases of the disease, given a specific immunogenetic profile[1]: but reports of case-clustering are scarce, and seasonal variation in disease onset has been excluded by other investigations[19,20] and also by our current study.

We believe it is not possible to sustain the hypothesis of an infectious cause for polymyalgia, notwithstanding that sample sizes required to show significant differences in highly seroprevalent agents need to be larger than in this study and in others' reports. We believe a multicenter study could give us more conclusive information.

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Silicone Breast Implants

To the Editor:

We are troubled by Dr. Vasey's reply to our letter[1,2]. He implies that systemic symptoms can develop either with or without rupture of the implant. Our study did not evaluate women with ruptured implants as a separate group and we cannot make any judgements on whether rupture is or is not associated with systemic symptoms[3,4]. In addition, we find the comparison to the flu bizarre. Dr. Vasey suggests that a unique disease exists in women with breast implants in the same way as the flu exists in people infected with the flu virus. In our view no credible evidence exists for a unique disease or syndrome in women with breast implants, regardless of Dr. Vasey's beliefs to the contrary.

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Book reviews

Oxford Textbook of Rheumatology. David A. Isenberg, Peter J. Maddison, Patricia Woo, David Glass, and Ferdinand C. Breedveld, editors, Oxford and New York: Oxford University Press, 2004, 3rd edition, 1278 pages, price $675.00 US.

This age of information has blessed us with knowledge but cursed us with how to manage it. This textbook is a good example of how to organize the breadth of rheumatology knowledge into one volume. The print is small

but clear. The plethora of excellent illustrations and tables helps to organize the data, concentrate facts at an eye's glance and shorten the text. In the British tradition, the language in the text is simple, succinct, and a pleasure to read. The reference lists have been limited to around 100 key overview references per chapter. These references will supplement any limitations in the depth of information that sometimes must be sacrificed when managing endless data. In addition, a CD-ROM containing the full contents of the book is included.

The organization of sections and chapters is practical, logical, and geared to clinical problem-solving. Section 1 deals with the clinical presentation of rheumatic disease including the clinical presentations in different age groups. In fact, a number of chapters throughout the book focus on pediatric rheumatology. Another interesting feature of this section is the handling of overlap of rheumatology with different specialties. A series of chapters are co-authored by rheumatologists and specialists in a wide range of other disciplines. Section 2 deals with the outcomes and delivery of rheumatologic care, rehabilitation, and sexuality. Pertinent aspects of basic science are described in sections 3 (pathophysiology) and 4 (inflammation). The investigation of rheumatic diseases is discussed in section 5. The gamut of rheumatic diseases including management is described in detail in section 6. Section 7 covers joint surgery, corticosteroid injection therapy, and sports medicine.

The book reflects the current state of rheumatology around the world by utilizing over 150 internationally renowned contributors. Furthermore, because these authors are encouraged to express their opinions and expose areas of dispute, the sober medical evidence is enlivened.

Faults are few. There are several minor spelling mistakes. In some of the diagrams and tables, abbreviations are not clarified. Some of the illustrations could be improved by labelling the abnormalities on the picture. The book is very expensive. The *Textbook* is highly recommended to rheumatology trainees and clinical and academic rheumatologists. Some may find it appealing to alternate new editions of this textbook with new editions of an American one every 4 to 5 years. This book is a must for medical libraries.

HOWARD STEIN, MD, FRCPC, Professor of Medicine (Honorary), University of British Columbia, Vancouver, BC, Canada.

Cutaneous Manifestations of Rheumatic Disease. Richard D. Sontheimer and Thomas T. Provost. Philadelphia: Lippincott Williams & Wilkins, 2004, 318 pages, $135.00 US.

This textbook is written entirely by dermatologists and consists of 14 chapters covering the skin manifestations of all major musculoskeletal diseases. The content was determined using the Arthritis Foundation's *Primer for Rheumatic Diseases* (9th edition), and as a result is comprehensive. Most chapters include a historical perspective, pathophysiology, treatment, and systemic manifestations of the diseases. To the rheumatologist this adds little to standard rheumatology texts. The real strength of this book is the eloquent and comprehensive descriptions of common and rare cutaneous manifestations of the diseases treated by rheumatologists on a daily basis. Dermatologists involved in writing the chapters clearly have extensive clinical experience and strike a balance between more evidence-based research and personal experience.

Several chapters deserve special mention. The chapter on miscellaneous disorders that commonly affect both skin and joints covers topics frequently seen by rheumatologists, but that are covered only superficially in the usual texts. Those on lupus, dermatomyositis, and vasculitis are especially comprehensive. One full chapter is devoted to rheumatic diseases in children. Because chapters are organized by diseases, and the text is well indexed, facts regarding specific rheumatic conditions can be found easily.

Another major strength of the text is the 250 full-color illustrations. These cover commonly-seen manifestations and are thus invaluable to the trainee, but in addition display much rarer findings and are thus of interest to the most seasoned clinician.

Overall, this is a comprehensive, beautifully illustrated book, which will serve as an excellent reference for rheumatologists interested in dermatology as it applies to their patients.

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Osteoarthritis, Second Edition. K.D. Brandt, M Doherty, L.S. Lohmander, editors, New York, NY: Oxford University Press, 511 pages, Price $375 US.

The second edition of this textbook offers a comprehensive overview of this disease from all angles. Osteoarthritis covers aspects of the disease from basic to clinical science, including therapeutic and potential targets for new therapies. This edition represents a major update, with extensive revision of many chapters and the addition of new ones that reflect the rapid evolution of knowledge in this field of medicine and addressing in particular new findings with regard to the etiopathogenesis of the disease. Moreover, new chapters have also been added to cover the recent developments in the pharmacological and non-pharmacological management of osteoarthritis.

The reader will particularly appreciate the logical succession in which the different chapters are presented, making this textbook one that presents a very lucid chronology of events. The presentation of the chapters is attractive, and each one is easy to read. The color illustrations, including pictures, tables and figures, are pleasant and help the reader more easily and effectively understand the data and/or concepts presented. The chapter bibliographies are complete and comprehensive and have been nicely updated from the first edition. The only drawback is that the work cited is a few years old. This, however, is common with almost all textbooks.

The authors have made a considerable effort to add new chapters that reflect the most recent developments in the field of osteoarthritis. We found the chapter on imaging, as well as those addressing the different issues regarding the development and assessment of disease modifying antiosteoarthritis drugs, to be most relevant to the outstanding work which is now underway at both the basic and clinical research levels. This book will be an excellent reference to a wide audience interested in osteoarthritis, from trainees to general practitioners and sub-specialists. It provides useful information which will not only improve the understanding of the disease process but also guide the practitioner in providing optimal management and treatment of this disease condition.

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