Which patients stop working because of RA?

The paper by Young et al is a useful contribution to the quest for work disability related to rheumatoid arthritis.1 However, one of the areas in which intervention is theoretically possible to reduce disability—namely, that of work place intervention—was not discussed. In the study by Young et al the types of work performed by the study cohort are grouped into four categories—mainly, manual, semi-manual, semi-sedentary, and mainly sedentary. Perhaps, the patients were allocated to a group based on job title using the British classification of occupations and coding index.2 It is well known to occupational physicians and others taking occupational histories that a job title does not adequately reflect the true nature of work.3 In addition, problems likely specifically to affect patients with rheumatoid arthritis are not usually classified in a subject or ordinal scale such as that used in the study. Examples of such problems might be fine repetitive movements of the hand or work starting times. To gain an accurate insight into work factors affecting work disability, a study is required in which information on the nature of the work tasks is obtained. Ideally this should be gathered prospectively by direct analysis of the workplace duties rather than from trained observers. Tools have been developed that can assist with this type of data gathering.4,5 This would reduce recall and misclassification bias of previous studies. Once this information is obtained, work place intervention as an approach to minimising disability can be implemented and assessed for efficacy and effectiveness.

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References

Authors’ reply
Dr Smith and colleagues make a valid point about studies on work disability in general, although I am not sure that this is highly relevant to our report. We do not dispute any of the other points made. Job title in our patients was based on the Office of National Statistics classification.

We agree that a very detailed account of work tasks taken at the onset by specially trained observers, and repeated regularly until work loss, might reduce possible recall and misclassification bias. However, ERAS, which was started in 1986, aimed at recording outcomes in several quite different dimensions in ordinary busy clinical settings and not in the degree of detail outlined. In the same way, very detailed accounts of home and social circumstances, factors also known to affect work disability, were not included. Despite this, as we make clear in our report, we feel we have adequately highlighted the importance of work disability in RA. Although the above authors do not say as such, the sort of study they describe needs to be set up with the primary aim of investigating possible specific interventions.

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Adult onset Still’s disease: response to Etanercept

Over the past year several publications have appeared recording the use of tumour necrosis factor (TNF) blockers, particularly infliximab (Revellex) in the treatment of adult onset Still’s disease (AOSD), a condition often resistant to a variety of treatments.

We wish to report a favourable response to etanercept (Enbrel) in a single patient who has proved resistant to a wide variety of agents over a 10 year period and who has had several, very serious complications of this condition, including the development of cardiac amyloidosis.

The patient, a 35 year old nursing sister, was initially diagnosed with AOSD at the age of 23 and was treated with non-steroidal anti-inflammatory drugs, salicylates, methotrexate, antimarial drugs (chloroquine), and p-aminosalicylic. On this regimen she developed frequent flares and side effects to most of the disease modifying antirheumatic drugs to which she had been exposed—for example, antimarial drugs resulted in increased loss of peripheral vision in her right eye. Intramuscular gold injections (Myocerin) were then given but also to no avail. High dose steroids (3g daily over five days intravaneously (IV) given at 6–8 weekly intervals caused weight gain and Cushing’s syndrome. Attacks of myalgic pain affecting the neck, shoulders, and mid-back areas were common, and were present throughout her illness. Eventually this was diagnosed as fibromyalgia.

At the age of 29 she was admitted to hospital with severe dyspnoea and chest pain. She tested positive for cytomegalovirus and coxackievirus B. Steroids were ineffective and an emergency tracheotomy was performed in 1996. She was admitted to the intensive care unit with chest emphysema, bilateral pulmonaryoraces, pleural effusions, and a pericardial effusion. She was kept sedated for most of her admission. The tracheotomy tube was reinserted but had to be reinserted owing to the collapse of both arytenoid cartilages. Eventually a Montgomery stent (permanent tracheotomy) was inserted and this remained in situ for some three years later. Treatment was started with daily oral cyclophosphamide. This resulted in severe neutropenia which required Neupogen as the white cell count had fallen to 1x10⁹/l. Extensive alopecia also developed. Steroids were again given in a dose of 1 g twice weekly. Then she consulted a different rheumatologist (RAA) when she was admitted to the intensive care unit again with pericarditis and effusion, pleural effusions, peritonitis (polysarositis), hepatosplenomegaly, and a restrictive cardiomyopathy, which was later diagnosed as being due to amyloid. Gas- troscopy showed reflux oesophagitis with ulceration and severe candidiasis. Severe bone marrow depression with thrombocytopenia (15x10⁹/l) necessitated intravenous gamma-globulin (Polygam) treatment, which was ineffective.

It was decided to attempt plasmapheresis combined with cyclophosphamide at 6–8 weekly intervals. Although the frequency of relapses was markedly reduced, she developed pseudomasomas, and the line had to be removed. Myocarditis was treated with β blockers (Sotacor) 160 mg twice a day. In February 1999 treatment with cyclosporin 125 mg twice a day and methotrexate 50 mg weekly was started. This resulted in fair but not complete control. Lithium was not measured weekly, but the high doses of methotrexate were well tolerated. Because of side effects, the cyclosporin had to be discontinued.

The relapses were not as severe or as frequent as previously. IV cyclophosphamide, together with mesna and zoferan were given every 6–8 weeks. However, relapses occurred more frequently again requiring high dose steroids. Thalidomide was then attempted but even with minimal doses peripheral neuropathy ensued and it had to be discontinued. Premature ovarian failure was then diagnosed.

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The use of Enbrel revolutionised control of the disease. However, a reduction of the dose to one injection weekly instead of the recommended two was ineffective and major relapses occurred. The use of TNFα antagonists in the treatment of AOSD dates back to 1997 when it was first suggested by Stambe and Wickes, who documented the use of thalidomide in a 44 year old woman unresponsive to the usual treatment, although in this particular patient the TNFα levels were low. Hoshino et al. found high levels of TNFα as well as interferon γ and interleukin 6 in 12 patients with AOSD.

Elliot et al. in 1998 used infliximab effectively in a patient with juvenile rheumatoid arthritis and systemic features. The first paper demonstrating its usefulness in AOSD was that of Cavagna et al. in 2001. It was shown that long intervals between infusions resulted in relapses and that reduction of the interval of administration from eight to four to weekly was effective. Skin reactions (for example, urticaria) were prevented by the administration of antihista- mines before the infusions. Kraetsch et al. also treated six patients with a diagnosis of AOSD with infliximab. The fevers, arthralgias, myalgias, hepatosplenomegaly, and rash resolved in all six patients after the first course of treatment with the compound. All serological abnormalities also returned to normal. Up to the time of publication of that series, treatment had been given for between five and 28 months.

It seems now that infliximab and entanercept have revolutionised the treatment of recalcitrant AOSD and should not be withheld from any patients who do not initially respond to conventional treatments which may have included ciclosporin and cyclophosphorin, both of which have been used in the treatment of this condition. High dose steroids combined with cyclophosphamide, on occasion, aborted the acute episodes in this patient but resulted in side effects of steroid overdose.

Our patient had a number of unusual features of the disease and her response to anti-TNF treatment has been nothing short of dramatic.

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References
1 Burcoglu A, Church C, Bontempo F. Therapeutic use of single-stranded naked denatured DNA (defibrotid) in antisynthetase syndrome (APLAS) (abstract). Lupus 1996;5:81

Authors’ response
The authors report an interesting case of a patient with severe adult onset Still’s disease refractory to multiple conventional treatments. A reduction of disease activity was not achieved with initial treatment with the tumour necrosis factor (TNF) antagonist etanercept at a dose of 25 mg twice weekly was started. After a period of treatment with the dose approved for the treatment of rheumatoid arthritis a marked improvement of the patient’s symptoms was seen. Subsequent reduction of the dose to a weekly administration of 25 mg etanercept was followed by a relapse of the disease. Treatment had to be re-escalated to the original dose of 25 mg etanercept twice weekly. Again, a relevant reduction of disease activity was achieved. Up to now treatment with etanercept 25 mg twice weekly is effective and well tolerated by the patient.

The case demonstrates again that treatment directed against TNFα is an effective treatment for adult onset Still’s disease. Up to now, promising data have been presented only for treatment with infliximab. To our knowledge, this is the first published case of successful treatment of adult onset Still’s disease (AOSD) with the TNF receptor construct etanercept, suggesting that inhibition of TNFα is a potential approach to treatment of this disease. Additionally, as seen with several patients treated with infliximab, the case again underlines the need to give continuously a “minimum dose” of this drug to maintain the achieved remission of AOSD.

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Epidemiology of the rheumatic diseases


Eight years after the first edition, this revision reflects the extraordinary growing importance of epidemiology of the rheumatic diseases. The present volume illustrates the complexity of the discipline and its many links with other specialties, particularly with genetics. It makes it very clear that the epidemiology of rheumatic diseases deserves more than a sentence or a section at the beginning of each chapter in textbook series. This second edition has been largely rewritten and augmented by new contributions. It expands the scope to new aspects of rheumatology, including syndromes and the particular burden of overall musculoskeletal diseases, which is of major importance at the beginning of the Bone and Joint Decade (BJD).

The aims are to understand the basic concept of, and specific difficulties related to, the epidemiology of rheumatic diseases. Each chapter has a useful format which describes the methodological difficulties in the disease considered from the standpoint of diagnosis and classification criteria, incidence, prevalence and time trends, and exposure factors classified into genetic and non-genetic, particularly environmental, factors. Minor departures from this scheme are sometimes justified by the particular aspects of some diseases. Chapters are well referenced.

There is a supplementary thematic index with well organised and comprehensive information. Although up-to-date in the presentation and taxonomy of diseases, the book will probably require periodic revision because of the continuous progress in the field, an undertaking which should be encouraged. As a comprehensive worldwide perspective of the rheumatic diseases as currently described in published reports, it has no competitor.

Because increasing interest from policy makers in rheumatic diseases is to be expected in the BJD, the new chapter on population studies of musculoskeletal morbidity is most welcome in documenting the burden of such diseases in other than medical taxonomy.

The chapter on rheumatoid arthritis has been largely rewritten to reflect the in-depth approach of genetics, new methods, and recent results while that on juvenile rheumatoid arthritis takes into account advances in classification as well as in genetics.

Spondylarthropathies and related seronegative or B27 related diseases are covered in three chapters on psoriasis, ankylosing spondylarthritis (inflammatory bowel disease and acute anterior uveitis), and reactive arthritis and Reiter's syndrome. Although this forms a single topic, the presentation used by the authors is thoughtful. Further evolution in classification may be necessary. Chapters on other rare diseases like lupus, scleroderma, polymyalgia rheumatica, myositis, and systemic vasculitis provide in-depth information about recent advances in familial clustering, twin studies, genetic models, immunogenetics, etc.

The osteoarthritis chapter includes a prognosis section, which provides an understanding of outcomes. A tabular summary of occurrence data on osteoarthritis would have been welcome. This chapter is an important contribution to information about one of the most common conditions.

A clear synthesis of complicated data is given in the chapter on osteoporosis. New insights from contributors with innovative views are given on back pain, arm disorders, and fibromyalgia.

Epidemiology of the rheumatic diseases reflects the evolution of taxonomy, conceptualisation, knowledge, and increasingly documented epidemiology in the broad area of the rheumatic diseases and is abundantly documented. It is useful for both clinicians and epidemiologists. Authors and editors are to be commended for producing this second edition and should be encouraged to keep pace with changes in the field by preparing a third edition when opportune. Why not as a measure of progress by the end of the BJD?

F Guillemin

NOTICE

Carol-Nachman Prize and Carol-Nachman Medal 2002

The Carol-Nachman Prize awarded annually is possibly the most prestigious prize in rheumatology at the moment. This is underlined by the impressive list of previous prize winners, including clinicians and scientists such as Professor Lipsky, Professors Maini and Feldmann, Professors Sieper and Braun, Professor Hahn, and Professor Pelletier—just some of the most recent prize winners. The Carol-Nachman Prize of the city of Wiesbaden is donated by the Wiesbaden Casino.

In 2002 the jury unanimously agreed to award the prize to Professor van Venrooij, professor in biochemistry and head of the Department of Biochemistry, University of Nijmegen, Faculty of Science, Mathematics and Informatics, Nijmegen, The Netherlands. Being trained in biochemistry, Professor van Venrooij became interested in the structure of the cytoskeleton in the 1970s. He soon realised that antibodies would be needed to develop his research in this area further. It was at this point, in 1994, when he started to become interested in antibodies, autoantibodies, and their relevant target antigens, that Professor van Venrooij’s group began to focus on autoantibodies and autoantigen systems present in rheumatoid arthritis (RA). In recent years, Professor van Venrooij has succeeded in conducting very elegant research to define new antigens, filaggrin and citrullinated peptides, respectively, probably of great importance for the pathogenesis of RA. The autoantibodies directed against these newly defined antigens were shown to be highly sensitive and specific for RA, thus improving the possibility for an early diagnosis of RA and providing at the same time a significant parameter predicting the clinical course. This beautiful research work, reflecting a merge between clinical and fundamental research, was published in highly reputed international journals. It is largely for this new discovery that the jury awarded the 2002 Carol-Nachman Prize to Professor van Venrooij.

In addition to his recent excellent research work in the area of rheumatology, it should also be mentioned that Professor van Venrooij has been greatly involved over the past years in the standardisation of autoantibody test systems. He was one of the organisers of a worldwide network which was not only scientifically very productive but also resulted in mutual respect, trust, and friendship between scientists.

Mr Fred Wyss was awarded the Carol-Nachman Medal 2002. Mr Wyss studied economics and took part in different activities—for example, as an assistant of a public relations manager of the Swiss Traffic Central Zurich and as the head of the Finance and Personnel Department of Sabena in Switzerland, before his appointment in 1985 as the executive secretary of the European League against Rheumatism (EULAR). In this position, in which Mr Fred Wyss is still active, he has successfully reconstructed EULAR, which at present includes 40 scientific member societies and 24 national social leagues. EULAR, with Mr Fred Wyss as general secretary, coordinates a multitude of research, patient care, and educational activities; it has its own peer-reviewed journal, the Annals of the Rheumatic Diseases. The organisation promotes basic research in rheumatology through grants and awards. Seven standing committees comprising experts in their field coordinate work in diagnostic imaging and clinical trials, paediatric rheumatology, epidemiology, and investigative rheumatology. In addition, EULAR actively supports the care and understanding of the social needs of rheumatic patients.

Three years ago EULAR started organising an annual EULAR Congress, the first being held in Nice, followed last year in Prague, and this year, 2002, in Stockholm.

In view of all these changes EULAR needed complete reorganisation, and the general secretary, Mr Fred Wyss, has been a driving and tireless force. For his achievement in developing EULAR into a modern Europe-wide organisation, and dealing with the different scientific, educational, and social activities, Mr Fred Wyss was unanimously selected for the Carol-Nachman Medal in 2002.

J R Kalden

Chairman of the Board of Trustees of the Carol-Nachman Award

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FORTHCOMING EVENTS

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 1287
Email: askmtr@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.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

7th EULAR Postgraduate Course in Rheumatology
22–27 September 2002; Budapest, Hungary
The course will cover clinical aspects of rheumatic diseases, concentrating on outcome, assessment and evidence based management, and the scientific basis of rheumatology. It is aimed at junior rheumatologists at the end of at least four years of postgraduate training but is open to all rheumatologists. The course will be conducted in English.
Course fee 550 euros, including tuition, accommodation, and full board.
Details: The preliminary programme and registration information are available on the EULAR website: www.eular.org

Third International Conference on Familial Mediterranean Fever and Hereditary Inflammatory Disorders
23–27 September 2002; La Grande Motte, France
Contact: Dr Isabelle Touitou, Laboratoire de Génétique Moléculaire et Chronosomique, Hôpital A de Villeneuve, Montpellier, France
Tel: 33 4 67 33 58 59
Fax: 33 4 67 33 58 62
Email: isabelle.touitou@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@kenses.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, Waaapole 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
Email: 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@rso.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 230, 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 Liege, 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

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