Correspondence

Intestinal permeability

Sir,—Judging from recent review articles on the subject of intestinal permeability, it seems to have become the fashion to ignore completely the original contributions made by Dr Axon and successive coworkers in Leeds. I was, therefore, not too surprised to see the recent article by Ramage and colleagues (Gut 1988; 29: 57–61) which covered very similar ground (albeit with different probe molecules) to a study on intestinal permeability changes in an experimental rat model reported some time ago.1 After all, it is always important to see confirmatory studies and there were some interesting new aspects in the recent paper. I was surprised, however, to see that Ramage and colleagues (and presumably the referees of their paper) did not think it necessary to acknowledge the existence of such a closely related study, which was one of the first to describe the use of the Nippostrongylus infected rat as an experimental model for studying passive intestinal permeability, perhaps it appeared in too obscure a journal?

In their discussion, they hint that future experiments on animal models might yield further information on the relationship between structural damage and intestinal permeability. Perhaps if they were to scan other obscure journals,2,3 they might find some help.

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References


Activity of phospholipase A2

Sir,—We read with interest the paper by Otamiri et al (Gut 1987; 28: 1445–53) concerning the activity of phospholipase A2. The authors suggest that the increase in enzyme activity may be the result of a cellular influx of calcium ions or that the ischaemia may have inactivated an endogenous phospholipase A2 inhibitor.

It has been shown in a rat model1 that platelet activation results in a profound increase in phospholipase A2 activity. Our work on experimental acute pancreatitis in the rat confirms this finding.2 The authors make no reference to the administration of anticoagulants in their experimental protocol; we therefore suggest that platelet activation may have made a significant contribution to the measured phospholipase activity.

The differences between plasma and serum phospholipase A2 activity in the rat are not seen in man. This model therefore may be of limited relevance to the clinical problems associated with intestinal ischaemia.

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Lymphokine activated killer cell activity in patients with GI cancer

Sir,—Several fundamental aspects of tumour immunology are important to the interpretation of the valuable article by J R T Monson et al (Gut 1987; 28: 1420–5) on lymphokine activated killer (LAK) cell activity in patients with gastrointestinal carcinoma.

The study confined itself to peripheral blood (PB) lymphocytes, the relevance of which has been brought into serious doubt by the work of Vose and Moore1 and Holmes,2 indicating that PB lymphocyte activity and type bear little similarity to the immune-tumour relationship and micro-environment in vivo. It is also important to bear in mind that cytotoxic effector lymphocytes in tissues would appear to be different in number and type to those in peripheral blood.

Of the many theories thought to underlie down regulation of the immune system in carcinoma patients, that of longterm specific cellular immunosuppression, relating to cancer cell minor histocompatibility antigen expression has been shown to be the case in vitro.3 This, in association with the idiotype network concept of immune function4 may be an explanation for the inability of most patients
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with disseminated carcinoma to respond to the LAK process, and indicates the requirement for techniques to increase lymphocyte cellular renewal in such patients.

Lymphokine activated killer source cannot simply be explained on the basis of cell type, but surely represents a functional disruption of a down regulated networks when performed outside the body. This results in large numbers of effector lymphocytes derived from those cell types, both T-cell and NK cell, in which anti-tumour activity can be augmented.

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References


Reply

SIR,—We were pleased to receive Mr O'Byrne's interesting reflections on our paper (Gut 1987; 28: 1420–5). Mr O'Byrne's points are well taken. We do indeed recognise the differences which may exist between the antitumour cytotoxic responses present in peripheral blood, and those which may be elicited from tumour infiltrating lymphocytes. Our point in studying peripheral blood was that certainly at present, and for the foreseeable future, lymphokine activated killer cells for therapeutic purposes would continue to be generated from peripheral blood until techniques for the reliable expansion of tumour infiltrating lymphocytes have been perfected. Our viewpoint was therefore a practical one rather than a theoretical one.

In order to invoke the idiotype/anti-idiotype network as a cause of suppression of a cytotoxic cellular immune response, however, specificity of that response has to be assumed. Unfortunately for Mr O'Byrne's argument, the very characteristic which separates LAK cells and NK cells from T-cell mediated cytotoxic responses is their very lack of specificity. Thus LAK cells from cancer patients and from normal controls are capable of killing tumour cells of a very wide variety of origins, indeed under certain circumstances, even normal cells.

There is much evidence to suggest that the tumour mediated immunosuppression present in cancer patients has a far more simple explanation. We have found tumour cells to actively suppress the generation of LAK cells in vitro (Guillou, Ramsden, and Sedman – in preparation). Because there is ample evidence that tumour cells secrete autocrine growth factors, which themselves regulate such events as natural killer cell activity, it may well be that these are a more likely candidate for mediating the suppression than idiotype/anti-idiotype mechanisms.

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An epidemic of pseudomembranous colitis or simply a nosocomial case clustering

SIR,—In their paper (Gut 1987; 28: 1467–73) Dr Nolan and colleagues report on the occurrence of an 'epidemic of pseudomembranous colitis' (PMC) in three hospitals involving 23 patients in 10 months. Evidence in support of an epidemic caused by nosocomial transmission of Clostridium difficile should, however, rely on distinctive antimicrobial resistance patterns, in addition to agarose- or polyacrylamide gel electrophoresis, crossed immunoelectrophoresis and/or phage-typing.1 4 The retrospective nature of the above study, in which cross infection was supported only in 16 patients by a positive culture and in no case by use of bacterial typing techniques, makes the assumption of an 'importance of person to person spread' purely speculative. Furthermore, there is hardly convincing evidence that all 23 patients included actually developed PMC because endoscopic and histological proof of PMC were missing in five other patients. Also we are aware of negative cultivations of Clostridium difficile from patients with PMC and cytotoxin production, but in this study only a single patient was assayed for the cytotoxin. Although Clostridium difficile is the most abundant bacteria in this condition also Staphylococcus aureus and Clostridium perfringens have been reported to be responsible for PMC, but were not even looked for. A final open question concerning this paper relates to the 20 patients without clinical symptoms, in whom Clostridium difficile was identified. Why were these patients not regarded as nosocomially infected? In our ward we have had a clustering of antibiotic associated diarrhoea and PMC in six patients in two months, similarly suggestive of a nosocomial spread.