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 immuno-electrophoresis 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.
Nevertheless, further bacteriological characterisation, including antimicrobial resistance patterns and fermentative reactions in sugars, permitted a clear distinction between six different Clostridium difficile species. We would recommend, therefore, that case clustering of PMC, suggestive of nosocomial cross infection, is evaluated prospectively using bacteriological typing methods.

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References


Reply

SIR,—Dr Tvede and colleagues expand on several of the points made in the discussion in our paper and pose questions regarding the prospective evaluation of case clusters of pseudomembranous colitis (PMC). The cases we described, however, were not studied prospectively because for several reasons their epidemic nature was not initially apparent. The cases occurred in three separate hospitals in patients under the care of many clinicians, the epidemic was of a protracted rather than explosive kind and when clustering was first recognised attention focused not on the possibility of cross infection but on the prominence of exposure to the third generation cephalosporin, cefotaxime, an association previously little reported. It was only after epidemiologic investigation that the compelling evidence of person to person spread, which is documented in our paper, became clearly evident. As we stated, however, this could not be conclusively proved microbiologically. A typical view of the pathogenesis of PMC is that almost any of the ubiquitous toxin producing strains of Clostridium difficile may (because of alteration of flora or other factors) gain a competitive advantage after therapy with certain antibiotics. The ensuing damage to the colonic mucosa by toxin is manifested as PMC. This pattern may have occurred in the six cases described by Tvede et al. The relative frequency of isolated cases of PMC compared with cases caused by person to person spread of a particular strain is currently obscure but obviously has important prophylactic and therapeutic implications. The previous description of epidemics of PMC and in particular the latent and protracted nature of the epidemic we describe suggests to us that person to person spread may be more common than previously realised. We feel that wider recognition of the possibility of cross infection together with the use of prospective studies of the type advocated by Tvede et al are necessary to define the relative roles of cross infection and isolated cases in the epidemiology of PMC.

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Olsalazine and GI transit in UC

SIR,—I was most impressed with the report of Rao et al who noted an accelerated gastric emptying, mouth to caecum transit time and whole gut transit time caused by olsalazine sodium in ulcerative colitis. Although no change in bowel habits was seen among their patients, they attempted to study the diarrhea reported to occur with olsalazine therapy in some earlier uncontrolled reports. I would like to emphasise, however, that diarrhea has not yet been proved to be a definite or common problem with this therapy. In my controlled study of olsalazine sodium, diarrhea was no more common among patients with ulcerative colitis treated with the active drug than those receiving placebo. Similarly, in another controlled trial, four patients receiving placebo and only two receiving active drug were withdrawn because of diarrhea. In one other controlled trial, however, one patient did have increased diarrhea thought to be caused by olsalazine sodium.

More rigorous study design may at least partially account for the lower incidence of unwanted effects
An epidemic of pseudomembranous colitis or simply a nosocomial case clustering.
M Tvede, F Trautner and J Rask-Madsen

*Gut* 1988 29: 694-695
doi: 10.1136/gut.29.5.694-a

Updated information and services can be found at:
http://gut.bmj.com/content/29/5/694.2.citation

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