LETTERS TO THE EDITOR

Cancer risk in patients treated surgically for duodenal ulcer

EDITOR,—Macintyre and O’Brien (Gut 1994; 35: 451–4), although discussing our paper1 in some detail, seem to have misunderstood it.

They claim that Caygill et al reported an “increased risk of cancers of the colon, rectum, biliary tract and female breast”, in contrast with their own results in duodenal ulcer patients. In fact, firstly we did not separate colon and rectum but, like them we reported a decreased risk (relative risk 0.8) in duodenal ulcer patients of colorectal cancer (see our Table I).

We did report an excess risk of biliary tract cancer in duodenal ulcer patients but it was not significant. The excess risk of female breast cancer that we reported was seen only after a 20 year latency. Elsewhere in the paper they claim that we reported carcinomas with oesophageal cancer, again in contrast with their own results. But like them we found no significant excess of oesophageal cancer in duodenal ulcer patients (see our Table I).

We did report significant excess risks at these sites in gastric ulcer patients or in our whole cohort of peptic ulcer patients.

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Intestinal permeability in patients with Crohn’s disease

EDITOR,—We read with great interest the article by Munkholm et al (Gut 1994; 35: 68–72). While this is very interesting work we feel that several important facts must be pointed out.

An important conclusion reached by the authors is that these data do not support the hypothesis that asymptomatic first degree relatives of patients with Crohn’s disease have increased intestinal permeability. Furthermore, they state that as a large number of participants were included in their study, it had minimal risk of a type 2 error. We would like to point out that in another study, similar in design to this one, we have examined a considerably sized group and by combining data from two separate studies we have in fact studied almost twice as many relatives of patients with Crohn’s disease as reported here.1 Most importantly, our interpretation of the data differs dramatically from that presented in this paper. We described in our paper a fundamental flaw in the analysis of this type of data that has potentially contributed to much of the confusion in published works concerning these issues. We are disappointed not to see the same flaw repeated in this work.

Not all relatives of patients with Crohn’s disease ultimately develop the disease. In fact it has been estimated that only 10% of this group will develop disease during their lifetime.2 Therefore, even if increased intestinal permeability is a prerequisite for disease and, furthermore, is manifested lifelong only 10% of the relative group would be expected to show increased intestinal permeability. In the study by Munkholm et al only 39 relatives of patients with Crohn’s disease were studied, therefore, given these assumptions only four subjects should have increased permeability. It is almost impossible to imagine how 15% of the small fraction would conceivably have so significantly changed the mean of the entire group. We discuss this more fully in our paper. The point that must be made is that this type of data analysis cannot disprove the hypothesis that relatives of patients with Crohn’s disease have increased intestinal permeability.

The most effective means to analyse the data obtained in this study is to construct a normal range of permeabilities and to ask whether a subgroup of relatives exists with increased permeability and disregard group statistics. These points were clearly made in our paper and we are disappointed that they have been ignored. From our perspective, unless the study by Munkholm et al deals with these issues it is merely a repetition of numerous previous studies that have completely missed the point. With only 10% of relatives having abnormal permeability the approach used in this paper will be unlikely to even show a statistical difference between control and relative groups. Thus, we believe that conclusions reached by the authors are unwar- ranted as the statistical analysis fails to consider the question that the authors intended to ask.

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Reply

EDITOR,—We only became aware of the publication of May et al 1 when our article was in press.

Although the analytical methods for determination of urine concentrations used by May et al seem to be identical to those of our study, the results obviously differ in that we did not find any difference in permeability among Crohn’s disease patients, healthy or inflammatory bowel disease (IBD) diseased relatives, ulcerative colitis patients, and controls.

The proposed method for statistical evaluation is in our opinion not acceptable because non-parametric statistics should be applied in data not normally distributed. Furthermore the correct comparison between the IBD group and patients data seem to be a direct test.

Defining absolute normal limits for permeability based on data from 31 controls does not seem reasonable, which is further illustrated by the “borderline” values considered abnormal by May et al.

The calculations of the Canadian group on the probability of relatives of Crohn’s disease patients developing the disease are based on all first degree relatives. In our study we examined only relatives from 18 families with known familial IBD occurrence where the expected inheritance will be higher. Furthermore the individual value of expressed relatives were not different from controls.

We thus conclude that even with the most positive and optimistic view of our permeability data we cannot see anything that points to the very interesting hypothesis tested by the study of Hollandar et al in 1984.3

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1 May GR, Sutherland LR, Meddings JB. Is small intestinal permeability really increased in relatives of patients with Crohn’s disease? Gastroenterology 1993; 104: 1627–32.
