PostScript

MATTERS ARISING

Steroids cause osteoporosis

We read with great interest the article by Gudbjörnsön and colleagues and concur with the accompanying leader by Dr Paget on the issue of corticosteroid associated osteoporosis.1 Osteoporosis is a major public health problem, associated with significant morbidity and mortality, and is estimated to cost £614 million annually in England and Wales alone. Despite well published guidelines on the prevention and treatment of corticosteroid associated osteoporosis, as a profession, we are failing to meet the targets set by these guidelines.1

In the light of the American College of Rheumatology guidelines in 2001, we performed an audit of our current practice relating to the issue of steroid prescription, calcium supplementation, measurement of bone density, and the prescription of antiresorptive treatment to see if we had been adhering to the recommendations of the National Osteoporosis Society. Our rheumatology department has a continually updated database on all current and past patients who have attended our unit. This contains information on patient demographics, primary rheumatological diagnosis, comorbid conditions, current drug treatment, past disease modifying treatment (including corticosteroids), and records all patient generated events, including outpatient and inpatient episodes. From our database of over 10 000 patients, we identified 258 patients who were currently receiving prednisolone and had been taking the drug for a minimum of three months.

Forty patients (29 female) were randomly selected. The median patient age was 63 years (range 33–85). The patients were taking a mean daily dose of 6.7 mg prednisolone (range 1–45) and had been prescribed prednisolone for a median of 6 years (range 3 months–20 years). The most common reason for the prescription of prednisolone was for polymyalgia rheumatica for 14 (35%) of those selected, followed by systemic lupus erythematosus (SLE) in nine (23%), rheumatoid arthritis or associated complications for four (10%), and mixed connective tissue disease for three (8%). There were also isolated prescriptions for juvenile idiopathic arthritis, dermatomyositis, polymyositis, psoriatic arthritis, Wegener’s granulomatosis, iritis, and unspecified systemic vasculitis.

Encouragingly, 34 (85%) of our cohort were receiving some form of bone protective treatment: 22 (55%) were taking an oral bisphosphonate and one patient received intravenous pamidronate and one patient received intravenous alendronate. Of the postmenopausal women, we were taking hormone replacement therapy and two patients were receiving calcitriol. Twenty (50%) were prescribed calcium and vitamin D supplements, and this was the only treatment in eight (20%) of the cohort. However, of the six patients not receiving any form of bone therapy, five were over the age of 65 years and the one patient under the age of 65 years had been treated with prednisolone continuously for 20 years for SLE, up to a maximum dose of 80 mg/day.

Twenty-four (60%) of the 40 patients had bone density measured by dual x ray absorptiometry (DXA) scan. Of these, seven (29%) were normal, eight (33%) showed osteopenia, and nine (38%) demonstrated osteoporosis at the lumbar spine or the neck of the femur, or both. All patients who had either osteopenia or osteoporosis had been treated with prednisolone and were treated with bone protective agents.

We interviewed 24 patients by telephone. Eighteen (75%) recalled being informed of steroid side effects. Seven had received written information on steroids, but only three had received written information on osteoporosis.

Although our results are encouraging, a significant number of patients are not being treated to prevent osteoporosis and reduce future fracture risk. The fact that all patients with an abnormal bone density scan are treated is reassuring, but we cannot be sure what proportion of patients who have not been scanned require treatment. In 1996, Walsh and colleagues found that only 14% of patients receiving long term prednisolone were receiving some form of preventive treatment against osteoporosis.1 Although matters have improved to a degree, a substantial proportion of patients treated with steroids is still undertreated and considerable progress has to be made nationally and internationally to prevent further bone associated morbidity among patients treated with corticosteroids.

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References

Authors’ response

We appreciate the comment by Dr Gordon and her coworkers on our article on the prevalence of decision making against steroid-induced osteoporosis, which was recently published in the Annals and which included a leader from Dr Paget.1 In their letter, they further highlight the importance of prevention against corticosteroid-induced osteoporosis. They also reported their experience at their rheumatological clinic with more than 10 000 patients. Surprisingly, only 2.6% of their patients with various rheumatological disorders were receiving long term treatment with corticosteroids, in comparison with 0.7% of our unselected population based cohort. More than half of their patients were receiving bisphosphonate, but unfortunately they did not report whether this was primary or secondary prevention or treatment against manifest osteoporosis, nor did they report the prevalence of fragility fractures in their patient group. Although this is a much higher proportion than the1 and others have previously reported,4,5 still 20% of their patients were not treated with any antiresorptive agent and 15% were neither receiving specific bone protective treatment nor calcium or vitamin D supplementation. These figures show that even in a specialist clinic with attention to osteoporosis, further work needs to be done in primary prevention against steroid-induced osteoporosis. Since we performed our study in northeast Iceland an Osteoporosis Clinic with DXA has been established in the study area, and the Director of Public Health in Iceland has published clinical guidelines concerning this issue. Thus, it will be of interest to re-perform our study in the near future for evaluation of the actual improvement in preventing bone morbidity in patients in need of long term treatment with corticosteroids.

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Sjögren's syndrome criteria

In the June issue of the Annals Manthorpe comments on the recently proposed US-European criteria for Sjögren's syndrome (SS). We would like to deal with some of the issues he raises, and add some comments.

Not the classification criteria have evolved from rather subjectively biased ones to more objective assessments, it is surprising that the two most disease-specific objective parameters currently available for SS are subject to considerable criticism. Of course, when serological and histological items are emphasised in the new SS classification criteria, their individual disease sensitivity and specificity should always be kept in mind.

In fact, all six items that are included in the classification criteria may be subject to discussion. For example, the Schirmer-I test, and unstimulated whole saliva flow test have been criticised in a number of papers, but these items are recommended in Manthorpe's paper.

Manthorpe expresses his concerns about the accuracy of sublabial salivary gland biopsies (SLGBs), referring to one paper in which a change of diagnosis of >50% is reported after a second examination of the SLGBs. However, the authors themselves report that not using the focus scoring system was probably the most important reason for the change of diagnosis on the second examination. They did not conclude that the focus score itself—which is mandatory to fulfil item VI—changed dramatically upon re-examination of the specimens.

Other ways of bypassing interobserver variability are also available—for example, measuring two parameters instead of one (for example IgA% and focus score) provides a syndrome for the accuracy of diagnosis, and, moreover, computer aided scoring methods may provide non-observer dependent data. For measuring the IgA% reliably and reproducible objective data from the biopsies are obtained by combining microscope, computer, and calibrated software. These biopsies show what is going on in the target organs of this disease and may provide early diagnostic markers; one should not put them aside too easily.

Manthorpe also criticises the SS classification criteria for the interdependent relation between anti-Ro/anti-La antibodies (item IV) and the focus score (item VI). They are certainly associated with each other, but why is that a problem? The worldwide accepted American Rheumatism Association criteria for rheumatoid arthritis also contain interdependent items—for example, positive rheumatoid factor serology is generally considered as strongly associated with radiological joint damage. Interdependency can also be found in the American College of Rheumatology classification criteria for systemic lupus erythematosus (presence of antinuclear antibodies is a distinct item from presence of anti-dsDNA or anti-Sm, items 11 and 10 respectively). Furthermore, it appears inconsistent that Manthorpe recommends including the patient's smoking habits in the SS classification criteria. This would also introduce an interdependent item.

The dependency does not equal a one-on-one relation—that is, seronegative patients may have a positive focus score and vice versa. In particular, because numerous reports have shown that the focus score alone can be false positive or false negative, the presence of anti-Ro/anti-La antibodies which are still the most disease-specific and sensitive parameters available, has additional value for the accuracy of diagnosis. Finally, it has yet to be proved that the suggested new antibodies (anti-fodrin, anti-muscarin) are more sensitive and disease-specific than the existing classic anti-Ro and anti-La antibodies. Therefore it is too early to include such items in classification criteria.

While our knowledge of Sjögren's syndrome increases, classification criteria may develop in a way that enhances early diagnosis of possibly reversible target organ damage. Not the final stage symptoms and signs (items I–III and V) but rather the early target organ histological signs and serum markers are likely to retain their place in the classification criteria. Therefore, in our view the US-European consensus group is right to emphasise items IV and VI, which should not be neglected if better alternatives have been introduced.

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References


Author’s reply

Zandbelt and van den Hoogen raise and discuss some important issues put forward in the June Leader of the Annals concerning Sjögren’s syndrome (SS) criteria published by a consensus group consisting of European and North American SS experts. The subtitle read: “American-European (US-Eur) and Japanese Groups’ criteria compared and contrasted.” Zandbelt’s and van den Hoogen’s points are well taken, although the issues put forward are not new. I agree with Manthorpe that final diagnostic criteria should set up are research tools, but nevertheless find their way into daily clinical practice. I am of the opinion that it is best to have as few preliminary classification criteria as possible. When coming up with new proposals these should include changes that are up to date in all aspects, otherwise other proposals will arise too soon. It is here, among other things, that I am disappointed by the consensus group’s latest proposal.

Most SS specialists agree that it is difficult to diagnose SS without close collaboration between clinical specialists within ophthalmology, oral medicine/oral surgery, and rheumatology. The US-Eur proposal is written by 13 authors but not a single person is an ophthalmologist! We have known for some years that patients with genuine SS do not complain of dry eyes because the cornea—although heavily innervated—lacks nerves that register dryness. This makes items I and VI in the proposed criteria set invalid and should have been changed.

As far as smoking is concerned, it seems of great importance that clinicians know such details just as they know the medical history. When did smoking start and stop? What was the weekly consumption of cigarettes? Patients, who are present or past smokers, and who have at least two abnormal objective test results from both the main affected exocrine organs, lachrymal and salivary glands, very often lack circulating anti-SSA/SSB antibodies and simultaneously have a low ACR score. As the greatest percentage of the world population is present or past smokers with a consumption of >21 cigarettes/week some will have eye and oral symptoms similar to patients with SS (item I updated plus item III), and I find it difficult to accept that such
patients would not be diagnosed as having SS if the US-Eur criteria were followed. Given that the patient in question is a present or past smoker should lead to the consequence that a smoker should lead to the consequence that a

A brief history of spa therapy

We read with great interest the paper entitled “A brief history of spa therapy” by van Tuberger and van den Hoogen.

We agree with Zandbelt and van den Hoogen that the original set of SS criteria, the Copenhagen criteria (also termed Japanese III), which look so different from the new criteria were presented and discussed. The proposal put forward by the president of the symposium, Professor Susumu Sugai, that an international group of SS experts will not regarded. Besides personal/family consequences it might have great social effects in some countries. In Sweden, for example, patients might get their dental repair bill subsidised by the State if they have SS diagnosed according to the Copenhagen criteria and, in addition, have abnormal unstimulated and stimulated whole sialometry, measured by 15 and 5 minutes, respectively.

I agree with Zandbelt and van den Hoogen that we do not have specific SS autoantibodies and neither do I think that the last autoantibodies (item IV and VI) cannot be against only two cases of SS. My qualified experience in an international group of SS experts will not regarded. Besides personal/family consequences it might have great social effects in some countries. In Sweden, for example, patients might get their dental repair bill subsidised by the State if they have SS diagnosed according to the Copenhagen criteria and, in addition, have abnormal unstimulated and stimulated whole sialometry, measured by 15 and 5 minutes, respectively.

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also support the idea of multicentre studies. We regret, and we have experienced this, that those who finance research projects are extremely reluctant to fund trials in this field. We hope that, as has been suggested, with the creation of European cooperation in rheumatology spa and mineral water research we will be able to provide strong scientific evidence for the effectiveness of spa therapy in the near future.

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References

BOOK REVIEW

Pathological basis of orthopaedic and rheumatic disease

The author provides an overview of the pathology of orthopaedic and rheumatic diseases which could help pathologists in finding the correct diagnosis and also support clinicians and rheumatic disease oriented researchers in obtaining information about a broad range of distinct pathological disorders.

There are eight chapters starting with skeletal structure development and progressing to injuries, infections, disorders of the skeletal development, and metabolic and other generalised diseases of the skeleton. Final chapters deal with diseases of articular tissues, including osteoarthritis and rheumatoid arthritis, and also describe tumours and tumour-like lesions of bone and soft tissue. The last two chapters covering tumour pathology comprise 40% of the content.

Each chapter stands by itself and, therefore, it is possible to focus directly on the matter of interest. The structure of description of the particular disease is consistent and logical and helpful to the reader. The normal format is a short introduction to the disease, some clinical features, radiological features, gross pathology, and histopathology. Every chapter ends with a list of references. The author quotes more than 1500 citations. More than 250 figures including histology, gross pathology, radiological pictures, and schematic diagrams and many tables enrich the quality of the volume.

In a future edition, inclusion of colour figures and an indication of the magnification of the histology pictures would be helpful. From our point of view working in the field of rheumatoid arthritis, the subchapter dealing with the disease could be extended, because the incidence of rheumatoid arthritis is 1–3% in Western countries.

What is missing is any reference throughout the text to the molecular and cellular mechanisms of the diseases. However, we suggest that this single volume would be useful for everyone interested in a summary of histological features of numerous orthopaedic and rheumatic diseases as seen in the clinic.

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FORTHCOMING EVENTS

7th International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation and Related Diseases
14–17 Oct 2002; Nashville, Tennessee, USA
Contact: Lawrence J Marnett, Biochemistry Department, Vanderbilt University, School of Medicine, Nashville TN 37232-0146, USA
Tel: (615) 343 7329
Fax: (615) 343 7354
Website: www.eicosanoids.science.eayne.edu

3rd International Conference on Sex Hormones, Pregnancy, and the Rheumatic Diseases
21–24 Oct 2002; New Orleans, LA, USA
Contact: Anne Parke
Tel: 860 679 8190
Fax: 860 679 1287
Email: parke@nso.uchc.edu

66th American College of Rheumatology AGM
25–29 Oct 2002; New Orleans, USA
Contact: ACR, Ronald F Olejko, Director of Conferences and Meetings, 1800 Century Place, Suite 250, Atlanta, Georgia 30045–4300, USA
Tel: + 1 404 633 3777
Fax: + 1 404 633 1870
Email: acr@rheumatology.org
Website: www.rheumatology.org

Third International Meeting on Social and Economic Aspects of Osteoporosis and Osteoarthritis
7–9 November, 2002; Barcelona, Spain
Contact: Yolande Piette Communication, Boulevard Kleeyer 108, 4000 Liége, Belgium
Tel: 32 4 254 12 25
Fax: 32 4 254 12 90
Email: ypc@compuserve.com

Certifying Examination in Pediatric Rheumatology
18 Nov 2002
Contact: American Board of Pediatrics, 111 Silver Cedar Court, Chapel Hill, NC 27514-1513, USA
Tel: 919 929 0461
Fax: 919 918 7114 or 919 929 9255
Website: www.abp.org

10th APLAR Congress of Rheumatology
1–6 Dec 2002; Bangkok, Thailand
Contact: APLAR 2002 Secretariat
Fax: 66 2 716 6525
Email: secretariat@aplar2002.com
Website: www.aplar2002.com

Eleventh Intensive Applied Epidemiology Course for Rheumatologists
24–28 Feb 2003; ARC Epidemiology Unit, Manchester
No previous experience in epidemiology is required. The course is residential and limited to 25 places
Contact: Ms Lisa McCair, ARC Epidemiology Unit, Manchester, Oxford Road, Manchester M13 9PE, UK
Tel: +44 (0)161 275 5993
Fax: +44 (0)161 275 5043
Email: Lisa@fs1.ser.man.ac.uk

Future EULAR congresses
18–21 June 2003; EULAR 2003 Lisbon, Portugal
9–12 June 2004; EULAR 2004 Berlin, Germany
8–11 June 2005; EULAR 2005 Vienna, Austria
21–24 June 2006; EULAR 2006 Amsterdam, The Netherlands