

PostScript

MATTERS ARISING

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French guidelines for diagnosis and treating latent and active tuberculosis in patients with RA treated with TNF blockers

In a recent paper in the *Annals of the Rheumatic Diseases*, Furst *et al* proposed preliminary consensus guidelines, elaborated during the "Advances in targeted therapies IV" meeting 2002, for diagnosis and treating latent tuberculosis in patients with rheumatoid arthritis (RA) treated with tumour necrosis factor (TNF) blockers.¹ Such guidelines cannot be universal and must take into account the prevalence of tuberculosis, the type of immigrants, and the prevalence of vaccination with BCG (bacille Calmette-Guerin) in the country where they are proposed. A multidisciplinary French cooperative group termed RATIO (Recherche sur Anti-TNF et Infections Opportunistes), including specialists in infectious diseases, pneumology, gastroenterology, and rheumatology, recently proposed such guidelines adapted for France,² which have been validated by the French agency for healthcare product safety (AFSSAPS). These guidelines are intended to help doctors detect and manage tuberculosis in their patients before and after TNF blocker therapy. Moreover, they are now mandatory for all doctors and have to be implemented in addition to the labelling recommendations. They differ in several points from the preliminary consensus guidelines.

Definition of latent tuberculosis and of patients at risk

These patients are defined by the presence of one of the following items:

- A history of tuberculosis treated before 1970, including at least two months with the rifampicin-pyrazinamide combination, or not treated for at least six months
- A weal larger than 10 mm in diameter or a blister in response to an intradermal tuberculin test done more than 10 years after the last BCG vaccination, with no history of correct treatment for active tuberculosis
- Residual radiographic tuberculous lesions larger than 1 cm³ in size with no certainty that eradicating treatment was received.

The small differences between the previous recommendations are:

- The date of the BCG, which is frequently performed in Europe and mandatory in France where 95% of the children are vaccinated by age 6, is taken into account
- Interpretation of the PPD test: choice of a single threshold of 10 mm to consider the test positive in order to simplify the doctor's practice.

Management of latent tuberculosis

Before starting TNF blocker therapy, anti-tuberculous chemoprophylaxis should be initiated in all patients who are at risk of tuberculous reactivation, as defined above.

Three regimens can be used for chemoprophylaxis:

- Rifampicin (Rifadine) 10 mg/kg/day and pyrazinamide (Pirilène) 20 mg/kg/day, each in a single daily dose, for two months. However, the efficacy of this regimen for prophylactic treatment has been validated only in HIV infected patients.³
- Rifampicin (Rifadine) 10 mg/kg/day in a single daily dose and isoniazid (Rimifon) 4 mg/kg/day for three months.
- Isoniazid alone for nine months in very elderly patients and in patients with hepatic toxicity or cirrhosis.

The main difference with the previous recommendations is the preferred choice of two drugs including pyrazinamide when possible. This drug may have hepatic toxicity but interest in use of the combination of rifampicin and pyrazinamide for two months has been recently emphasised in immigrants with resistant BK coming from Asia and Africa.⁴

Chemoprophylaxis should be started at least three weeks before the first infusion of TNF blockers. If latent tuberculosis is diagnosed, it is recommended that gastric aspirates are obtained. If *Mycobacterium tuberculosis* is recovered from the gastric aspirates, the patient should be switched from the prophylactic regimen to a curative regimen.

Management of active tuberculosis diagnosed before or during TNF blocker therapy

Curative treatment includes triple combination therapy with rifampicin (10 mg/kg/day in a single dose), isoniazid (4 mg/kg/day), and pyrazinamide (20 mg/kg/day in a single dose), after which the pyrazinamide is stopped and the two other drugs continued in combination. Ethambutol (20 mg/kg/day) should be added during the first two months if there is a relapse or a suspicion of drug resistance (patient from an endemic area).

It is not advisable to start the treatment in hospital departments where other patients with TNF blocker associated immune deficiency are seen.

Can TNF blocker therapy be resumed?

In the absence of prospective data, resumption of TNF blocker therapy is not recommended. If the clinical value of TNF blockers is considered large, the drug should be started no sooner than two months after the end of the anti-

tuberculous treatment. It is essential to make sure that there is no clinical or radiographic evidence of active tuberculosis and that tests for the tubercle bacillus are negative.

Current knowledge suggests that isoniazid alone, or with rifampicin, should be given as long term treatment to patients who resume TNF blocker therapy. Careful monitoring by a multidisciplinary team is essential.

Prescription of systemic or local glucocorticoid therapy in patients with tuberculosis receiving TNF blockers

There is no contraindication to intra-articular or systemic glucocorticoid therapy. Glucocorticoid therapy is recommended in patients with tuberculous miliary, meningitis, or pericarditis. Because rifampicin accelerates the breakdown of glucocorticoids, the glucocorticoid dose should be increased by 40%.

Such recommendations, adapted in every country, should substantially reduce the frequency and severity of tuberculosis occurring during TNF blocker therapy. However, many issues remain unsettled, and changes in these recommendations are likely to occur in the near future.

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References

- 1 Furst DE, Cush J, Kaufmann S, Siegel J, Kurth R. Preliminary guidelines for diagnosing and treating tuberculosis in patients with rheumatoid arthritis in immunosuppressive trials or being treated with biological agents. *Ann Rheum Dis* 2002;61(suppl II):ii62-3.
- 2 Salmon D on behalf of the GTI and AFSSAPS. Recommendations about the prevention and management of tuberculosis in patients taking infliximab. *Joint Bone Spine* 2002;69:170-2.
- 3 Halsey NA, Coberly JS, Desormeaux J, Losikoff P, Atkinson J, Moulton LH, *et al*. Randomised trial of isoniazid versus rifampicin and pyrazinamide for prevention of tuberculosis in HIV-1 infection. *Lancet* 1998;351:786-92.
- 4 Khan K, Muennig P, Behta M, Graff Zivin J. Global drug-resistance patterns and the management of latent tuberculosis infection in immigrants to the United States. *N Engl J Med* 2002;23:1850-66.

BOOK REVIEW

Bone and joint futures

Ed A D Woolf. (Pp150, 16-95.) London: BMJ Publishing Group, 2002. ISBN 0 727 91548 7.

"Joint diseases, back complaints, osteoporosis and limb trauma resulting from accidents have an enormous impact on individuals and societies and on healthcare services and economies". This statement was given by the

UN secretary general, Kofi Annan, before the formal launch of the Bone and Joint Decade early 2000. He also stated that there are effective ways to prevent and treat these disabling disorders "but we must act now". The book *Bone and joint futures* is a helpful contribution to understand the burden of musculoskeletal diseases and their current and future management, and these topics are especially important issues for the Bone and Joint Decade.

This book is divided into eight different sections. The first chapter focuses on the future provision of care for musculoskeletal conditions, the second on the future burden of the conditions and priorities for health care, and the third chapter on the potential of developments in bioscience and technology. The last five chapters discuss the future diagnoses and management of five different conditions: rheumatoid arthritis, osteoarthritis, osteoporosis, chronic musculoskeletal pain, and trauma. Each chapter is written by very competent clinicians and epidemiologists.

The chapters are generally well referenced and provide a lot of useful information to support both clinicians and decision makers in health policy. For example, the demand for care for musculoskeletal conditions is discussed within the framework of change in population demographics, lifestyle changes, peoples' increasing expectations for health, provision of new treatments, and new technologies as well as the increased costs of health care. Models for care are discussed from different perspectives: the community, the health systems, self management of patients delivery systems, and also how new information technology can be integrated into the management.

The description of the burden of diseases focuses on the global burden of disease project, the changing demography and, more specifically, on rheumatoid arthritis, osteoarthritis, osteoporosis, and back pain.

All chapters are easy to read, they are divided into subsections, and an index at the end of the book is also helpful for finding specific information. In this way, the book may also be used as a reference for clinicians and managers of health care to identify specific information when needed.

The authors have focused on the major conditions of the musculoskeletal system, but of course, not all conditions have been covered. For example, there are no major discussions on the spondyloarthropathies, on undifferentiated polyarthritis, and on gout. The comprehensiveness of references is a little variable across chapters. The limitation of this book, as with most other books, is that the more recent references are not included. For example, no references from 2002 are included and only a few from 2001. Despite this limitation, the message of this book clearly meets the expectations of the title—focusing on the futures of bone and joint management.

To my knowledge no other book or special issue of a journal covers, the same topic in a similar way. Thus, this book fills an important gap. It will definitely support clinicians when arguing for resources for the care of patients with musculoskeletal diseases and be of special importance to understanding the background and importance of the Bone and Joint Decade.

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FORTHCOMING EVENTS

25th Annual Meeting of the American Society for Bone and Mineral Research (ASBMR)

19–23 September 2003; Minneapolis, Minnesota, USA

Tel: +1 202 367 1161

Fax: +1 202 367 2161

Email: asbmr@dc.sba.com

Website: www.asbmr.org

10th European Pediatric Rheumatology Congress

2–5 October 2003; Stresa, Italy

Contact: Organising Secretariat, ECON srl, Via della Moscova 16, 20121 Milan, Italy

Tel: +39 022 900 5745

Fax: +39 022 900 5790

Email: econsrl@tin.it

Website: www.pres.org.uk

International Congress on Arthritis in the Elderly

9–11 October 2003; Milan, Italy

New perspectives in diagnosis and treatment

Contact: Organising Secretariat: Elena Romero

Tel: +39 02 65 71 200

Fax: +39 02 65 71 270

Email: eldrheum@oic.it

7th EULAR Sonography Course

9–12 October, 2003; Rome, Italy

An introductory and practical course on musculoskeletal ultrasonography

Scientific secretariat: Professor Guido Valesini

Email: annamaria.iagrocco@uniroma1.it

Contact: Organising secretariat: Michela Civelli, EDRA Spa, Medical Publishing and News Media, Viale Monza, 133 - 20125, Milan, Italy

Tel: +39 (0)2 281 72300

Fax: +39 (0)2 281 72399

Email: edracongressi@dsmedigroup.com

OARSI World Congress on Osteoarthritis

12–15 October 2003; Berlin, Germany

Tel: +1 202 367 1177

Fax: +1 202 367 2177

Email: oarsi@oarsi.org

Website: www.oarsi.org

Fourth International Symposium on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis

14–17 November 2003; Nice, France

Contact: Organisation Secretariat, YP Communication, 108 boulevard G Kleyer, 4000 Liège, Belgium

Tel: +32 (4) 254 12 25

Fax: +32 (4) 254 12 90

Email: yoland@piettecommunication.com

Website: <http://nice.piettecommunication.com>

2nd International Forum on Geronto-Rheumatology

27–29 November 2003; Amsterdam, The Netherlands

Contact: Erna Kleinjan, project manager Mark Two Communications, PO Box 358, 3830 AK Leusden

Tel: +31 33 434 5730

Fax: +31 33 434 5720

Email: ekleinjan@markttwo.nl

Website: www.marktwo.nl

IOF World Congress on Osteoporosis

14–18 May 2004; Rio de Janeiro, Brazil

Abstract deadline 14 November 2003

IOF awards are available for scientists:

IOF Claus Christiansen Research Fellowship: €45 000

IOF Servier Young Investigator Fellowship: €40 000

Contact: Congress Secretariat at info@osteofound.org

Website: www.osteofound.org

XIth International Conference on Behçet's Disease

27–31 October 2004; Antalya, Turkey

Contact: Congress Secretariat, Figur Congress and Organization Services Ltd, STI, Ayazmaderesi Cad. Karadut Sok. No: 7 80888 Dikilitas, Istanbul, Turkey

Tel: +90 (0212) 258 6020

Fax: +90 (0212) 258 6078

Email: behcet2004@figur.net

Website: www.behcet2004.org

Future EULAR congresses

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

Future ACR meetings

24–28 October 2003; 67th Annual Scientific Meeting; Orlando, Florida

16–21 October 2004; 68th Annual Scientific Meeting; San Antonio, Texas