Markers to study human colonic cell proliferation

EDITOR—We noted with interest the paper by Kubben et al (Gut 1994; 35: 530–5) on a comparison between proliferating cell nuclear antigen (PCNA) and ex vivo bromodeoxyuridine (BrdU) labelling. We have compared PCNA labelling in 86 human colorectal tumours to iododeoxyuridine (IudR) labelling after in vivo administration using both flow cytometric and immunohistochemical methods.1

In contrast with the authors’ findings, we have not found a significant correlation between the two labels. This was despite correcting for the presence of IudR labelled daughter nuclei (a problem that has not been discussed in this paper) and using a variety of fixatives when assessing PCNA labelling. In our experience, the stronger correlation seen has been on comparison between IudR labelling assessed immunohistochemically and PCNA labelling after fixation in methanol (r=0.38, P<0.01). Fixation methods seem to affect the identification of PCNA in different parts of the cell cycle2 and the apparently higher expression of PCNA than BrdU in Kubben’s paper reflects this.

As we have stated before,1 we feel that in comparisons such as this, it is necessary to analyse a much greater number of specimens from a greater number of subjects and attach less clinical significance to a weak correlation that is statistically significant.

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Reply

EDITOR—We thank Drs Barson and Harris for their interest. We reply to their four points below.

1 The mean result (±SD) for BrdU was 5·24±3·25 mCi (same group, same hour because the first half hour is not a reliable estimate of the basal) was: H pylori positive (n=41), basal acid output 5·14 mmol/h, Vg 111 mU; H pylori negative (n=21), basal acid output 4·97 mmol/h, Vg 110 mU. (2) We do not know why ‘only’ 68% of our duodenal ulcer group were H pylori positive, although some evidence bearing on this point has been submitted for publication. We agree that 95% is commonly quoted, but in five recent publications the values were 67%, 52·6%, 66·4%, 76·3% and 50% (weighted average 65·6%) (3) The plateau/average values (SD) of duodenogastic reflux (Vs) m/min were: H pylori positive first (0·61 (2·6), 2·1 (3·2); 4·5/8·6, 5·7 (6·7). The positive and negative patients did not differ significantly from each other. (4) Body biopsy specimens were not taken, hence the speculative nature of our suggestion. Some of the patients had their H pylori eradicated. Acid output was not measured after eradication.

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Duodenal ulcer, gastric acid, and Helicobacter pylori

EDITOR—Professor Hobsey’s group (Gut 1994; 35: 1033–6) found significant decrease in basal histamine-stimulated acid secretion corrected for pyloric loss, duodenogastic reflux, and stature in patients with duodenal ulcer or non-ulcer dyspepsia who were H pylori positive. We have four questions.

1 What were the results with the one hour basal acid output? (2) Why were only 68% (21 of 31) of the duodenal ulcer group H pylori positive with active chronic gastritis? The usual proportion of H pylori positivity in duodenal ulcer is 95%, and superficial or antral gastritis is almost invariable in duodenal ulcer. (3) The decrease in acid was significant only in the controlled data. Was either pyloric loss significantly reduced or duodenogastic reflux significantly increased in those infected with H pylori? (4) They speculate that the reduced acid in the H pylori positive duodenal ulcer group results from destruction of parietal cells; we would expect this because we ascribe the tissue

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development of PCNA expression with increasing dysplasia to be related to both hyperproliferation and neoplastic deregulation of PCNA synthesis. Although they do not provide sufficient technical details, the interesting results of Wilson and Schofield are in agreement with our study and the work of Weisgerber et al and Risio et al.

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2 Galand P, Degnaf C. Cyclin/PCNA immuno-

4 Weisgerber UM, Boring H, Nemitz R, Raedsch R, Waldber H. Proliferation cell nuclear antigen (clone 19A2) correlates with 5-bromo-2-


Correlation of BrdU and PCNA immunohistochemistry on human colorectal tissue

<table>
<thead>
<tr>
<th>Author</th>
<th>Tissue</th>
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<th>r</th>
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Mab=monoclonal antibody against proliferating cell nuclear antigen; r=correlation coefficient.