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 steatorrhoea 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 diarrhoea with malabsorption is of significance. These symptoms are related to an increase in the luminal flora and the presence of obligate anaerobes (colonising 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 conjugation 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), tryptophic 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 colonised with gastric flora (anaerobic, bile associated with an altered and increased bacterial flora, does not necessarily cause symptomatic bacterial overgrowth). Thus only the three patients with positive bile acid determination should 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,4 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.

Relapsing poly chondritis as a secondary phenomenon of primary systemic vasculitis

Papo et al recently reported1 that in 33 patients with relapsing poly chondritis (RP) they found a significantly higher titre of rheumatoid factor (RF) compared with controls. We agree that our patients with RP did not have the bacterial overgrowth syndrome.

The aim of our study was 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 However, 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 rheumatoid factor titres, just 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, possibly by changing the intestinal microflora in the ‘wrong’ direction.


4 Henriksson A E K. Unpublished observations.

Correspondence to: Dr Henriksson.

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Table  
Vasculitic organ involvement and immunological features in patients with primary or secondary RP  

<table>
<thead>
<tr>
<th>Patient</th>
<th>Organ involvement</th>
<th>ANCA</th>
<th>pANCA</th>
<th>Coll</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>RP</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>B, [K], N, E, H, S</td>
<td>+</td>
<td></td>
<td>RP</td>
</tr>
<tr>
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<td></td>
<td>B, E, H</td>
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</tr>
<tr>
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<td>+</td>
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</tr>
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<td>B, N, [K]</td>
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<td>+</td>
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</tr>
<tr>
<td>6</td>
<td></td>
<td>B, N, H</td>
<td></td>
<td>+</td>
<td>RP</td>
</tr>
</tbody>
</table>

Extended ELK-Classification (Nölle et al. 1989):  

- B = constitutional symptoms, E = ENT, E = eye, G = gastrointestinal, M = mPA = microscopic polyangiitis, pANCA = classic panarteritis nodosa, RP = relapsing polychondritis  


Authors' reply: In their series of seven patients with relapsing polychondritis (RP), Handrock and Gross could detect ANCA in six patients, two with Wegener’s granulomatosis (WG), three with microscopic polyangiitis and one with classical polyarteritis nodosa. They conclude that the presence of ANCA in RP indicates that polychondritis occurs as a secondary event of a primary systemic vasculitis.

Our experience is very different. Among our eight biopsy positive RP patients, 5 had vasculitis. Among these three, WG could be diagnosed in only one with low titres (1/20) pANCA. The two others, one with C-ANCA and one with P-ANCA, had minor cutaneous and no visceral involvement. Among our 25 ANCA-negative patients, nine had vasculitis (cutaneous in seven, quiescent WG in one, mononeuritis multiplex in one). These data indicate that ANCA may be detected in RP without defined systemic vasculitis, including microscopic polyangiitis. In the Mayo Clinic experience, eight of 22 patients with RP had ANCA with perinuclear or nuclear pattern. Such discrepancies might result from recruitment bias and/or differences in the size of the studied groups, but also from the major problem of diagnostic procedures which requires further study.

Obviously, vascular involvement is frequent in RP and can affect vessels of any size, from aorta to capillaries. Its frequency has been said to be as high as 56% in McAdam’s series. In RP, microscopic angitis has proved to represent the anatomical basis responsible for dermatological and renal manifestations, and is supposed to cause neuropathies, auditory, vestibular disturbances and episceritis.  

RP is frequently associated with various inflammatory or autoimmune disorders, ranging from ulcerative colitis and rheumatoid arthritis, two ANCA-associated diseases, to thyroiditis, spondylarthropathies and primary systemical vasculitides, including Behcet’s syndrome. Some of these diseases are clearly distinct from RP but associated with, others share, many manifestations with RP which results in obscure nosological considerations and difficult differential diagnosis. The main problem is trying to distinguish RP from WG, since both diseases frequently have striking similarities, mainly saddle nose deformity and laryngotracheal involvement (although resulting from different processes), arthritis, episceritis and skin vasculitis. Necrotising glomerulonephritis, auricular chondritis, nasal septal perforation and proptosis, which are more suggestive of WG, also occur in a small percentage of patients with RP. Unfortunately, typical ANCA are not available in reports for those patients with atypical manifestations of RP. Last but not least, auricular chondritis, which is supposed to be the hallmark of RP, has been described in a few patients with WG. Facing this critical problem, physicians can get help from histological data and from some more specific clinical manifestations such as lung cavitory infiltrates or peculiar dermatological involvement for WG, and conversely for RP diffuse tracheobronchial dynamic collapse, ascending aorta aneurysm or dysmyelopoietic syndrome in the absence of previous immunosuppressive treatment. These features may diagnose some intriguing patients as probably having auricular chondritis in the course of an otherwise unremarkable WG. In the absence of clearly discriminating data, an overlap between RP and WG is the only conclusion, as described in a case we recently reported. Such puzzling problems, however, are restricted to less than 5% of cases in our experience of 100 RP and 75 WG. Extending the question to the whole spectrum of systemic vasculitides encountered in RP increases the ratio of patients concerned to 11 of 112 in Michet’s series, which remains far less frequent than suggested by Handrock and Gross.  

Nevertheless, we agree with these authors that chondritis can probably occur as an epiphenomenon in RP not specific for definite inflammatory disorders. This is true not only for primary systemic vasculitides, but also for systemic lupus erythematosus, possibly for other rheumatic diseases, and even for leprosy (Kerl et al. 1989). Under these circumstances, cartilage involvement frequently differs from the typical features of RP, regarding the usual sparing of the respiratory tree and the lack of a relapsing/relenting course of the disease. On the basis of clinical and pathological data on auricular chondritis is rare.  

A clear-cut categorisation of patients with vasculitic manifestations and chondritis seems impossible. Definitions of RP, WG, other arthritis and episceritis, can remain purely descriptive of clinical symptoms and pathological data that sometimes overlap, in the absence of a comprehensive view of their pathophysiology and aetiology. Recent studies on ANCA have provided new and promising insights into the processes involved, but their application to diagnosis is mainly restricted to the close association of WG with ANCA positivity. However, more recent studies on ANCA have provided new and promising insights into the processes involved, but their application to diagnosis is mainly restricted to the close association of WG with ANCA positivity.
Relapsing polychondritis as a secondary phenomenon of primary systemic vasculitis.

K Handrock and W L Gross

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