Markers to study human colonic cell proliferation

EDITORS—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 (IdUrd) immunohistochemistry in 86 human colorectal tumours. The higher expression of PCNA than BrdU in our study ascribes to the fixation method used.

Two populations of PCNA are present during S phase. One is nucleoplasmic, present in short term G1 cells, and not apparent in cells fixed in organic solvents such as methanol or ethanol. The other form is associated with DNA replication sites and cannot be extracted with organic solvents.1-3

Our results are comparable with those of Weisgeberger et al,4 who used an organic solvent as fixative as well, and slightly lower than those of Risio et al,5 who used formalin fixation (Table). Risio showed a decreasing correlation between PCNA and BrdU immunohistochemistry with increasing dysplasia of the tissue under investigation.

The progressive increase of PCNA expression with increasing dysplasia seems to be related to both hyperproliferation and neoplastic deregulation of DNA 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 Weisgeberger et al and Risio et al.

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Reply

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

(1) The mean results were 4 hours (range 3 to 5 hours). We found the results in our first half hour (because the first half hour is not a reliable estimate of the basal) were: H. pylori positive (n=41), basal acid output 5-14 mmol/h, Vg 111 ml/h; H. pylori negative (n=21), basal acid output 4.97 mmol/h, Vg 110 ml/h. (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%,5 52.6%,6 66.4%,6 76%,6 and 50% (weighted average 65%). (3) The plateau/average values (SD) of duodenogastic reflux (Vg ml/min) in H. pylori positive (n=61) 2.6 (2.1), 2.6 (2.1); H. pylori negative (n=21), basal acid output 4.97 mmol/h, Vg 110 ml/h. We did not measure acid output after eradication.

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