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 suffering from glomerulonephritis, IgA nephropathy and renal amyloidosis.1,2 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 1991.3 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 her BS was classified as IBD LA. 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 added. 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 methylprednisolone and was discharged prescribed azathioprine 150 mg/day, aspirin 300 mg/day and prednison 30 mg/day. She was well except for frequent ocular episodes and a mild folliculitis on the scalp. Two years after transplantation, she was 21 years old when she presented with mild exacerbation of her back pain and intermittent arthritis of the knees.

We had some hesitation in performing a renal transplantation on 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.4 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.5 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 replacement6 have been reported in BS patients. As these complications are probably related to the pathergy phenomenon reaction, 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.7 We have not experienced any of the feared complications after the transplantation procedure in this instance. 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.8 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 the anastomosis. Whatever might be related to the outcome in our patient suggests that BS patients can undergo renal transplantation with a satisfactory outcome.

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References

Lymphocyte phenotypes in systemic sclerosis

Although the pathophysiology of systemic sclerosis (SSc) is not fully clarified, there are considerable data implicating abnormalities of microvascular changes, fibroblast activation and immune system abnormalities. Immune system activation may play a role as a stimulus in both fibrotic and vascular damage.9 To investigate the immune system abnormalities in the pathogenesis of SSc we evaluated lymphocyte phenotypes in patients with SSc and end stage renal failure (serum creatinine (Epics Profile II) for total T (CD3), T helper (CD4), T suppressor (CD8), B lymphocyte cell surface marker (CD19), activator (CD25) and natural killer cell surface marker NK-H-1 (CD56).

We studied 29 patients (27 women, two men) 16 limited, 12 diffuse and one overlap who fulfilled preliminary criteria for classification of SSc.10 Anti-nuclear antibody was positive in 25 (86.2%) and anti-Scl70 antibodies was positive in seven (24.1%) patients. The age range of the patients was 20–63 years (mean (SEM) 40 (5)) and the mean (SEM) disease duration was 5.6 (5.5) years. Patients were receiving no medication nor had received any immunosuppressive agent for at least three months. Controls were 12 aged and sex matched healthy volunteers with an age range from 27–51 years.

Data were compared for significance Student’s unpaired t test.

Table 1 summarises lymphocyte phenotypes in patients with SSc and healthy controls.

We found a higher expression of T cell activation marker CD25+ and NK cell main surface marker CD56+. In lymphocyte phenotype there was not any difference among disease subsets and CD25+ and CD56+ were not correlated with the disease duration.

Immune system abnormalities have been suspected in the development of SSc because of the presence of autoantibodies, changed cytokine production and evidence of overlap with other autoimmune diseases. It was suggested that immune system changes play the major part in the development of vasculopathy and fibrosis. Previous reports on T lymphocyte subpopulations in SSc are partially conflicting. Melendro et al demonstrated that there was no significant difference in the levels of CD25+ and CD56+ in 22 SSc patients and control group but in rheumatoid arthritis (RA) CD3+ and CD8+, in Sjögren’s syndrome CD3+, CD4+ and CD8+ levels were significantly decreased compared with those of controls and they suggested that the abnormalities in immune regulatory T cell circuits leading to autoimmunity are different in each connective tissue disease.

Table 1 Lymphocyte phenotypes in patients with SSc and healthy controls

<table>
<thead>
<tr>
<th>Serum</th>
<th>Systemic sclerosis (n=29)</th>
<th>Control (n=12)</th>
<th>t test</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3(%)</td>
<td>71 (9) 69 (9) 0.660 ≥0.05</td>
<td>CD4(%)</td>
<td>44 (9) 45 (9) 0.110 ≥0.05</td>
<td>CD5(%)</td>
</tr>
</tbody>
</table>

*Unpaired Student’s t test. Data shown as mean (SD).
various results in di... and known as the alpha chain of IL2R. CD25+ is one of the subunits of high affinity...B lymphocytes might play only a...can say that B lymphocytes and we could not observe any...CD19+ is a cell surface marker of B...lymphocytes expressing CD25+ and T...between CD25+ and soluble IL2R in serum.

Presence of autoantibodies and hypergammaglobulinemia support the role of humoral immunity but B lymphocytes were rarely found in the skin biopsy specimens.\textsuperscript{6} CD19+ is a cell surface marker of B lymphocytes and we could not observe any difference in the levels of CD19+ and CD25+.

CD25+ is one of the subunits of high affinity IL2R and known as the alpha chain of IL2R. CD25+ is one of the subunits of high affinity IL2R and known as the alpha chain of IL2R.

Bruns et al.\textsuperscript{7} 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 dermatological diseases such as LA, 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 homophilic adhesion molecule that belongs to the immunoglobulin superfamily. NK cells are the main cellular effectors of the late NK-dependent cell cytotoxicity, they mediate antigen presentation and secrete immune modulator cytokines like interferon, IL2, colony stimulating factor, these functions suggested the involvement of NK cells in the pathophysiology of SSc.\textsuperscript{8,9}

We found the percentage of CD56+ significantly higher in SSC patients (mean [SD] 22 (9)) than controls (mean [SD] 14 (5)). Although this finding suggested the role of CD56+ cells in the pathogenesis of SSC, various results in different investigations pointed out that further investigations on CD56+ and CD16+ NK cell percentage and activity are needed.

**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).\textsuperscript{1} The clinical picture varies from subclinical pericardial effusion and classic acute pericarditis to cardiac tamponade. In recent studies of pericardial fluid (PF) have been limited to determination of autoantibodies, complements and immune complexes.\textsuperscript{2} To further study the pathogenic mechanisms involved in lupus pericarditis, we measured the lymphocytic 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 polymyalgia, photophobia, oral ulcers, nephritis, non-hemolytic anemia, positive ANA, increased anti-dsDNA and hypocomplementemia. The patient improved with corticosteroid and intravenous cyclophosphamide treatment. However, on 18 June 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. Pericardioeffusion was performed and 180 ml of an orange fluid was aspirated. Examination of PF showed white blood cell count of 5280/mm\textsuperscript{3} (polymorphonuclear cells = 96%). The absolute number of lymphocytes was lower in PF than in PB (211 x 1000/mm\textsuperscript{3}). PF contained white blood cells (polymorphonuclear cells = 96%). The absolute number of lymphocytes was lower in PF than in PB (211 x 1000/mm\textsuperscript{3}). PF contained white blood cells.

**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></td>
<td></td>
</tr>
<tr>
<td>CD4+ T cells</td>
<td>57.8</td>
<td>50.0</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></td>
<td></td>
</tr>
<tr>
<td>IL1B</td>
<td>3.0</td>
<td>24.00</td>
</tr>
<tr>
<td>IL2</td>
<td>6 pg/ml</td>
<td>&lt;4.0</td>
</tr>
<tr>
<td>IL4</td>
<td>&lt;6.0</td>
<td>&lt;6.0</td>
</tr>
<tr>
<td>IL6</td>
<td>16.9</td>
<td>4714.0</td>
</tr>
<tr>
<td>IL10</td>
<td>&lt;5.0</td>
<td>139.8</td>
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<tr>
<td>TNF*F</td>
<td>3.8</td>
<td>15.4</td>
</tr>
<tr>
<td>INF*F</td>
<td>1.5</td>
<td>32.8</td>
</tr>
</tbody>
</table>

*Manufacturer (Genzyme, Boston, MA) detection limits: 3 pg/ml for IL1B, INF*F and TNF*F; 4 pg/ml for IL2; 6 pg/ml for IL6; 8 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 malignancies were seen to progress to rapidly high dose corticosteroids and azathioprine. Prednisone was gradually decreased to 10 mg daily over a three month period. After a 22 month follow up, he remained clinically stable without recurrence of pericardial involvement or SLE exacerbations.

Before starting immunosuppressive treatment, PF and PB were obtained simultaneously for immunological analysis. Mononuclear cells from both sources were isolated by gradient centrifugation and the frequency of lymphocyte populations was determined by flow cytometry. The cytokine concentrations in 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, IL1B and IL10 concentrations were higher in PF. IL2 was detected in plasma but not in PF.

The considerable increase in pericardial IL6, with respect to plasma, was very interesting. PF concentrations of IL6 in our case were substantially higher than those observed in PF from patients with inflammatory and non-inflammatory heart conditions.\textsuperscript{1} The IL6 concentration was much higher in PF than plasma. Also, IL1B and IL10 concentrations were higher in PF. IL2 was detected in plasma but not in PF.

The increased pericardial lymphocyte count and fluid characteristics observed here are in agreement with other studies.\textsuperscript{9} 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 have been shown to secrete IL10 compared with normal controls.\textsuperscript{10}

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.


### Table 1 Lymphocyte populations in AU patients and controls

<table>
<thead>
<tr>
<th></th>
<th>AU patients (n=146)</th>
<th>Controls (n=31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes (no/mm³)</td>
<td>2425.60 (964.44)</td>
<td>2567.74 (820.72)</td>
<td>NS</td>
</tr>
<tr>
<td>CD3 (no/mm³)</td>
<td>1734.20 (726.67)</td>
<td>1835.64 (586.68)</td>
<td>NS</td>
</tr>
<tr>
<td>CD4 (no/mm³)</td>
<td>1032.91 (489.16)</td>
<td>1072.97 (47.56)</td>
<td>NS</td>
</tr>
<tr>
<td>CD8 (no/mm³)</td>
<td>702.21 (359.67)</td>
<td>675.90 (243.54)</td>
<td>NS</td>
</tr>
<tr>
<td>CD24/CD8</td>
<td>29.25 (8.81)</td>
<td>26.72 (6.81)</td>
<td>NS</td>
</tr>
<tr>
<td>CD4/CD8</td>
<td>1.70 (0.89)</td>
<td>1.92 (0.78)</td>
<td>NS</td>
</tr>
<tr>
<td>CD19 (no/mm³)</td>
<td>266.87 (227.44)</td>
<td>335.90 (142.35)</td>
<td>NS</td>
</tr>
<tr>
<td>CD4CD45R+ (no/mm³)</td>
<td>10.81 (5.65)</td>
<td>13.64 (5.99)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CD4CD45R− (no/mm³)</td>
<td>406.17 (304.18)</td>
<td>657.70 (301.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4CD45R+ (%)</td>
<td>16.70 (9.99)</td>
<td>25.20 (7.76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4CD45R− (%)</td>
<td>661.53 (338.48)</td>
<td>529.41 (219.04)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NK (no/mm³)</td>
<td>300.45 (179.63)</td>
<td>323.80 (182.53)</td>
<td>NS</td>
</tr>
<tr>
<td>NK (%)</td>
<td>13.30 (7.76)</td>
<td>12.81 (5.86)</td>
<td>NS</td>
</tr>
</tbody>
</table>

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

### Figure 1 Absolute values of CD4CD45R+ cells.

![Figure 1](http://www.example.com/figure1.png)

### Figure 2 Percentages of CD4CD45R− cells.

![Figure 2](http://www.example.com/figure2.png)
diseases. The immunological features studied were systemic 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 is the same entity.

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

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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 polymyalgia rheumatica (two patients), presence of erosions (one patient) and evolution to haematological diseases (two patients concomitantly developed a T lymphoblastic syndrome and 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 focused on articular symptoms, treatment and evolution. The current cohort was composed of 22 patients (male 16; female 6; mean age:77.9; range 64–91). Four patients died (the three with haematological diseases, one stroke) and one was not located. Thirteen patients were asymptomatic and without treatment, in contrast nine required treatment, namely corticosteroids (6), gold salts (1), colchicine (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 polymyalgic syndromes at different times. Last but not 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, unlike 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.

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Correspondence to: Dr A Olivé.

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 heterogenous condition associated with different inflammatory rheumatic diseases and also with neoplastic disorders.

In our study none of the 23 patients with RS3PE syndrome developed erosions 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 a worse prognosis observed by Olivé et al.

We designed a prospective follow up study excluding patients satisfying the criteria for the diagnosis of polymyalgia rheumatica, rheumatoid arthritis and seronegative spondylarthropathies. Moreover, patients with a clinical history of cancer were excluded from the study. In their original report1 these authors performed a retrospective study including all patients with remitting distal extremity swelling with pitting oedema. They recruited also patients not evaluated for spondylarthropathies, 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,3 the similarities of demographic, clinical and MRI findings between patients with “pure” RS3PE syndrome and those with polymyalgia 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 alternatively relapses of RS3PE syndrome with pitting oedema or polymyalgic 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 polymyalgia 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 arthritides, proximal symptoms of polymyalgia rheumatica and distal extremity swelling with pitting oedema.5

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Crysalids in arthritis: new age nonsense or novel therapeutic target?

Apatite crystals are present in up to 70% of fluid 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.1 Whether the presence of crystals is a cause of cartilage damage or an effect of cartilage damage is unclear.2 Several lines of evidence suggest that apatite crystals cause joint destruction. For example, apatite crystals induce both mitogenic and pro-inflammatory synthesis in synovial fibroblasts and chondrocytes in vitro.3 They also induce matrix metalloproteinase (MMP) synthesis and secretion, thus promoting tissue destruction.4 The cellular mechanisms whereby apatite crystals induce such responses are currently under investigation. Like many other growth promoting agents, apatite crystals induce a variety of transcription factors such as nuclear factor-κB (NF-κB) and activator protein 1 (AP-1).5 They also induce mitogen activated protein kinases (MAPK) and protein kinase C (PKC).6,7 Furthermore, such activation is specific as the crystals do not activate protein tyrosine kinases (PTK) or phosphatidylsino-3-kines (PI3K).8 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.9 Thus, current data support the potential of apatite crystals in stimulating joint destruction.

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 view even when the vast body of literature that supports the biological activity of apatite crystals.10 To add to the confusion, they place crystals in a list of pathogenic crystals in the same sentence as the assertion that their identification will be of little benefit to current understanding.11 The paper “Mortality in rheumatoid arthritis patients” by McCarthy and colleagues also raises concerns about the identification of apatite crystals.12

We agree with all the points made by Dr McCarthy. Basic calcium phosphate crystals (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 current understanding they are of “doubtful significance”, and that their identification should have no influence on contemporary therapeutic decisions.

Author’s reply

We agree with all the points made by Dr McCarthy. Basic calcium phosphate crystals (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 current understanding they are of “doubtful significance”, and that their identification should have no influence on contemporary therapeutic decisions.

Paul Dieppe
MRC Health Services Research Collaboration, University of Bristol, Bristol

Mortality in rheumatoid arthritis patients

The paper “Mortality in rheumatoid arthritis patients with disease onset in the 1980s” is of considerable interest.1 A decrease in mortality risk for rheumatoid arthritis (RA) patients in more recent years would be important, not 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.
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.

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Daniel A Bloch
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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 7.32 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.

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KERSTIN EBERHARDT
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>
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<tbody>
<tr>
<td>15–19</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>20–24</td>
<td>3</td>
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<tr>
<td>55–59</td>
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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 PÉREZ-ALVAREZ, J L DEL ARBOL, MANUEL TORIBIO and FRANCISCO SAMANIEGO

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