Letters

A successful renal transplantation in Behçet’s syndrome

Renal involvement is not frequent in Behçet’s syndrome (BS) and consists of occasional reports of patients having glomerulonephritis, IgA nephropathy and renal amyloidosis. We present the successful outcome of a renal transplantation in a patient who had end stage renal failure secondary to glomerulonephritis. To our knowledge, this is the first patient with BS to receive an organ transplantation.

The detailed history of this patient at the time of the diagnosis of glomerulonephritis was the subject of a case report in 1991. In brief, she was 21 years old when she developed recurrent oral and genital ulcers, bilateral uveitis, erythema nodosum, folliculitis, and intermittent arthritis of the knees. Two years later, she was referred to our centre for further evaluation of eye symptoms. She had no active mucocutaneous lesions at that time, the pathergy reaction was positive and she was carriers of HLA B4. It was decided to prescribe only local drops for her mild eye involvement. Three months later she experienced two ocular episodes resulting in a sharp decline of visual acuity and azathioprine 2.5 mg/kg/day was increased. Two weeks later she was admitted to the hospital because of microscopic haematuria. She was ANA negative, the anti-DNA and serum complement levels were normal. Her glomerular filtration rate was 67 ml/min. An open renal biopsy showed diffuse proliferative glomerulonephritis and weak focal segmental positivity of IgA and IgM. She was treated with three boluses of 1 g methylprednisone and was discharged prescribed azathioprine 150 mg/day, aspirin 300 mg/day and prednisone 30 mg/day. She was well except for occasional mucocutaneous symptoms and a mild intermittent ocular episode during the next four years. However her renal function deteriorated progressively despite uninterrupted treatment with azathioprine and changing doses of prednisone and she was put on regular haemodialysis. She returned to us in the 14th month of haemodialysis, she received a kidney from her mother. The graft function started immediately and she was prescribed maintenance immunosuppression with azathioprine, cyclosporin A and methylprednisolone. An acute interstitial type rejection on the 11th day of transplantation was treated successfully with pulse corticosteroids. Now 40 months after transplantation, she has normal renal function and is free of any symptoms of BS except for occasional oral ulcers.

We had some hesitation in performing a renal transplantation in our patient initially because of the lack of any previous experience and particularly because of our concern for the heightened inflammatory response of BS patients to simple penetrating trauma that is best characterised by the pathergy reaction. This reaction, however, is not only limited to the skin and development of aneurysms after vascular punctures and episodes of synovitis after arthrocentesis have been observed. Furthermore, postoperative complications leading to a poor outcome such as occlusions of grafts/anastomoses after the surgical treatment of aneurysms or perivalvular leakage and suture breakdown after aortic valve replacement have been reported in BS patients. As these complications are probably related to the pathergy phenomenon on skin, you would also reasonably expect problems after an organ transplantation, an operation with arterial and venous anastomoses. On the other hand, we had previously shown that despite the increased inflammation, wound healing after full thickness skin punch biopsies is not changed in BS. We have not experienced any of the feared complications after the transplantation procedure in this case. One reason for this favourable outcome might be that our patient was female. It is known that BS runs a milder disease course in women compared with men. Additionally, the rather intensive immunosuppressive/anti-inflammatory post-transplant drug use might also have contributed to the diminished disease activity of our patient as well as to the prevention of a reaction at the site of transplantation. Whatever it might be related to, the outcome in our patient suggests that BS patients can undergo renal transplantation with a satisfactory outcome.

SUHELYA APAYDIN

EKREM KAYALI

UGUR ULKCI

Division of Nephrology, Department of Internal Medicine

VEDAT HAMURYUDAN

HASAN YAZICI

Division of Rheumatology, Department of Internal Medicine

MUZAFFER SARIYAR

Department of Surgery, Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey

Correspondence to: Dr V Hamuryudan, Veseysap sokaq 100, Yil Sitesi, I Blok D16 Uskudar, 81190 Istanbul, Turkey.

various results in di (SD) 22 (9)) than controls (mean (SD) 14 (9.8)).

Bruns IL2R and known as the alpha chain of IL2R.

CD25+ is one of the subunits of high affinity IL2R and CD19+ is a cell surface marker of B lymphocytes.

Presence of autoantibodies and hypergammaglobulinemia support the role of humoral immunity but B lymphocytes were rarely found in the skin biopsy specimens. CD19+ is a cell surface marker of B lymphocytes and we could not observe any difference in the levels of CD19+ B cells. We can say that B lymphocytes might play only a minor part in the pathogenesis of SSc. CD25+ is one of the subunits of high affinity IL2R and known as the alpha chain of IL2R.

Bruns et al. established a clear correlation between CD25+ and soluble IL2R in serum. T lymphocytes expressing CD25+ and T helper cell derived cytokines and growth factors stimulate matrix protein synthesis by fibroblasts, resulting in generalised fibrosis and sclerosis. In our study we did not find significant increases of CD25+ and this surface marker can be used in the follow up the inflammatory stage and activity of SSc. In further studies the investigation of CD25+ T cell subsets CD4+, CD8+, TCR gamma-delta and other T cell activation markers HLA-DR, CD45RO/CD45RA will be useful to shed light on the pathogenesis of SSc. NK cell abnormalities have been described in a number of rheumatic diseases such as RA, Sjögren’s syndrome, systemic lupus erythematosus. NK cells are large granular lymphocytes easily identified morphologically by the presence of azurophil granules in their cytoplasm and they commonly express certain cell surface markers such as CD16+ and CD56+. CD56+ is a homofilar adhesion molecule that belongs to the immunoglobulin superfamily. NK cells are the main cellular effector population in the pathophysiology of SSc. "

**Lymphocyte populations and cytokine concentrations in pericardial fluid from a systemic lupus erythematosus patient with cardiac tamponade**

Pericardial involvement is the most common cardiovascular complication in systemic lupus erythematosus (SLE). The clinical picture varies from subclinical pericardial effusion and classic acute pericarditis to cardiac tamponade. Pericardial fluid (PF) has been limited to autoantibodies, complements and immune complexes. To further study the pathogenic mechanisms involved in lupus pericardial effusion we examined the lymphocyte populations and cytokine concentration pattern in PF and peripheral blood (PB) from a SLE patient with cardiac tamponade.

We report a case of a 38 year old man with SLE diagnosed in December 1995 when he presented with polyarthralgia, photosensitivity, oral ulcers, nephritis, non-hemolytic anemia, positive ANA, increased antibodies to dsDNA and hyocomplementemia. The patient improved with corticosteroid and intravenous cyclophosphamide treatment. However, on 18 July 1997 he presented with syncope, hypotension (80/40 mm Hg), a tachycardia, jugular vein distension and cardiomegaly. The two dimensional echocardiogram showed a large pericardial effusion with right atria and ventricle collapse in diastole. Pericardiocentesis was performed and 180 ml of an orange fluid was aspirated. Examination of PF showed white blood cell count of 5280/mm³ (polymorphonuclear cells = 96%). The absolute number of lymphocytes was lower in PF than in PB (211 x 10⁶/mm³). PF}

**Table 1. Frequency of lymphocyte populations and cytokine concentrations in peripheral blood and pericardial fluid**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peripheral Blood</th>
<th>Pericardial Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocyte population (%)</td>
<td>T-helper cells</td>
<td>CD4+ T cells</td>
</tr>
<tr>
<td>CD4+ T cells</td>
<td>17.6</td>
<td>25.0</td>
</tr>
<tr>
<td>CD8+ T cells</td>
<td>34.3</td>
<td>25.0</td>
</tr>
<tr>
<td>B cells</td>
<td>7.8</td>
<td>8.3</td>
</tr>
<tr>
<td>NK cells</td>
<td>34.3</td>
<td>41.7</td>
</tr>
<tr>
<td>Cytokine concentration (pg/ml)</td>
<td>IL1β</td>
<td>IL6</td>
</tr>
<tr>
<td>IL1β</td>
<td>3.0</td>
<td>2400</td>
</tr>
<tr>
<td>IL6</td>
<td>&gt;4.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>TNFα</td>
<td>3.8</td>
<td>15.4</td>
</tr>
<tr>
<td>IFNγ</td>
<td>1.5</td>
<td>32.8</td>
</tr>
</tbody>
</table>

*Manufacturer (Genzyme, Boston, MA) detection limits: 3 pg/ml for IL1β, INFγ and TNFs; 4 pg/ml for IL2; 6 pg/ml for IL6; 8 pg/ml for IL8; and 5 pg/ml for IL10.

The level of protein was 4.1 g/dl (serum = 5.3 g/dl), glucose was 53 mg/dl (serum = 110 mg/dl) and LDH was 471 IU/l (serum = 110 IU/l). PF cultures were negative. No malignant cells were seen to proliferate with high dose corticosteroids and azathioprine. Pneumonosis was gradually decreased to 10 mg daily over a three month period. After a 22 month follow up, he remained clinically stable without recurring pericardial involvement or SLE exacerbations.

Before starting immunosuppressive treatment, PF and PB were obtained simultaneously for immunological analysis. Mononuclear cells from both samples were evaluated by gradient centrifugation and the frequency of lymphocyte populations was determined by flow cytometry. The cytokine concentrations from plasma and PF were determined by ELISA. Table 1 shows the results. Among lymphocytes, the percentage of CD4+ T cells and NK cells was higher in PF, while the frequency of CD8+ T cells was higher in PB. IL6 concentration was much higher in PF than plasma. Also, IL1β and IL10 concentrations were higher in PF. IL2 was detected in plasma but not in PF.

The considerable increase in pericardial IL1β, with respect to healthy controls was interesting. PF concentrations of IL6 in our patient were substantially higher than those observed in PF from patients with inflammatory and non-inflammatory heart conditions. IL6, not only can increase antibody production, but in SLE, B cells have increased reactivity to this cytokine. As in our case, IL6 is usually expressed or increased in the affected organ or system rather than PB. IL6 has been found to be higher in cerebrospinal fluid and urine than in serum of SLE patients with CNS disease and active nephritis respectively.

The decreased pericardial lymphocyte count and fluid characteristics observed here are in agreement with other studies. The higher frequency of CD4+ T cells and NK cells in PF could be associated with the observed cytokine concentration pattern. For example, CD4+ memory T cells from SLE patients highly secrete IL10 compared with normal controls.

In summary, different patterns of lymphocyte populations and cytokines were found in both sources, with type 2 cytokines predominating in PF and type 1 in PB. Further studies would be required to confirm the results presented here. In addition, immunocytochemical studies of pericardial
tissue are necessary as the composition of lymphocyte and cytokine profiles may differ between pericardial fluid and tissue.

LUIZ M VILÁ
Department of Internal Medicine, Universidad Central del Caribe School of Medicine, Bayamón, Puerto Rico

LUIZ M VILÁ
ZILKA RIOS
ELIZABETH RIVERA
Department of Microbiology and Immunology, Universidad Central del Caribe School of Medicine, Bayamón, Puerto Rico

Correspondence to:
Dr L M Vila, Department of Internal Medicine, Division of Rheumatology, Universidad Central del Caribe School of Medicine, Call Box 60327, Bayamón, Puerto Rico 00960–6032, USA.

系のHLA-B27陽性を伴う前葡萄膜炎（IAU）が観察された。これらの患者では、免疫学的検査の結果、ウイルス性前葡萄膜炎（IAU）群と比較して、CD4+CD45R−（メモリータリンフォサイト）の比率が有意に高く、CD4+CD45R+（ナチュラルキラー細胞）の比率が有意に低かった。

IAU = anterior uveitis, NK = natural killer cells, NS = not significant. Data shown as mean (SEM).

Table 1 Lymphocyte populations in AU patients and controls

<table>
<thead>
<tr>
<th>AU patients (n=146)</th>
<th>Controls (n=31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes (no/μm³)</td>
<td>2425.60 (964.44)</td>
<td>2567.74 (820.72)</td>
</tr>
<tr>
<td>CD3 (no/μm³)</td>
<td>1734.20 (726.67)</td>
<td>1835.64 (586.68)</td>
</tr>
<tr>
<td>CD4 (no/μm³)</td>
<td>1032.91 (419.18)</td>
<td>77.02 (359.67)</td>
</tr>
<tr>
<td>CD8 (no/μm³)</td>
<td>42.56 (9.50)</td>
<td>47.00 (6.13)</td>
</tr>
<tr>
<td>CD4/CD8</td>
<td>29.25 (8.81)</td>
<td>26.72 (6.81)</td>
</tr>
<tr>
<td>CD4/CD28</td>
<td>1.70 (0.89)</td>
<td>1.92 (0.78)</td>
</tr>
<tr>
<td>CD4/CD3</td>
<td>226.87 (227.44)</td>
<td>335.90 (142.35)</td>
</tr>
<tr>
<td>CD4CD45R+ (no/μm³)</td>
<td>10.81 (5.65)</td>
<td>13.64 (5.09)</td>
</tr>
<tr>
<td>CD4CD45R− (no/μm³)</td>
<td>406.17 (304.18)</td>
<td>657.70 (301.36)</td>
</tr>
<tr>
<td>CD4CD45R+ (no/μm³)</td>
<td>16.70 (9.99)</td>
<td>25.20 (7.76)</td>
</tr>
<tr>
<td>CD4CD45R− (no/μm³)</td>
<td>661.53 (338.48)</td>
<td>529.41 (219.04)</td>
</tr>
<tr>
<td>NK (no/mm³)</td>
<td>27.20 (7.84)</td>
<td>20.77 (6.40)</td>
</tr>
<tr>
<td>NK (no/mm³)</td>
<td>300.45 (179.63)</td>
<td>323.80 (182.53)</td>
</tr>
<tr>
<td>CD4CD45R+ (no/μm³)</td>
<td>13.30 (7.76)</td>
<td>12.81 (5.86)</td>
</tr>
</tbody>
</table>

IAU = anterior uveitis, NK = natural killer cells, NS = not significant. Data shown as mean (SEM).

Figure 1 Absolute values of CD4CD45R+ cells. Patients with IAU had absolute values lower than those of SA patients (p<0.001). IAU = idiopathic anterior uveitis; AU = anterior uveitis; SA = spondyloarthropathy.

Figure 2 Percentages of CD4CD45R− cells. Patients with IAU had higher percentages than the healthy subjects and SA patients (p<0.001). Abbreviations as in figure 1.
diseases. The immunological features studied with synovial and cellular, in HLA-B27+ patients without associated SA were similar to those of patients with SA, which suggest a common pathogenetic link between both forms of AU. It is possible that the long term follow up of these patients will clarify whether or not it is the same entity.

We are indebted to Ms E Velasco for assistance in the preparation of the manuscript.

FRANCISCO RIVERA-CIVICO
JUAN JIMÉNEZ-ALONSO
MARIA MARTIN-ARMADA
MARIA TERESA HERRANZ
JOSE CASTRO
FRANCISCO PÉREZ-ALVAREZ
J L DEL ARBOL
Service of Internal Medicine
MANUEL TORIBIO
Service of Ophthalmology
FRANCISCO SAMANIEGO
Service of Clinical Chemistry and Immunology,
"Virgen de las Nieves" University Hospital,
Granada, Spain

Correspondence to: Dr Jiménez-Alonso, Jefe del Servicio de Medicina Interna, Hospital General de Especialidades "Virgen de las Nieves" Avda Fuerzas Armadas 2, 18014 Granada, Spain.

16 Monos et al. FABRIZIO CANTINI
ALEX OLIVE
Rheumatology Section, Hospital Universitari i Politecnico Germans Trias i Pujol, C/ de Canyet s/n, Badalona 08016, Spain

Correspondence to: Dr A Oliveira.

Letters, Matters arising

RS3PE: six years later

We read with interest the paper by Cantini et al and would like to comment on it.1

In 1992 we performed a retrospective multicentre study of 27 RS3PE patients. We concluded that personal history of polygamiya rheumatica (two patients), presence of erosions (one patient) and evolution to haematomyoligic diseases (two patients concomitantly developed a T lymphoproliferative disorder, one myelodysplastic syndrome) suggested that RS3PE syndrome might not be a distinct clinical entity. At that moment 12 patients were asymptomatic and 12 required treatment. This was reported elsewhere.2

Now, six years later, we have reviewed the original cohort of patients with the RS3PE syndrome. A questionnaire was sent to the participating rheumatologists. The survey was focused on articular symptoms, treatment and evolution. The current cohort was composed of 22 patients (16 male; female 6; mean age:77.9; range 64–91). Four patients died (the three with haematomyoligic diseases, one stroke) and one was not located. Thirteen patients were asymptomatic and without treatment, in contrast none required treatment, namely corticosteroids (6), gold salts (1), ciclosporine (1) and NSAID (1). Interestingly, two of the patients were identified by their rheumatologist as having a seronegative rheumatoid arthritis, another patient had a chronic disease with separate corticosteroid responsive episodes of bilateral hand oedema and polygamiya syndromes at different times. Last but not least one patient developed Raynaud’s phenomena, both hands had sclerodactyly. A nailfold capillary microscopy showed a decreased number of capillary loops, which were widened, suggesting systemic sclerosis.

Our results suggest that RS3PE syndrome has a good prognosis, and probably half of the patients are asymptomatic and without treatment six years later. However, there is a subset of patients that have other diseases. Although pure RS3PE syndrome does exist the evolution should be carefully monitored.

MONICA GUMÁ
ENRIQUE CASADO
XAVIER TENA
ALEX OLIVE
Rheumatology Section, Hospital Universitari i Politecnico Germans Trias i Pujol, C/ de Canyet s/n, Badalona 08016, Spain

Correspondence to: Dr A Oliveira.

We thank the following rheumatologists for the contribution to the study: Jordi del Blanco, Miquel Pons, Isabel Rotés, Raïmon Samnani, Eduard Kantarievicz, Miquel Sala, Ivonne Breyssse, Rosa Rosello, Javier Arasa, Marta Larrosa, Genovefa Caffiezas, Josep Pujol, Anna Lafort.


Authors’ reply

We appreciate the comment by Olivé et al on our article on RS3PE. They reviewed 27 previously described RS3PE patients after a follow up of six years. As we suggested in a previous report, they confirm that RS3PE syndrome should be considered a heterogeneous condition associated with different inflammatory rheumatic diseases and also with neoplastic disorders. In our study none of the 23 patients with RS3PE syndrome developed concomitant conditions supporting the diagnosis for another disease. The different study design and selection of patients may in part explain the subset of patients with other diseases and with a worse prognosis observed by Olivé et al.

We designed a prospective follow up study excluding patients satisfying the criteria for the diagnosis of polygamiya rheumatica, rheumatoid arthritis and seronegative spondyloarthropathies. Moreover, patients with a clinical history of cancer were excluded from the study. In their original report these authors performed a retrospective study including all patients with remitting distal extremity swelling with pitting oedema. They recruited also patients not evaluated for spondyloarthropathies, which may be associated with distal extremity swelling with pitting oedema.3

However, in their retrospective evaluation Olivé et al found that 13 of 22 (59%) patients were asymptomatic and drug free over a six year follow up period, confirming that RS3PE not associated with other conditions and with a good prognosis does exist. The problem is how to label this clinical picture. As discussed in our article, the similarities of demographic, clinical and MRI findings between patients with “pure” RS3PE syndrome and those with polygamiya rheumatica and the concurrence of the two syndromes suggest that these conditions may be part of the clinical spectrum of the same disease. In the series of Olivé et al the patient with a clinical course characterised by alternate relapses of HLA-B27 associated oedema or polygamiya symptoms further supports our hypothesis. Even those RS3PE patients successively diagnosed as having seronegative rheumatoid arthritis (elderly onset rheumatoid arthritis) do not conflict with our conclusions. Healey described patients who developed episodes of polygamiya rheumatica and seronegative rheumatoid arthritis at different times during follow up.4 Similar clinical characteristics have been recently described in a population based cohort of patients with giant cell arteritis followed up over a 42 year period. Four of the six patients who fulfilled the criteria for the diagnosis of rheumatoid arthritis during the follow up experienced multiple separate episodes of symmetrical arthritis, proximal symptoms of polygamiya rheumatica and distal extremity swelling with pitting oedema.4

FRABRIZIO CANTINI
2nd Divisione di Medicina, Ospedale di Prato, Italy

CARLO SALVARANI
Servizio di Reumatologia, Azienda Ospedaliera,
Aspiedale S Maria Nuova, Reggio Emilia, Italy

IGNAZIO OLIVIERI
Servizio di Reumatologia, Ospedale S Carlo,
Pozzona, Italy

Downloaded from http://ard.bmj.com/ on June 20, 2017 - Published by group.bmj.com
Crystals in arthritis: new age nonsense or novel therapeutic target?

Apatite crystals are present in up to 70% of fluids from degenerated joints. Their presence correlates strongly with radiographic evidence of cartilage degeneration and is associated with larger joint effusions when compared with joints without crystals. Whether the presence of apatite crystals is a cause of cartilage damage or an effect of cartilage damage is unclear. Several lines of evidence suggest that apatite crystals cause joint destruction. For example, apatite crystals induce both mitogen-activated protein kinases and activator protein 1 (AP-1). They also induce mitogen activated protein kinases (MAPK) and protein kinase C (PKC). Further, such activation is specific as the crystals do not activate protein tyrosine kinases (PTK) or phosphatidylinositol 3-kinases (PI3K). If the crystals were present simply as a consequence of joint destruction, we would expect them to be present in other arthropathies characterised by cartilage dissolution and synovial lining proliferation such as rheumatoid arthritis (RA). However, apatite crystals are rarely found in RA joint fluids. Thus, current data support the potential pathogenicity of apatite crystals.

On the other hand, the clinical significance of apatite crystals in joint degeneration continues to be questioned. Dieppe and Swan doubt that apatite crystals are of pathogenic significance but they fail to refute the idea even to the vast body of literature that supports the biological activity of apatite crystals. To add to the confusion, they place apatite in a list of pathogenic crystals in the same group as the crystal-induced joint diseases but fail to indicate that the importance of balance in the presentation of scientific papers has recently been emphasised.

As noted by Dieppe and Swan, part of the problem is that apatite cannot be readily identified in the same way that monosodium urate (MSU) or calcium pyrophosphate dihydrate (CPPD) can be by polarised light microscopy. Furthermore, the presence of apatite crystals does not change the management of either osteoarthritis (OA) or any other arthropathy in patients at present. However, Swan concludes therefore that apatite crystals are irrelevant to clinical practice. Historically, the role of cytokines in the pathogenesis of OA was also considered to be speculative. As with apatite crystals, levels of IL-1 and TNFα are interlinked 1 (IL1) or tumour necrosis factor α (TNFα) are not routinely measured in joint fluid from patients with arthritis. After considerable further investigation, however, the roles of IL1 and TNFα in joint destruction in OA are now considered important. As a consequence of such a research effort, Pelletier and coworkers have prevented the development of OA in an experimental model by transfer of the IL1 receptor antagonist gene. We have shown that apatite crystals induce MMP-1 in human OA (HOA) fibroblasts with a potency equivalent to that of IL1 and TNFα in vitro. Furthermore, apatite crystals IL1 and TNFα act in synergy to increase MMP-1 production by HOA fibroblasts. Efforts continue to discover methods to inhibit the pathogenic effects of IL1 and TNFα. Why not inhibit the effects of apatite crystals also?

Currently, there is no drug available to retard the progression of OA. A greater understanding of the pathogenesis of OA is essential to the development of rational treatment and we must allow apatite to target important pathogenic mediators. While it might be tempting to write apatite crystals off as new age nonsense, a considerable body of evidence suggests that they could serve as a new therapeutic target as well as a prognostic marker. Without further study, only those with crystal balls can tell.

Author’s reply

We agree with all the points made by Dr McCarthy. Basic calcium phosphates (BCPs) in synovial fluids may be important, and it may be that their identification will be validated in relation to future treatments. However, she seems to agree with the only two points made about BCPs in our article (which is about the identification of urate and pyrophosphate crystals): that is, that on the basis of their current understanding, the identification of BCPs is “doubtful significance”, and that their identification should have no influence on contemporary therapeutic decisions.

Mortality in rheumatoid arthritis patients

The paper “Mortality in rheumatoid arthritis patients with disease onset in the 1980s” is of considerable interest. A decrease in mortality risk for rheumatoid arthritis (RA) patients in more recent years would be important, e.g. only in the first 10 years of RA. However, this inception cohort differs from those previously published so that no direct comparison is possible. As earlier (and older and larger) studies have shown standardised mortality ratios of two to three, a finding of “normal” mortality might imply that more recently used treatment strategies are reversing the excessive mortality in RA previously observed.

Yet, even at first perusal, there are a lot of deaths in this series of relatively young people. In the 10 years after a mean age of 51, 18 patients (10%) had died. Over 20 deaths were said to be expected. However, using US mortality rates for a population mean aged the same, projected over 10 years, two thirds women, and white, one would expect only 11 deaths using 1996 mortality rates and 12 deaths using 1985 rates, over the 1710 patients years of follow up. While we did not have the age distribution of this RA cohort to calculate precise expectations, these figures should be conservative. Female mortality rates in the US white female popula-
tion, at 3.4 per 1000 per year at age 51 and 9.0 per 1000 per year at age 61 are presumably higher than those in long lived Malmöhus County, Sweden.

Of interest, in our own larger study with meticulously computed “expected” values in four different populations we also had an “expected” death rate of about 10% to 15% over 10 years. But, these were not inception cohorts and their age at start of follow up was 60.4, 62.6, 59.8, and 69.1 years. Thus, they were much older cohorts. Given the expected doubling of mortality rates each eight years (Gompertz’s law), expected deaths should have been two to three times more in our cohorts than in a cohort beginning at age 51.

Finally, recent studies have not suggested that “rheumatoid” deaths in themselves are the cause of the increased mortality in RA. The observed “excess” deaths are spread around in multiple disease categories, with accelerated atherosclerosis numerically the largest problem and only a slight relative increase in systemic RA complications, gastrointestinal haemorrhage, and infections.

JAMES F FRIES
Stanford University, School of Medicine, Palo Alto, California, USA

ELISABET LINDQVIST
Department of Rheumatology, Lund University Hospital, Sweden

Table 1

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of patients</th>
<th>Expected mortality</th>
<th>Observed mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–19</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20–24</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25–29</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30–34</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>35–39</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>40–44</td>
<td>20</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>45–49</td>
<td>27</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>50–54</td>
<td>34</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>55–59</td>
<td>24</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>60–64</td>
<td>19</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>65–69</td>
<td>16</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>70–74</td>
<td>11</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>75–79</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>All</td>
<td>183</td>
<td>20</td>
<td>18</td>
</tr>
</tbody>
</table>


Authors’ reply

We were pleased to notice the interest in our paper shown by Drs Fries and Bloch. In reply to their comments we do not consider the death rate of 10% in the cohort as an excessive one compared with the age and sex matched general population. It is not possible to calculate more precise figures of expected deaths knowing the mean age of the cohort only. To clarify this and make comparison possible we enclose a table of the age distribution in our cohort in five year intervals giving the number of observed and expected deaths for each age interval separately.

Women do live longer in Malmöhus County, Sweden than in the US. Female mortality rates in Malmöhus County were 3.76 per 1000 at age 51 and 3.92 per 1000 at age 61 in 1985. In 1996 the corresponding figures were 2.03 per 1000 at age 51 and 3.39 per 1000 at age 61.

We agree that the main cause of death in RA patients very seldom is the rheumatoid disease in itself. This was true also for our study where no certain connection between RA and death was found in any of the cases.

ELISABET LINDQVIST
KERSTIN EBERHARDT
Department of Rheumatology, Lund University Hospital, Sweden
HLA-B27+ anterior uveitis with or without associated spondyloarthritis: clinical and immunological features

FRANCISCO RIVERA-CÍVICO, JUAN JIMÉNEZ-ALONSO, MARÍA MARTÍN-ARMADA, MARÍA TERESA HERRANZ, JOSÉ CASTRO, FRANCISCO PEREZ-ALVAREZ, J L DEL ARBOL, MANUEL TORIBIO
and FRANCISCO SAMANIEGO

Ann Rheum Dis 1999 58: 721-722
doi: 10.1136/ard.58.11.721

Updated information and services can be found at:
http://ard.bmj.com/content/58/11/721

These include:

References
This article cites 15 articles, 3 of which you can access for free at:
http://ard.bmj.com/content/58/11/721#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/