With regard to the comment by Mongey and Hess about treating the patient with prednisolone, it is recommended that patients with severe constitutional symptoms are given a course of steroids. These should be continued until the symptoms have subsided when they can be tailed off [3]. This is the treatment our patient received. She is now off treatment and symptom free apart from her pre-existing arthritis with normal serology at 12-month follow-up.

E. WALKER

'Bethany', Derby Road, Mansfield, Notts NG18 5BJ

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Arthritis in Pigs Induced by Dietary Factors

SIR—Peltonen *et al.* [1] have not been able to repeat our experiments with diet-induced arthritis in pigs [2]. They found certainly significant changes of the faecal *Clostridium perfringens* counts but only minimal synovial signs of inflammation in the experimental animals. However, the difference in results may be caused by differences in both materials and methods.

We think that the age of the pigs is the most important parameter. In our experiments three control pigs received the fish meal diet at an age of 4 months and although the change of the faecal flora was obvious their joint changes were much less pronounced. The histological picture was characterized mainly by enlargement of the synovial lining cells and oedematous congestion of the synovial tissue. We reported a first series of fish meal diet experiments in 1967 [3], not mentioned by Peltonen *et al.*, in which the joint changes were milder in character than the exudative reactions found in the second series [2]. The long period before the development of the clostridial flora in the trial of Peltonen *et al.* [60 days, i.e. at age 4 months] might explain that the synovial reaction was insignificant in their studies. The absence of visceral parakeratosis in their study is also remarkable.

Peltonen *et al.* used Danish fish powder made from North Sea fish in contrast to our trials where we used fish powder of Norwegian origin. There are fundamental differences between fish meals from different sea regions. As reported in ref. [4] there were no increased counts of *Cl. perfringens* nor any signs of arthritis or parakeratosis in pigs fed Peruvian sardine meal.

Peltonen *et al.* suggest that the severe joint lesions in our experiments might be explained by a special arthritogenic strain. We think that this is improbable as the experimental diet induces a change in the normal indigenous intestinal flora: an exogenic infection is unlikely.

I MÅNSSON*, R. NORBERG†, B. OLHAGEN‡

**Biomedical Centre P.O. Box 583, S-751 23 Uppsala and †Swedish Institute for Infectious Disease Control, S-10521 Stockholm, ‡Department of Rheumatology, Karolinska Institute S-171 76 Stockholm, Sweden*

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Correspondence to B. Olhagen.

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This letter was shown to Professor Toivanen and colleagues who reply:

SIR—We thank Professor Månsson and colleagues for their response and agree that, in spite of our best efforts to follow their protocol, certain differences in the materials and methods were inevitable. We have contemplated and discussed the same factors as they have seeking a possible explanation for the discrepancy in results. More than 20 years have passed since the original study, and our report is the first published attempt to reproduce their results. We would also endorse the need for successful studies that apply chromatographic analysis to the intestinal flora which has influenced our own research [1–3].

R. PELTONEN, E. EEROLA, P. TOIVANEN

Department of Clinical Microbiology, Turku University, Turku, Finland

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Even Garlic

SIR—Most rheumatologists will be familiar with the problems that are caused when patients take preparations which interfere with prescribed therapy. In an editorial on 12 March in the *BMJ* 'Towards the safer use of traditional remedies' [1] D. J. Atherton emphasized the need for greater awareness of toxicity associated with traditional remedies particularly when used with conventional drugs.

A timely reminder of this occurred in a female patient age 61 yr. She is an insulin-dependent diabetic who has had RA for 41 yr. She suffered side-effects or failed to gain benefit from gold, D-penicillamine, sulphasalazine and azathioprine and was therefore very pleased to find that low dose methotrexate 5mg per week helped her.

When seen in February routine blood tests showed elevation of alanine amino-transferase (glutamate pyruvate transaminase) [ALT (GPT)] to 115 U/l (normal range 0–41 U/l) and it seemed that methotrexate would have to be stopped. Alkaline phosphatase and α glutamyl transferase were not elevated. Questioning revealed that she had been taking garlic (*Allium sativum*). It had been recommended to her by an old gentleman; she diced a small clove into five or six pieces and ate it on a piece of toast each evening.

It was explained that there might be risks in delaying stopping methotrexate, but it was suggested that first the garlic alone should be stopped and weekly blood tests were organized. There was a steady fall in ALT (GPT) to normal levels over the next 4 weeks (98,53,46,36 U/l).

Studies indicate that garlic oil (diallyl-sulphide) can have a dose-dependent effect on the hepatic drug-metabolizing enzyme system [2]. Garlic oil seems to have some protective effect against the elevation of liver GPT with cyclophosphamide in high doses [3].

It was not thought sensible to attempt to rechallenge our patient with garlic. However, the implication is that, despite its popularity, even garlic may be suspect.

B. J. SWEETMAN
Rheumatology Department, Morriston Hospital, Swansea SA6 6NL

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Hypercomplementaemia as a Marker of the Evolution from Benign to Malignant B Cell Proliferation in Patients with Type II Mixed Cryoglobulinaemia

SIR—Type II mixed cryoglobulinaemia (MC) is an immune complex (IC) disease classically defined by the presence of arthralgia, purpura, and weakness, and serum mixed cryoglobulins consisting of polyclonal IgG and monoclonal IgM RF. In this disorder production of large amounts of IC usually leads to an extensive complement consumption and to the consequent finding of serum hypocomplementaemia [1]. Although type II MC is commonly regarded as a benign lymphoproliferative disease [2, 3], in some cases it can switch to a frank malignant lymphoproliferative disorder such as non-Hodgkin's lymphoma, Waldenstrom's macroglobulinaemia or chronic lymphocytic leukaemia [2–5].

We report here three cases of type II MC in which the development of a small lymphocytic lymphoma of low malignancy was accompanied by the appearance of hypercomplementaemia. The main clinical and serological features of the patients are summarized in the Table I.

Patient 1 was a 36-yr-old-woman who had been complaining of weakness, arthralgia and orthostatic purpura for 2 yr. She also showed liver and spleen enlargement, and pleural and peritoneal sero-haematic effusions. The main laboratory abnormalities at the onset of the symptoms were raised ESR (100 mm/h) and γ-globulins (2.7 g/dl with a monoclonal IgMk component), positive CRP (1 mg/dl, normal values <0.5 mg/dl), presence of type II cryoglobulins, hypocomplementaemia (C3 44 mg/ml, C4 1 mg/ml and CH50 98 hu/ml) and antibodies to hepatitis B virus. In March 1986 she underwent a splenectomy, together with the surgical removal of some enlarged lymph nodes located at the vascular pole of the spleen. A liver biopsy was performed during the surgical procedure. Histologic and immunohistochemical examination of the spleen, lymph node and liver tissues showed the presence of diffuse polyclonal lymphoplasmocytic cell infiltration. The patient was maintained under treatment with corticosteroids (20 mg of 6-methyl-prednisolone daily) over the following months, and she was relatively well until September 1986, when she was again hospitalized because of severe weakness, arthralgia, abdominal pain, and the appearance of sicca complaints. Laboratory investigations disclosed marked hyper-γ-globulinaemia (4.1 g/dl), with significantly increased levels of IgM (5544 mg/dl, normal value 80–280 mg/dl) and serum hyperviscosity. It was therefore decided to treat the patient with weekly plasma exchange associated with corticosteroid and cyclophosphamide. During this therapeutic regimen an increase in serum complement levels was observed (Table I). The patient was followed-up at the outpatient clinic until April 1987, when she was again hospitalized because of severe abdominal pain and fever. Laboratory investigations confirmed the presence of raised complement levels. A new liver biopsy disclosed the presence of a low grade lymphoplasmocytic B cell lymphoma [6]. Afterwards, the patient was referred to the haematologic department of a different hospital to be treated with a standard chemotherapeutic schedule.

Patient 2 was a 70-yr-old woman who had been complaining of orthostatic purpura, arthralgia and weakness for 2 yr. Previous laboratory findings had demonstrated the presence of antibodies against hepatitis B and C viruses, as well as type II cryoglobulins and frankly reduced levels of CH50. The patient was treated with corticosteroids (30 mg/day of deflazacort) for several months. In September 1992 physical examination disclosed enlargement of the lymph nodes, liver and spleen. Laboratory findings revealed a raised ESR (99 mm/h), and increased levels of CRP (14.2 mg/dl), serum RF (564 U/l), C3, C4 (see Table I) and IgM (938 mg/dl). A serum monoclonal IgMk paraprotein was detected by immunoelectrophoresis. Haematoxylin-eosin stained sections from a latero-cervical lymph node biopsy disclosed the presence of a low grade lymphocytic and plasmocytoid malignant lymphoma [6], which was confirmed by bone biopsy from the iliac crest. Since in the following weeks the clinical picture consistently worsened (weight loss, fever, and further lymph node and spleen enlargement), it was decided to treat the patient with a more aggressive therapeutic schedule (P/VABEC, 7). The patient died 2 months later due to severe non-responsive opportunistic infections and consequent septicaemia.

Patient 3 was a 64-yr-old woman who had been complaining of dry mouth, dry eyes and purpuric lesions on

TABLE I
Main clinical and serological findings for the patients

Case no.	Age (yr)	Sex	LAP	SM	Sicca syndrome	Purpura	Cryotype	Cryo-composition	HBV-Ab	HCV-Ab	C3* (mg/dl)	C4* (mg/dl)	CH50* (hu/ml)
1	36	F	Yes	Yes	Yes†	Yes	II	IgG, Mk	Yes	N.D.	185	262	N.D.
2	70	F	Yes	Yes	No	Yes	II	IgG, Mk	Yes	Yes	168	163	N.D.
3	64	F	Yes	Yes	Yes‡	Yes	II	IgG, A, Mk	No	Yes	140	218	225

LAP, Lymphoadenopathy; SM, splenomegaly; HBV-Ab, antibodies to hepatitis B virus; HCV-Ab, antibodies to hepatis C virus (detected using commercial immunoenzymatic assays from Ortho Diagnostic Systems Inc., Raritan, NJ); N.D., not done.

*Normal values: C3, 55–120 mg/dl; C4, 20–50 mg/dl; CH50, 160–220 hu/ml.

†The diagnosis of associated Sjögren's syndrome was confirmed by the presence of reduced salivary flow and ductal ectasias on sialograms, in the absence of anti-SSA(Ro) and -SSB(La) antibodies.

‡The diagnosis of associated Sjögren's syndrome was confirmed by the presence of inflammatory infiltrates in minor salivary gland biopsy, in the absence of anti-SSA(Ro) and -SSB(La) antibodies.