


Increased intestinal permeability in ankylosing spondylitis

SIR,—We read with great interest the excellent paper by Morris et al (Gut 1991; 32: 1470–2) on intestinal permeability in ankylosing spondylitis but we do not agree, however, with their conclusions.

Using the "Cr-EDTA resorption test" we recently studied gut permeability in inflammatory rheumatic disorders. Intake of non-steroidal anti-inflammatory drugs (NSAIDs) significantly increases gut permeability irrespective of the underlying disease. Patients with ankylosing spondylitis and with other spondylarthopathies not taking NSAIDs also presented a significant increase of gut permeability compared with controls. This indicates that the increased permeability is disease rather than drug related.

Gut permeability was not significantly increased in patients with histological gut lesions on ileocolonoscopy, or in patients with a normal ileum, although patients with a local ankylosing spondylitis and chronic gut lesions (resembling Crohn's disease) showed a significant increase in gut permeability compared with patients with ankylosing spondylitis and acute gut lesions.

There are several explanations for the absence of a relationship between increased gut permeability and ileocolonoscopic evidence of gut inflammation. On ileocolonoscopy only the terminal aspect of the ileum is seen, which is only a very small part of the small bowel, can be examined. Moreover, the distribution of the observed lesions was patchy. Intake of NSAIDs causes such major disturbances of gut permeability that the local inflammation of the ileum would not influence the results of the Cr-EDTA resorption test.

Inflammatory gut lesions were not found in patients with rheumatoid arthritis taking high doses of NSAIDs for prolonged periods, while such lesions were present in more than 50 patients with spondylarthropathies who had not taken anti-inflammatory drugs. This suggests that the ileal lesion in the ileocolonic region is associated with the spondylarthropathies, while intake of NSAIDs probably induces more extensive and diffuse functional disturbances of the entire small bowel.

H MIELANTS
MEYERS
M DE VOS
C CUEVIER
Departments of Rheumatology, Gastroenterology, and Pathology, Ghent University Hospital, Belgium


Crohn's disease after ileocolic resection

SIR,—Olaison, Smedh and Sjödahl (Gut 1992; 33: 331–5) have provided endoscopic evidence that in many cases of Crohn's disease the newly ulcerated lesion occurs soon after surgical resection. Of 30 examined patients, 28 showed higher activity following resection. In the same group, the authors consider the evidence of the disease to be vincingly convincing that there is no lesion present before the operation.

That evidence concerns the increased peristalsis and the increased rate of intestinal transit, which may be related to a period of rehabilitation after surgery. It is therefore possible that the new activity may also be related to a period of rehabilitation after surgery. It is therefore possible that the new activity may also be related to the" Cr-EDTA" results, which may not show a real increase in intestinal permeability.

Replay

SIR,—We do not feel that the evidence presented by Mielants et al in this letter convincingly shows that there is a primary pathology of the terminal ileum in patients with spondylarthopathies. Although patients with spondylarthropathies not taking non-steroidal anti-inflammatory drugs (NSAIDs) did have significantly increased permeability compared with the controls, this was, by the authors' own admission, a very small group in whom no details of gut histology are given. Chronic lesions, resembling subclinical Crohn's disease, as described by the authors, may have been present and thus affected the results by increasing intestinal permeability in some of these patients.

The argument that local or patchy inflammation of the ileum may not affect results of a "Cr-EDTA" absorption does not seem valid when previous studies have shown that "Cr-EDTA" excretion increases towards the end of a sputum to six hours collection consent with increased absorption more distally in the intestinal tract. In the case of the ileum would be expected to have a relatively greater effect on "Cr-EDTA" results and the lack of a correlation between ileocolonoscopic findings and permeability (by Mielants et al) requires further explanation.

The fact that no inflammation was observed in rheumatoid arthritis patients at ileocolonoscopy should be considered in the context of more proximal inflammation and ulceration observed by our group using small bowel enteroscopy. It may be that NSAID treatment is affecting different areas of the gut preferentially in ankylosing spondylitis and rheumatoid arthritis, thus explaining the increased permeability in rheumatoid arthritis patients on NSAIDs without ileocolonoscopic evidence of inflammation observed by Mielants and colleagues. Overall we feel that the evidence for NSAID small bowel damage is more compelling than for a primary abnormality in spondylarthropathy.

A J MORRIS
R J DUNCAN
R I RUSSELL
Gastroenterology Unit, Royal Infirmary, Glasgow G31 2ER


Letters.

The pathogenesis of Crohn’s disease can come from, whose before 1955 treated most patients over many years. Physicians at that time lacking effective drugs had little to offer.

J W PAULLEY
Chicksworth Park Hospital,
Ipswich IP1 3YN


Osteomalacia after gastrectomy

SIR,—I congratulate Bisballe et al (Gut 1991; 32: 1303–7) for their postgastrectomy patients for metabolic bone disease. All too often, we, as physicians caring for patients with gastrointestinal problems that lead to abnormal bone nutrition and metabolism — that is, postgastrectomy osteomalacia, small bowel malabsorption, and states of diminished oral intake, ignore the patients’ developing bone disease because the process is insidious and the patients are often asymptomatic until the disease is so profound that much of it may be irreversible.

I must take issue, however, with the authors’ conclusion advocating supplemental vitamin D for patients. The authors have found evidence of bone abnormalities by histomorphometry in up to 62% of 51 patients, but only eight patients were considered to have osteomalacia. It is not clear that vitamin D supplementation is beneficial in non-osteomalacia bone disease.

The authors suggest that the low mean levels of 25-hydroxyvitamin D are relevant and thus warrant supplementation. Yet, five of eight patients with histomorphometric bone abnormalities had normal levels, highlighting the lack of value serum measurements may have in predicting bone disorder diagnoses. The authors do not state how many of these osteomalacia patients had levels that were abnormal (they state only that the mean overall was abnormal).

That 1,25-dihydroxyvitamin D levels, the active circulating vitamin D metabolite, were normal in these patients, underscores how complex vitamin D metabolism is and how serum values may not be predictive of an abnormality.

Although the authors agree in their final paragraph that serum biochemical results are of limited value, they use these results as the premise for a therapeutic intervention. They showed that patients who took vitamin D supplementation had higher levels of serum 25-hydroxyvitamin D. It is not sufficient to recommend vitamin D therapy simply because patients have metabolic bone disease. Vitamin D supplements in excess doses can be toxic and may not normalize bone.

There is no indication that those patients on supplements had less bony abnormalities on histomorphometry. In fact, half of the patients with osteomalacia were using supplementation.

To determine whether vitamin D is of therapeutic benefit, a study is needed whereby vitamin D therapy is compared with placebo in a randomised blinded group of postgastrectomy patients and not where the use of vitamin D in a group of patients is compared with a non-diseased control group. Oral ingestion of dietary vitamin D needs to be controlled.

Investigators of such a study would need to show that bone histomorphometry improved or did not worsen over time while on therapy.

Vogelsang et al showed that overall, a group of Crohn’s disease patients randomised to vitamin D 1000 IU/day therapy did not have a statistically significant improvement in bone mineral density. Their dosage and compliance of vitamin D 400 IU/day with calcium supplement maintained bone mineral density in a group of corticosteroid using rheumatology patients, higher doses of more potent 1,25-dihydroxyvitamin D were of no benefit and led to raised serum and urine calcium concentrations.

Although low dose vitamin D therapy (400–600 IU/day) in postgastrectomy patients is likely nontoxic — that is, in terms of effects on calcium, this remains to be proved in a systematic fashion. The benefit of this therapy in postgastrectomy patients certainly needs to be proved and has not been in Bisballe et al’s paper.

G N BERNSTEIN
Division of Gastroenterology,
UCLA Department of Medicine,
Los Angeles, California, USA


Reply

SIR,—We thank Dr Bernstein for his constructive comments on our paper on osteomalacia in postgastrectomy patients and his emphasis on the importance of the problem. We also consider bone disease after gastrectomy a problem very often ignored in daily clinical practice.

The diagnosis of osteomalacia in our study was based on very stringent histological criteria, which delineate severe mineralisation defects affecting virtually all bony surface. The remaining patients with abnormal bone histology revealed varying degrees of secondary hyperparathyroidism with focal areas of mineralisation defects — that is, earlier stages in the osteomalacic process. Further analysis of serum biochemistry in these patients was hampered by the lack of good parathyroid hormone assays (the study was performed before the advent of assays for intact parathyroid hormone (1–84)). Theoretically, such patients would also benefit from vitamin D supplementation, because the high turnover state associated with secondary hyperparathyroidism leads to osteopenia. We do not feel that the study on Crohn’s disease by Vogelsang et al is of great relevance in this respect. The bone in patients with Crohn’s disease is characterised by osteopenia and every discrete osteomalacia is demonstrable.

We do not advocate the use of more potent analogues (1-alpha-vitamin D₃ or 1,25(OH)₂D₃) for postgastrectomy patients. We agree with Dr Bernstein that these compounds demand close monitoring because of the risk for severe intoxication. We have, however, administered daily doses of 18 000 IU calciferol (D₂) over a five year period to more than 200 osteoporotic women (mean age 65 years) without any cases of vitamin D intoxication. Thus, we do not think that vitamin D supplements are dangerous as long as they are given in the form of D₃, analogues in a dose range of 400–800 IU. We agree, however, that a controlled clinical study is necessary in order to test for optimal dose, efficacy and side effects.

E F ERIKSEN
S BISBALLE
Department of Endocrinology,
Gastrointestinal Surgery and Pathology,
Aarhus Amnoghus, Denmark