Steroids cause osteoporosis

We read with great interest the article by Gudbjornsson and colleagues and concur with the accompanying letter by Dr Paget on the issue of corticosteroid associated osteoporosis. 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.

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 anti-resorptive 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 zoledronic acid. One patient was on hormone replacement therapy. Of the postmenopausal women, 23 (56%) were on 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 was receiving prednisolone for 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 continuously for 20 years for SLE, up to a maximum dose of 80 mg/day.

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. 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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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).1 We would like to deal with some of the issues he raises, and add some comments.

Now that 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;23 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 higher level of diagnostic accuracy than that achieved by combining microcopy, 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,24 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. Nevertheless, it is true that a number of auxiliary signs and symptoms are necessary to maintain the accuracy of 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 or be replaced by better alternatives have been introduced.

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Author’s reply

Zandbelt and van den Hoogen raise and discuss some important issues which I 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: “A critical look at 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 them that final diagnostic criteria are not set in stone as the diagnosis of a disease is not a static entity. Significant changes in a disease entity may occur over time. It is therefore important to keep an open mind as to what is going on and to review the criteria as necessary.

The issue of smoking and the presence of antibodies is perhaps the most controversial. Several groups of authors have reported that patients with genuine SS do not come to medical attention as frequently as the general population is present or past smokers with a smoking history.29,30 When one makes a diagnosis of SS, one should therefore take note of the patient’s smoking history.31

In conclusion I would like to state that the criteria that I published in the Annals do not mean that smoking is not important. It is important to take all data into account before making a diagnosis of SS. The debate continues and I strongly encourage the rheumatology community to comment on the criteria which I published and participate in the ongoing discussion. It is not my intention to make smoking a criteria in and of itself but rather in combination with other criteria to determine if one can make a diagnosis of SS.

M Manthorpe

References

A brief history of spa therapy

We read with great interest the paper entitled “A brief history of spa therapy” by van Tubergen and van den Hoogen in the March edition of the Annals.1 Spas have certainly played an important part throughout the centuries not only in recreation but also in restoring physical and mental health. Both spas and doctors have greatly influenced the progress of rheumatology—for example, Bruce from Scotland described polyarthritis, Forester introduced gold treatment for rheumatoid arthritis in France, and Sita and Zitnan from Piestany described polyarticular chondrocalcinosis.

We regret that this paper failed to mention the famous spas of the Czech Republic, Slovakia, Hungary, and Romania. From their conception, Czech and Slovak spas became gathering places not only for aristocrats but also for kings and emperors. Hungary, one of the richest countries of thermal waters in the world, has a bath culture dating back to the pre-Roman Celtic times. Budapest is a capital unique for its thermal waters. It is renowned for Lukácisz, the second bigger hot lake in the world, second to Rotorua, New Zealand.

We are proud to have published in English the first double blind controlled trials with thermal water in the Netherlands.2 Therefore, we are surprised that the US-Eur criteria, which look more acceptable, are based upon a total of 15–22 bathes taken daily.5–8 bathes with an associated rise in the leucocyte count and vascular factor from the tumour necrosis factor family seems promising.

The fact that Japanese SS specialists simultaneously present their new classification criteria (also termed Japanese III), which look rather different from the US-Eur consensus criteria, might be considered very disturbing and disappointing for clinicians. However, they do look more acceptable, are based upon the results of a greater number of patients, and focus more on objective assessments—as asked for by Zandbelt and van den Hoogen. However, Zandbelt and van den Hoogen forget that the original set of SS criteria, the Copenhagen criteria of 1975, were based purely on subjective assessments. The history of the various classification criteria for SS from that date can simply be represented by a nearby closed circle (see fig 1 in the June leader).3

At the Vlith International SS symposium held in mid-May 2002 in Kanazawa, Japan, both 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 introduce them immediately as classification criteria would seem to have a rather short life.2

We profoundly disagree with the authors, that “taking the water, balneotherapy, spa therapy, hydrotherapy are more or less interchangeable.”4 We are certain that they are not. Even in their paper, they quote Priesnitz and Kneipp, who distinguish between thermal water (balneotherapy) and hydrotherapy.5 Hydropathy uses only the physical qualities of water (buoyancy of water, resistance, sometimes its temperature either cold or warm), whereas thermal waters are not only naturally warm (>20°C) but their mineral content is also significant. In Hungary a recognised mineral water should have minerals 1 g/l or more, but no nitrates, nitrites, or bacterial growth. It is not known whether the minerals of mineral water penetrate the body surface, but they are known to cause a so-called spa or mineral water reaction.6,7

In our paper we provide some examples of the effect of mineral water and spa treatment. In Hungary, the famous spas of the Czech Republic, Slovakia, Hungary, and Romania have greatly influenced the progress of rheumatology, for example, Bruce from Scotland, Forester introduced gold treatment for rheumatoid arthritis in France, and Sita and Zitnan from Piestany described polyarticular chondrocalcinosis.

We are, however, well aware of the central role of spas elsewhere in the world both in the past and the present. Furthermore, there are differences in mineral concentration, temperatures, cultures and beliefs. Underdevelopment of evidence-based physiotherapy is partly due to lack of funding for necessary trials. The situation is similar for balneotherapy and spa treatment trials. This problem may be overcome by conducting multicentre trials in many countries. Such trials may result in an evidence-based approach to therapeutic or recreational bathing.

References


Authors’ reply

We thank the Drs Bender, Balint, and Balint for their comments on our study and their additional remarks. We did not intentionally exclude the spas in countries such as the Czech Republic, Slovakia, Hungary, and Romania. In our paper we provided some examples of spas in European countries which we had found mentioned in published reports. We are, however, well aware of the central role of spas elsewhere in the world both in the past and the present. Furthermore, we agree that spas have an important role in rheumatology in many countries more research should be done and

PostScript

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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 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.

C A Seemayer, R E Gay, S Gay

FORTECOMMING 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 Mc Clair, ARC Epidemiology Unit, Manchester, Oxford Road, Manchester M13 9PT, 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