Serum and tissue autoantibodies to colonic epithelium in ulcerative colitis

Sir,—I read with interest and disappointment the above article by Snook et al which appeared recently. The authors confirmed previous reports from us and others regarding the presence of cytotoxic serum antibodies in a proportion of patients with inflammatory bowel disease, especially those with active disease, except that their percentage of positivity was much lower (20%) than all the other published reports (which were about 50% or more) and most frequent in ulcerative colitis.

One reason for this could be the use of different target cells — for example in this study the authors used HT-29 colon cancer cells compared with other studies (including ours) where RPMI-4788 colon cancer cells or normal colon epithelial cells were used as targets. Indeed this is important because one of the target molecules on the colon cells recognised by ulcerative colitis serum antibody in cytotoxicity assay is associated with the Mr 40 kDa protein which acts as an autoantigen in ulcerative colitis. Monoclonal and polyclonal anti-Mr 40 kDa antibodies block the cytotoxicity of ulcerative colitis sera on RPMI-4788 and DLD-1 colon cancer cells, while the role of Mr 40 kDa protein in this recognition. While normal colon epithelial cells, RPMI-4788, and DLD-1 colon cancer cells express Mr 40 kDa protein, several colon cancer cell lines, including HT-29, which was used by Snook et al, did not express detectable amounts of the Mr 40 kDa protein.

Therefore, the use of normal colon cells or selection of appropriate colon cancer target cells is very important for the cytotoxicity study. On the basis of the cytotoxicity data using a single cell line — that is HT-29 — it is indeed misleading for Snook et al to conclude that ‘lack of association with disease, extent and activity . . . lack of cytotoxic activity also strongly suggest this antibody is merely an epiphenomenon.

Using ‘ulcerative colitis (UC)-colon extracted IgG (CCA-IgG)’ these authors reported completely negative results in their ‘functional studies’ such as ‘cytotoxic assay’ using HT-29 target cells and ‘immunohistochemical staining’ of colon tissue. These results are in contrast to a number of our independent reports and the results of many other investigations.

There are several major problems with the study of Snook et al. Firstly, the authors did not provide any evidence of intact immuno-globulin or immunoreactive Fab regions being present in these ulcerative colitis colon extracted materials (‘CCA-IgG’s). The presence of IgG reactivity was reported only with ELISA. Fragmented IgG and Fc fragments will react in the ELISA as performed by them, but will not be reactive in the assays they have used. Indeed, some of the ‘CCA-IgG’ preparations prepared by these authors were examined by us for Ig analysis and immunoreactivity to tissue antigen(s). None of the samples had detectable intact IgG when we analysed them several times by SDS-poly-acrylamide gel electrophoresis. This was communicated to the authors well before the publication of the article.

Secondly, as mentioned above, HT-29 cells do not seem to be the right target cells for the cytotoxicity study as they do not express any detectable amount of Mr 40 kDa protein.

Therefore, the negative functional studies’ can easily be explained by the fact that the ‘CCA-IgG’ extracted by the authors are most likely fragmented by proteases, which are plentiful in colon particularly in ulcerative colitis. Such fragmentation of common IgG extraction procedure is performed at room temperature.

A striking increase of local IgG production in ulcerative colitis, with reactivity to colonic antigen, has been reported by many investigators, besides our several independent studies. The immunoreactive colon antigen, Mr 40 kDa protein has been analysed by us using two sensitive techniques, by immunoradiobinding analysis and by immunocytochemistry using monoclonal antibody. Recently, Trond Halstensen et alii beautifully demonstrated by two colour immunofluorescence technique the presence of colon epithelial cell-(IgG subtype) and also epithelial deposition of activated complement products (C3b and terminal complement complex) in active ulcerative colitis. All these studies indicate the presence of autoantibodies against epithelial cell protein(s) in ulcerative colitis which might play an important role in the pathogenesis.

While we share the ‘disappointment’ of the authors for their ‘uniform failure in their efforts of extraction of functional active tissue autoantibodies’ in ulcerative colitis, their conclusion of ‘no evidence of extractable, epithelial-bound autoantibody’ is unfounded.

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4 Biancone L, Ebert GC, Das KM. The Mr K40,000 colonic protein is associated with antibody dependent cell-mediated cytotoxicity (ADCC) by ulcerative colitis (UC) sera. Gastroenterology 1990; 98(5): A159.

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Oesophageal complications in epidermolysis bullosa

Sir,—Drs Walton and Bennett have written a good overview of oesophagealocutaneous diseases (Gut 1991; 32: 694-7). Such diseases are rare and infrequent. Walton on their appropriate management is therefore limited. We have an interest in epidermolysis bullosa (EB) and have recently reviewed 258 cases covering all major forms of EB to determine the prevalence of oesophageal lesions, amongst other features. Some comments made by Walton and Bennett need to be qualified.

Firstly, oesophageal lesions needing dilatation can occur in dominant dystrophic EB. Some 25% of our 52 patients with dominant dystrophic EB had dysphagia, and oesophageal dilatation was needed in about half of these. Dysphagia was most common in recessive dystrophic EB (72% of 36 patients), but oesophageal dilatation was needed in a similar proportion. Secondly, cervical strictures are not 'easily dilated'. We try to perform dilatation under general anaesthetic at the same time that the patient is having another operative procedure (such as division of acquired syndactyly), and this requires expert anaesthetic care to avoid trauma to the orificial tissues, apart from negotiating with a guide wire a stricture that may start 1 cm from the teeth. We are