

# PostScript

## MATTERS ARISING

### Guidelines for the treatment of osteoarthritis

Guidelines for the treatment of osteoarthritis (OA) have several purposes, but a major one relates to its use by regulatory or medical insurance agencies that use it to help guide their response to requests for drugs to treat patients.

Data have recently been published which record the efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) over paracetamol (acetaminophen) and report patients' preferences for NSAIDs rather than paracetamol in the treatment of OA.<sup>1-7</sup> Furthermore, inflammation is a common accompaniment of moderate to severe OA.<sup>8-10</sup> Therefore it would seem appropriate to consider the use of NSAIDs as the primary treatment in the group of patients with OA with moderate to severe pain or inflammation as part of their disease.

The EULAR Guidelines state that paracetamol is the first line of treatment for all patients with OA,<sup>11</sup> despite the recent evidence that NSAIDs are more efficacious than paracetamol and that paracetamol is associated with more gastrointestinal toxicity than was previously thought.<sup>12</sup>

Would it not be more appropriate to suggest that patients who have moderate to severe pain and/or OA with inflammatory components be given NSAIDs as the first line of treatment, leaving paracetamol for symptomatic use in those patients with lesser degrees of pain or lack of overt inflammation?

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**J R Caldwell**

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### References

- 1 **Felson DT.** The verdict favors nonsteroidal anti-inflammatory drugs for the treatment of osteoarthritis: a plea for more evidence on other treatments. *Arthritis Rheum* 2001;44:1477-80.
- 2 **Moskowitz RW.** Osteoarthritis: simple analgesics versus nonsteroidal anti-inflammatory drugs. *J Rheumatol* 2001;28:932-4.

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The editors will decide as before whether also to publish it in a future paper issue.

- 3 **Williams HJ, Ward JR, Egger MJ, Neuner R, Brooks RH, Clegg DO, et al.** Comparison of naproxen and acetaminophen in a two-year study of treatment of osteoarthritis of the knee. *Arthritis Rheum* 1993;36:196-206.
- 4 **Pincus T, Koch GG, Sokka T, Lefkowitz J, Wolfe F, Jordan JM, et al.** A randomized, double-blind crossover clinical trial of diclofenac versus misoprostol versus acetaminophen in patients with osteoarthritis of the knees or hip. *Arthritis Rheum* 2001;44:1587-98.
- 5 **Altman RD.** Ibuprofen, acetaminophen and placebo in osteoarthritis of the knee: a six-day double-blind study [abstract]. *Arthritis Rheum* 1999;42(suppl):S403.
- 6 **Wolfe F, Szabo S, Lane N.** Preferences for nonsteroidal anti-inflammatory drugs over acetaminophen by rheumatic disease patients: a survey of 1799 patients with osteoarthritis, rheumatoid arthritis and fibromyalgia [abstract]. *Arthritis Rheum* 1999;42(suppl):S296.
- 7 **Pincus T, Swearingen C, Cummins P, Callahan LF.** Preference for nonsteroidal anti-inflammatory drugs versus acetaminophen and concomitant use of both types of drugs in patients with osteoarthritis. *J Rheumatol* 2000;27:1020-7.
- 8 **Peyron J.** Inflammation in osteoarthritis. Review of its role in the clinical picture, disease progress, subsets, and pathophysiology. *Semin Arthritis Rheum* 1981;11(suppl 1):115-16.
- 9 **Goldenberg DL, Egan MS, Cohen AS.** Inflammatory synovitis and degenerative joint disease. *J Rheumatol* 1982;9:204-9.
- 10 **Ayral X, Pickering EH, Woodworth TG, McKillop N, Loose L, Dougados M.** Synovitis predicts the arthroscopic regression of medial tibiofemoral knee osteoarthritis [abstract]. *Ann Rheum Dis* 2001;60 (suppl 1):57 [abstract OP51].
- 11 **Pendleton A, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JWJ, et al.** EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2000;59:936-44.
- 12 **Garcia Rodriguez LA, Hernandez-Garcia S.** The relative risk of upper gastrointestinal complications, users of acetaminophen and nonsteroidal anti-inflammatory drugs. *Epidemiology* (in press).

### Authors' response

The pro's and con's of oral non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol are certainly of interest and relevance to the management of osteoarthritis (OA). However, the following points are relevant to the suggestions contained in Dr Furst's letter:

(1) The EULAR recommendations reflect an evidence based approach to key clinical questions. They clearly specify the end of 1998 as the time up until which published evidence was included for review. The recommendations will be revised in the light of more recent publications in the future and will then include the studies referenced by Dr Furst. It is clearly impractical regularly to change individual recommendations in response to every new publication—certain time points need to be taken to "close the door" on data while the formal review process takes place.

(2) Again it is clearly stated in the EULAR document that the package of care offered to a patient with knee OA must take into account

not only efficacy and side effects of individual interventions but also patient attitudes and preferences, comorbidity, concurrent drug treatment, costs, and availability. It will indeed be interesting to see if the EULAR Task Force *do* change their recommendations in the light of these recent data in the way suggested by Dr Furst. For example:

- In the recent study by Pincus it is noteworthy that although 57% of patients thought that Arthrotec was better than paracetamol, 20% thought that paracetamol was better and 22% reported no difference.<sup>1</sup> In other words almost half the patients found no perceived benefit from Arthrotec. Side effects were significantly more common with Arthrotec. Furthermore, this was a short term study of six weeks. The few long term studies show that many patients stop their NSAID—in one study only 15–20% of patients with OA continued their NSAID for one year.<sup>2</sup>
- Traditional oral NSAIDs indeed kill a significant number of patients each year from gastrointestinal bleeding/perforation. Over half of the patients with symptomatic OA are in the high risk category for NSAID associated mortality (elderly, with comorbidity). Although there are now data that paracetamol may have a gastrointestinal risk, it is less than that caused by traditional NSAIDs. There are no renal or cardiovascular side effects from paracetamol, but there are from NSAIDs.
- NSAIDs remain expensive compared with paracetamol.
- Data show that NSAIDs (at least indometacin) may hasten cartilage and bone attrition<sup>3</sup>—there are no data that paracetamol is such a *negative* "DMOAD".

It is for reasons such as this that most doctors keep oral NSAIDs in reserve for patients in whom the safer and cheaper drug, paracetamol, has failed.<sup>4</sup>

(3) It is perhaps unfortunate that many of us get hung up on the order of drug selection. In practice, of course, most patients receive a package of care, not a single treatment. Many patients take both NSAIDs and paracetamol (often as self medication of over the counter drugs)—hopefully in addition to exercise, weight reduction, pacing of activities, etc, etc. The argument about "first use" is therefore irrelevant to most patients. Unfortunately, few studies use a factorial design to better inform us of effect sizes of combined treatments. Few also examine predictors of response. These points are again made in the EULAR document.

(4) We would take issue with the suggestion that a major purpose of "guidelines" is that they be used by regulatory or insurance agencies. This may be true in America but is not a rationale for producing recommendations in Europe. The objectives of the EULAR recommendations are clearly listed. They summarise evidence to help directly (not indirectly through agencies) guide decision making by

practitioners and patients. They also highlight gaps in our knowledge and inform the future research agenda.

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#### Reference

- 1 **Pincus T**, Koch GG, Sokka T, Lefkowitz J, Wolfe F, Jordan JM, *et al*. A randomized, double-blind crossover clinical trial of diclofenac versus misoprostol versus acetaminophen in patients with osteoarthritis of the knees or hip. *Arthritis Rheum* 2001;44:1587–98.
- 2 **Scholes D**, Stergachis A, Penna PM, Normand EH, Hansten PD. Nonsteroidal anti-inflammatory drug discontinuation in patients with osteoarthritis. *J Rheumatol* 1995;22:708–12.
- 3 **Doherty M**, Jones A. Indomethacin hastens large joint osteoarthritis in humans—how strong is the evidence? *J Rheumatol* 1995;22:2013–16.
- 4 **Brandt KD**, Bradley JD. Should the initial drug used to treat osteoarthritis pain be a nonsteroidal antiinflammatory drug? *J Rheumatol* 2001;28:467–73.

#### Salmonella arteritis

I was interested to read the “Lesson of the month” on salmonella arteritis in a 70 year old Afro-Caribbean man.<sup>1</sup> The discussion mentioned that male sex and pre-existing atherosclerosis are risk factors for salmonella arteritis and that the condition is extremely uncommon below the age of 50.

No mention was made of the possibility of sickle cell disease in this man. Sickle cell disease may be complicated by salmonella infection, rarely producing an osteomyelitis, and I should be interested to know if haemoglobin electrophoresis was carried out, and whether in fact the sharp drop in haemoglobin might be accounted for by a sickle cell crisis.

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#### Reference

- 1 **Pyne D**, Mootoo R, Bhanji A, Farrow A. Salmonella arteritis: an unusual cause of low back pain. *Ann Rheum Dis* 2001;60:1086–7.

#### Author's response

It is a valid point that sickle cell disease can be complicated by salmonella infection and as a sequel salmonella osteomyelitis. This usually follows a painful crisis, which is more common in male than female patients and has an increased incidence between the ages of 15 and 25. An episode of painful crisis lasting for more than two weeks and associated with a temperature of 38°C or more should raise the suspicion of osteomyelitis, and the most common organism is salmonella followed by *Staphylococcus aureus*. Radiological changes are often only apparent up to four weeks after the onset of illness. Salmonella infection is also recorded in young children with sickle cell disease and episodes of

vascular occlusion affecting the bones of the hand and feet, leading to dactylitis. Blood cultures are therefore always indicated in dactylitis when associated with sickle cell disease, and salmonella infection as a complication is well documented.<sup>1</sup>

Our patient did in fact have a haemoglobin electrophoresis carried out during his illness and this showed a normal adult haemoglobin pattern and no evidence of haemoglobinopathy.

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#### Reference

- 1 **Noonon WJ**. Salmonella osteomyelitis presenting as hand foot syndrome in sickle cell disease. *BMJ* 1982;248:1464–5.

#### Rheumatic pneumonia

I read recently in the *Annals* a letter by Fuente *et al* on rheumatic pneumonia.<sup>1</sup> Despite the authors stating that they had completely reviewed Spanish and English publications, an article by us published in 1995 was not included.<sup>2</sup>

Our article would have added to the information contained in the letter by Fuente *et al* because it described the case of a 3 year old girl (an uncommon age for the onset of rheumatic disease), in whom arthritis and carditis occurred together, with valvular sequelae (mitral insufficiency) that required surgical intervention a year later.

In Pernambuco, in the northeast of Brazil, which has serious socioeconomic problems, rheumatic fever is endemic among the poor, particularly in children and adolescents, causing early damage to mitral and aortic valves. Rheumatic pneumonia, though uncommon, can be seen in about 2% of our acute cases, mostly recurrent, with severe concomitant valvulitis.

#### L R Saraiva

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#### References

- 1 **de la Fuente J**, Nodar A, Sopena A, Martinez CA. Rheumatic pneumonia. *Ann Rheum Dis* 2001;60:990–1.
- 2 **Saraiva LR**, Carneiro RW, Willcox G. Rheumatic pneumonia with carditis and arthritis in a three-year-old girl. *Cardiology in the Young* 1995;5:197–8.

#### Authors' response

We thank Dr Saraiva for his letter and think that the case reported<sup>1</sup> is very interesting as they describe rheumatic pneumonia associated with mitral insufficiency at an unusually early age of onset in a region where rheumatic fever continues to be prevalent. This emphasises even more the rarity of this complication.

Unfortunately, we were unable to include the article in our review because it was not indexed in the bibliographic sources we used (Medline, Medline plus, and PubMed of the United States National Library of Medicine databases) and it was not referred to in the bibliography of papers reviewed in our article.

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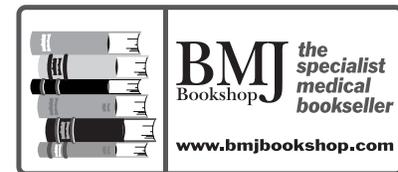
Pneumology Service, Xeral-Cíes Hospital

Correspondence to: Dr J de la Fuente

#### Reference

- 1 **Saraiva LR**, Carneiro RW, Willcox G. Rheumatic pneumonia with carditis and arthritis in a three-year-old girl. *Cardiology in the Young* 1995;5:197–8.

## BOOK REVIEW



### Conquering rheumatoid arthritis. The latest breakthroughs and treatments

Thomas Lee. (Pp 250, \$20.) Amherst, New York: Prometheus Books, 2001. ISBN 1-57392-886-0

Thomas Lee is a professor of microbiology and biotechnology and is also a patient with rheumatoid arthritis (RA). He has studied and read about rheumatic diseases, mainly about RA, and felt the need for a comprehensive work to explain to patients with RA more about the mechanism of their disease and current and future treatments. It is not meant for, and offers little new to, the professional reader. On the other hand, it may be too complicated for a patient without a medical background. Those targeted are also clearly American patients: prices are always given in US dollars, references are only to USA regulations and, moreover, the major part of research quoted was done in the USA.

The author first gives some definitions of rheumatic diseases, followed by chapters about immunology and the mechanisms of disease. A lot of attention is given to genes and their role in RA. Much seems to be expected from the human genome project and from genetic targeted treatments. A chapter is dedicated to bone marrow and stem cell transplantation. Though the author mentions the side effect of these treatments, he still considers them a “miracle”, giving, I fear, undue hope to patients. The next chapter gives a clear overview of the current treatments for RA and is followed by chapters about new treatments, clinical trials, and drugs in the pipeline. At the end useful websites are listed.

My main criticism is that it is too easy for professionals, but too difficult for patients without a medical background. While some chapters are clear, for instance those about treatments, others, or part of others, seem to be really difficult to understand for lay people. The information given is sometimes anecdotal, for instance, in the chapter about stem cell transplantation where there are no references. Only websites are given as references. These may be easily accessible, but I think classical referencing allows for easier checking of what is stated. Moreover, I fear that false hopes may be raised by describing some treatments that are still far from being used in practice.

E M Veys

## FORTHCOMING EVENTS

### International Congress: New Trends in Osteoarthritis

9–11 May 2002; Milan, Italy

Contact: Organising Secretariat, O.I.C. S.r.l., Via Fatebenefratelli 19, 20121 Milan, Italy  
Tel: +39 02 65 71 200  
Fax: +39 02 65 71 270  
Email: osteoarthritis@oic.it

### IOF World Congress on Osteoporosis

10–14 May 2002; Lisbon, Portugal  
Contact: IOF Secretariat, 71 cours Albert Thomas, F-69003 Lyon, France  
Tel: +33 472 91 41 77  
Fax: +33 472 36 90 52  
Email: info@ioflyon.org  
Website: www.osteofound.org

### 6th International Symposium on the Immunotherapy of the Rheumatic Diseases

15–19 May 2002; Limassol, Cyprus  
Contact: Tammi Wenham, Department of Rheumatology, 5th Floor, Thomas Guy House, Guy's Hospital, London SE1 9RT, UK  
Tel: +44 (0)207 955 4394  
Fax: +44 (0)207 955 2472  
Email: tammi.wenham@kcl.ac.uk  
Website: www.kcl.ac.uk/ip/jeremycridland/rsymp

### 5th European Conference on Systemic Lupus Erythematosus

26–30 May 2002; Athens, Greece  
Chairman Professor HM Moutsopoulos  
Secretariat: Amphitriion Congress Organising Bureau  
Email: hmoutsop@med.uoa.gr  
Email: congress@amphitriion.gr

### Annual European Congress of Rheumatology

12–15 June 2002; Stockholm, Sweden  
Contact: Fred Wyss, Executive Secretary EULAR, Witikonstrasse 15, CH-8032, Zurich, Switzerland  
Tel: +41 1 383 9690  
Fax: +41 1 383 9810  
Email: eular@bluewin.ch  
Website: www.eular.org

### 10th International Congress on Behçet's Disease

27–29 June 2002; Berlin, Germany  
Under the auspices of the International Society for Behçet's Disease  
Up to eight young investigator awards, each of \$500, will be awarded on the basis of abstracts submitted  
Contact: Professor Ch C Zouboulis, Department of Dermatology, University Medical Centre Benjamin Franklin, The Free University of Berlin, Fabeckstrasse 60–62, 14195 Berlin, Germany  
Fax: 49 30 84456908  
Email: zoubbere@zedat.fu-berlin.de  
Website: www.userpages.fu-berlin.de/~zoubbere  
ISBD website: www.behcet.ws

### 29th Scandinavian Congress of Rheumatology

15–18 Aug 2002; Tromsø, Norway  
Contact: Hans Nossent, Department of Rheumatology, University Hospital Tromsø, Norway  
Tel: 47 776 27294  
Fax: 47 776 27258  
Email: 29scr2002@rito.no or revhan@rito.no

### 24th Annual Meeting of the American Society for Bone and Mineral Research

20–24 Sep 2002; San Antonio, TX, USA  
Contact: ASBMR, 2025 M Street, NW, Suite 800, Washington DC 20036-3309, USA  
Tel: +1 202 367 1161  
Fax: +1 202 857 1880  
Email: asbmr@dc.sba.com

### Translational Research in Autoimmunity

21–22 Sep 2002; Pavia, Italy  
Contact: Organising secretariat: eventi S.R.L., Corso Cavour, 18/20 - 27100 Pavia, Italy  
Email: tra@e20pr.com  
Website: www.e20pr.com  
Congress website: www.medicine.ucsd.edu/albani/2001 meeting

### OsteoArthritis Research Society International (OARSI) World Congress

22–25 Sep 2002; Sydney, Australia  
Contact: OsteoArthritis Research Society International (OARSI), 2025 M Street, NW, Suite 800, Washington DC 20036, USA  
Tel: +1 202 367 1177  
Fax: +1 202 367 2177  
Email: oarsi@oarsi.org  
Website: www.oarsi.org

### Third International Conference on Familial Mediterranean Fever and Hereditary Inflammatory Disorders

23–27 September 2002; La Grande Motte, France  
Contact: Dr Isabelle Tzoutou, Laboratoire de Génétique Moléculaire et Chromosomique, Hôpital A de Villeneuve, Montpellier, France  
Tel: 33 4 67 33 58 59  
Fax: 33 4 67 33 58 62  
Email: isabelle.tzoutou@igh.cnrs.fr  
Website: www.congres.igh.cnrs.fr.FMF/2002

### 10th International Congress on Antiphospholipid Antibodies

29 Sep–3 Oct 2002; Sicily, Italy  
Contact: Secretariat, 10th International Congress on Antiphospholipid Antibodies, c/o Kenes International, PO Box 50006, Tel Aviv 61500, Israel  
Tel: 972 3 5140018/9  
Fax: 972 3 5140077 or 972 3 5172484  
Email: aps@kenes.com  
Website: www.kenes.com/aps

### Third international Congress on Spondyloarthropathies

2–5 Oct 2002, Gent, Belgium  
Topics covered will be:

- Innate immunity

- Genetics and HLA-B27
- Animal models and pathogenesis
- Clinical research and therapy

Contact: Organisation and secretariat, Medicongress, Waalpoel 28–34, B-9960 Assenede, Belgium  
Tel: +32 9 344 39 59  
Fax: +32 9 344 40 10  
Email: congresses@medicongress.com  
Website: www.medicongress.com

### 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 7534  
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 Kleyer 108, 4000 Liège, 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

### 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