Which patients stop working because of RA?

The paper by Young et al is a useful contribution to the question of 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—namely, manual, semi-manual, semi-sedentary, and mainly sedentary. Presumably, 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. In addition, problems likely specifically to affect patients with rheumatoid arthritis are not usefully classified in a subjective 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 work place by suitably trained observers. Tools have been developed that can assist with this type of data gathering.

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, though 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 Enbrel

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

We wish to report an 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, antimalarial drugs (chloroquine), and p-phenylalanine. On this regimen she developed frequent flares and side effects to most of the disease modifying anti-rheumatic drugs to which she had been exposed—for example, antimalarial drugs resulted in a 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 intravenously (IV) given at 6–8 weekly intervals) caused weight gain and Cushings 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 coxsackievirus B. Steroids were ineffective and an emergency tracheotomy was performed in 1996. She was admitted to the intensive care unit with right sided emphysema, bilateral pulmonary oedema, pleural effusions, and a pericardial effusion. She was kept sedated for most of her admission. The tracheotomy tube was removed but had to be reinserted owing to the collapse of both artenoid 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 count had fallen to 1×10⁹/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 (polyserositis), hepatosplenomegaly, and a restrictive cardiomyopathy, which was later diagnosed as being due to amyloid. Gastroscope showed reflux oesophagitis with ulceration and severe candidiasis. Severe bone marrow depression with thrombocytopenia (15×10⁹/l) necessitated intravenous gammaglobulin (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 pseudomonas infection 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. Lungs were 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 zofran 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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In 2000 treatment with Defibrotide, an experimental anticytokine preparation, was started. This was ineffective. It was then decided to give etanercept (Enbrel) for “flares only, combined with intramuscular steroid (Depo-Medrol 160 mg biweekly before and at the time of the flare); flares were anticipated by subjective symptomatology (sore throat, sweats, fatigue, polyarthralgias, vasculitic skin lesions) as well as by rises in the C reactive protein, erythrocyte sedimentation rate, white blood cell count, and serum ferritin levels. Methotrexate was maintained at 25 mg weekly, as recommended by the manufacturers. On this regimen, flares occurred every 3–4 months on average. Enbrel was then given once weekly together with steroids twice weekly.

On 29 June 2000 she sustained a fracture of her skull complicated by a subarachnoid bleed; a tymanopanostoidectomy was required. She discontinued all her drugs in November 2000 and sustained a massive flare requiring admission to hospital. She decided to discontinue her methotrexate because of side effects and continued with the Enbrel twice weekly. No flares occurred. She ran out of Enbrel in November 2001 for one week and again had to be admitted to hospital with a “flare” necessitating IV steroid and cyclophosphamide once again. When supplies of Enbrel were again made available she used only one injection weekly and once again, in January 2002 developed a severe “flare” necessitating admission to hospital and IV steroid (4 g), on this occasion without cyclophosphamide.

This case demonstrates several important points in the management of recalcitrant AOSD as well as clinical features occurring in the course of the disease.

It was marked by the appearance of vasculitic skin lesions accompanied by severe arthralgias and frank arthritis, in addition to systemic features such as night sweats and fatigue. No typical rash of Still’s disease ever appeared. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement. Her temporomandibular joints were affected more severely than any others ever appeared. Her temporomandibular joints eventually required total replacement.

It seems now that infliximab and etanercept 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 been intravenous 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.

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 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.1 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 the use 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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References

1 Burcoglu A, Church C, Bontempo F. Therapeutic use of single-stranded naked denatured DNA (defibrotide DF) in antiphospholipid antibody syndrome (APLAS) [abstract]. Lupus 1996;5:S1
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 textbooks. 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 continuous progress in the field, an undertaking which should be encouraged. As a comprehensive worldwide perspective of the rheumatic diseases as currently described in the BJD, it should 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 Vennrooij, 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 Vennrooij 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 Vennrooij’s group began to focus on autoantibodies and autoantigen systems present in rheumatoid arthritis (RA). In recent years, Professor van Vennrooij 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 Vennrooij.

In addition to his recent excellent research work in the area of rheumatology, it should also be mentioned that Professor van Vennrooij 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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<td><strong>FORTHCOMING EVENTS</strong></td>
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<td>24th Annual Meeting of the American Society for Bone and Mineral Research</td>
<td>20–24 Sep 2002; San Antonio, TX, USA</td>
<td>Contact: ASBMR, 2025 M. Street, NW, Suite 800, Washington DC 20036-3309, USA Tel: 1 202 367 1161 Fax: 1 202 857 1880 Email: <a href="mailto:asbmr@dc.sba.com">asbmr@dc.sba.com</a></td>
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<td>Translational Research in Autoimmunity</td>
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<td>OsteoArthritis Research Society International (OARSI) World Congress</td>
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<td>7th EULAR Postgraduate Course in Rheumatology</td>
<td>22–27 September 2002; Budapest, Hungary</td>
<td>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: <a href="http://www.eular.org">www.eular.org</a></td>
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<td>3rd International Conference on Familial Mediterranean Fever and Hereditary Inflammatory Disorders</td>
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<td>10th International Congress on Antiphospholipid Antibodies</td>
<td>29 Sep–3 Oct 2002; Sicily, Italy</td>
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<td>Third International Congress on Spondyloarthropathies</td>
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<td>7th International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation and Related Diseases</td>
<td>14–17 Oct 2002, Nashville, Tennessee, USA</td>
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<td>3rd International Conference on Sex Hormones, Pregnancy, and the Rheumatic Diseases</td>
<td>21–24 Oct 2002; New Orleans, LA, USA</td>
<td>Contact: Anne Parke Tel: 860 679 8190 Fax: 860 679 1287 Email: <a href="mailto:parke@rsu.uchc.edu">parke@rsu.uchc.edu</a></td>
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<td>66th American College of Rheumatology AGM</td>
<td>25–29 Oct 2002; New Orleans, USA</td>
<td>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: <a href="mailto:acr@rheumatology.org">acr@rheumatology.org</a> Website: <a href="http://www.rheumatology.org">www.rheumatology.org</a></td>
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<td>Third International Meeting on Social and Economic Aspects of Osteoporosis and Osteoarthritis</td>
<td>7–9 November, 2002; Barcelona, Spain</td>
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<td>Certifying Examination in Pediatric Rheumatology</td>
<td>18 Nov 2002</td>
<td>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: <a href="http://www.abp.org">www.abp.org</a></td>
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<td>10th APLAR Congress of Rheumatology</td>
<td>1–6 Dec 2002; Bangkok, Thailand</td>
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<td>Future EULAR congresses</td>
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