MATTERS ARISING

Small intestinal bacterial overgrowth in patients with rheumatoid arthritis

I read with interest the paper by Henriksson *et al.*¹ in which the authors demonstrated an altered character in the small bowel's bacterial flora in patients with rheumatoid arthritis. However, the authors did not demonstrate the presence of bacterial overgrowth. The syndrome of bacterial overgrowth is characterised by diarrhoea with malabsorption. The mechanism by which the bacterial overgrowth causes symptoms is not known. These symptoms are related to an increase in the luminal bacterial flora and the presence of obligate anaerobes (colonic luminal flora) as judged by jejunal fluid culture or breath tests. The patients in the study did not have any evidence of malabsorption or diarrhoea.

The investigations used, apart from the bile acid deconjugation test, had not been previously validated in patients with bacterial overgrowth. Quantitative bacterial culture was not done; the bacterial flora was of oral type, not colonic. The presence of enterobacteriaceae (a facultative anaerobe), tryptic activity, gas production (both not specific to obligate anaerobes) and the use of jejunal biopsy culture (biopsies culture produces different flora than fluid culture) are not proven features of bacterial overgrowth of the small bowel. The controls used did not have the syndrome of bacterial overgrowth as they were clinically well (achlorhydria, whilst associated with an altered and increased bacterial flora, does not necessarily cause symptomatic bacterial overgrowth). Thus only the three patients with positive bile acid deconjugation tests could be considered to have investigational evidence of bacterial overgrowth. In view of previously reported changes seen in the small bowel's bacterial flora of elderly and infirm people,² perhaps the findings were not surprising considering the multi-system involvement of rheumatoid arthritis. To confirm their hypothesis that disease activity is due to and not causing the bacterial flora changes, the authors could have studied the influence of either proton pump inhibitors or antibiotics on disease activity.

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1 Henriksson A E K, Blomquist L, Nord C-E, Midtvedt T, Uribe A. Small intestinal bacterial overgrowth in patients with rheumatoid arthritis. *Ann Rheum Dis* 1993; 52: 503-10.

2 Haboubi N Y, Montgomery R D. Small bowel bacterial overgrowth in elderly people: Clinical significance and response to treatment. *Age and Ageing* 1992; 21: 13-9.

AUTHORS' REPLY: We appreciate the remarks made by Dr S J Lewis about the small bowel microflora in patients with rheumatoid arthritis (RA) and would like to give the following comments.

We feel that the two concepts *bacterial overgrowth* and *bacterial overgrowth syndrome* are sometimes confused. We used the concept *bacterial overgrowth* to designate an altered microflora in the upper small intestine in patients with RA, and the criteria were clearly stated in the article. The *bacterial overgrowth syndrome*, also known as blind loop or stagnant loop syndrome, is characterised by steatorrhea and other signs of malabsorption. We agree that our patients with RA did not have the bacterial overgrowth syndrome.

Dr Lewis, however, seems to presume that only an altered small intestinal microflora complicated by the bacterial overgrowth syndrome is of interest in patients with RA. This view has to be questioned as we still do not know what types or quantities of microbes demonstrated in the upper small intestine are of interest in these patients.

The aim of our study was not to describe a bacterial overgrowth syndrome in patients with RA, but rather to denote an altered small intestinal microflora. A combination of techniques was preferred to get a comprehensive picture of small intestinal microflora, as it has been shown that different tests may be necessary to detect bacterial overgrowth in the upper small intestine.¹ It has been suggested that a qualitative change may be more important than a quantitative change;^{2,3} hence we used the growth of Enterobacteriaceae (*Escherichia coli* or *Klebsiella*) without counting the microorganisms as one of the criteria of bacterial overgrowth. These species originate from the colonic and not from the oral microflora.

The clinical significance of our findings is still uncertain. The RA patients with signs of bacterial overgrowth had significantly higher rheumatic disease activity as well as rheumatoid factor titre. Dr Lewis's suggestion that the changes in the small bowel bacterial flora may be secondary to multi-system involvement of RA certainly cannot be excluded. As for his contention that treatment with proton pump inhibitors or antibiotics would confirm our hypothesis, it should be noted that the small intestinal bacterial overgrowth in these patients was not only related to lack of gastric acid and that we know very little about the types of microorganisms involved; severe flare ups after treatment with antibiotics have been observed in patients with RA,⁴ possibly by changing the intestinal microflora in the 'wrong' direction.

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1 Suhr O, Danielsson Å, Hörstedt P, Stenling R. Bacterial contamination of the small bowel evaluated by breath tests, ⁷⁵Se-labelled homocholic-tauro acid, and scanning electron microscopy. *Scand J Gastroenterol* 1990; 25: 841-52.

2 Björneklett A, Fausa O, Midtvedt T. Bacterial overgrowth in jejunal and ileal disease. *Scand J Gastroenterol* 1983; 18: 289-98.

3 Skar V, Skar A G, Osnes M. The duodenal bacterial flora in the region of papilla Vater in patients with and without duodenal diverticula. *Scand J Gastroenterol* 1989; 24: 649-56.

4 Henriksson Å E K. Unpublished observations.

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Relapsing polychondritis as a secondary phenomenon of primary systemic vasculitis

Papo *et al* recently reported¹ that in 33 patients with relapsing polychondritis (RP) low titres of (c/p)ANCA occurred in 24% of the cases. They concluded that low titres of cANCA therefore are not specific for Wegener's granulomatosis (WG). We do not think that this line of reasoning is correct. We and others have earlier reported that cANCA is a highly specific and sensitive marker for WG.^{2,3} Thus we conclude that the presence of ANCA in RP, may instead indicate, that polychondritis occurs in the course of a primary systemic vasculitis (PSV), for example, WG.

We have seen such an association of PSV with polychondritis in six of seven patients with RP (three women, four men).⁴ The diagnosis of RP was either made histologically or according to the diagnostic criteria established by McAdam *et al.*⁵ In six patients, RP presented as a secondary phenomenon during an acute phase of a primary vasculitic entity. Autoantibody screening revealed cANCA (PR3 ANCA +) in two patients, pANCA in one patient and autoantibodies to native collagen type II in four. According to the Chapel-Hill-Definitions 1993⁶ and the ACR-Classification-Criteria for PSV 1990,⁷ the underlying PSV in these six patients was: histologically proven WG (PR3 ANCA +) in two cases, microscopic polyangiitis in three cases (one pANCA +), classic polyarteritis nodosa in one case (table).

We think that polychondritis can be diagnosed more often as a secondary phenomenon in PSV than has previously been recognised. The diagnosis of PSV has been considerably improved by the detection of ANCA and the establishment of ACR-Classification-Criteria and Chapel-Hill-Definitions for PSV. Subsequently, PSV with secondary polychondritis seems to be recognised more often. Although there are only very few case reports on the association of RP with recognised, classified PSV,^{8,9} the coincidence of RP with unclassified vasculitic symptoms is said to be about 10%.¹⁰ The occurrence of glomerulonephritis in RP seems to be even more frequent (29 of 112 patients).¹¹ These vasculitic symptoms may be attributed to an underlying PSV, that has not previously been recognised as such. We conclude that the occurrence of ANCA in RP should encourage thorough investigation for the presence of PSV, in which the polychondritis may be a secondary phenomenon. This is important, as the vasculitis determines the therapy and prognosis of the disease.

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