Letters to the Editor

Cimetidine and survival with colorectal cancer

SIR—We have done a multicentre clinical trial on cimetidine aiming to reduce appetite loss and reflux oesophagitis in colorectal cancer patients receiving 5-fluorouracil after operation, and have been surprised to find that treatment with cimetidine is advantageous in increasing the disease-free period and survival, as Adams and Morris reported.[1]

64 colorectal cancer patients (46 colon cancer and 18 rectal cancer patients) were registered and assorted randomly into two groups. All patients received 8 mg/m^2 of mitomycin intravenously within 24 h of surgical resection of the tumour. The patients in one group were given cimetidine 800 mg together with 5-fluorouracil 150 mg orally every day for about 1 year starting 2 weeks after the operation, while the patients in the control group received 5-fluorouracil alone. There were no significant differences between the two groups in the distribution of Dukes' stages or other factors defined by the general rules of the Japanese Research Society for Cancer of the Colon and Rectum. At a mean follow-up of 31 months, the 3·9-year survival in cimetidine-treated colon cancer patients (n=27) was 96·3% and in controls (n=19) 68% (figure), whereas the corresponding figures in the rectal cancer patients were 100% in the cimetidine-treated patients (n=7) and 53·3% in the controls (n=11).

It has been reported that cimetidine increases systemic host immunoreactivity via receptor antagonism of circulating suppressor T cells.[2] Cimetidine has also been reported to reverse the pharmacological activity of peritumoral histamine which promotes tumour growth and suppresses the local immune response.[3] In another series in our study of colon cancer, fluorescence-activated cell sorter analysis of cells in surgically resected tumours from 12 patients showed that the number of major histocompatibility complex (MHC) class I-expressing cancer cells was closely correlated with the number of infiltrating HLA-DR CD3 lymphocytes (r=0·722). This suggests that HLA-DR-expressing activated T cells may induce expression of MHC class I on cancer cells, which in turn may facilitate generation of cytotoxic CD8 T cells which recognise tumour-specific antigen complexed with MHC class I on the cancer cells. Elimination of suppressor T-cell activity and pharmacological activity of histamine by cimetidine would promote generation of tumour-specific cytotoxic T cells and lead to patient survival. Examination of the effects of perioperative treatment with cimetidine on cell surface phenotypes of cancer cells and infiltrating lymphocytes in surgically resected tumour may clarify the mechanism of the anti-cancer effect of cimetidine in colorectal cancer.

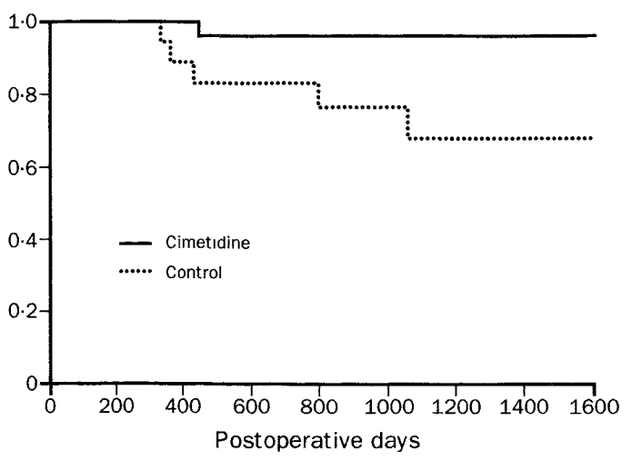

Figure: **Kaplan-Meier life-table analysis of survival from colon cancer after postoperative treatment with cimetidine for 1 year**
Cimetidine, n=27; control, n=19; log-rank test, p=0·025.

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1 Adams WJ, Morris DL. Short-course cimetidine and survival with colorectal cancer. *Lancet* 1994; **344:** 1768–69.
2 Kumar A. Cimetidine: an immunomodulator. *Ann Pharmacother* 1990; **24:** 289–95.
3 Adams W, Lawson J, Morris D. Cimetidine inhibits *in vitro* and *in vivo* growth. *Gut* 1994; **35:** 1632–36.

Brucella antibodies and oral cholera vaccination

SIR—The spread of epidemic cholera into the Americas[1] has renewed interest in evaluating new oral cholera vaccines. One of these candidate vaccines, composed of killed *Vibrio cholerae* O1 organisms and recombinantly produced B subunit (WC/rBS), is being evaluated in two community-based trials in Peru, to include about 50 000 vaccinees. One concern is the probable confusion that might occur when evaluating recently vaccinated individuals for intercurrent brucellosis. This disease is endemic in Peru,[2] and the old parenteral cholera vaccines are known to induce antibody-like substances against *Brucella* spp in as many as 60% of vaccinees, potentially interfering with the diagnosis of this infection.[3] The effect of the new oral cholera vaccines on brucella antibodies is unknown.

Sera were collected from 23 subjects (6–63 years old) at the time of initial vaccination and 2 weeks after two oral doses of WC/rBS, each dose containing 10^{11} organisms and 1 mg of cholera toxin B subunit. Cholera antibacterial antibodies by vibriocidal assay and antibodies to cholera