

serious consequences for a large number of patients. There is no substitute for histology or for the early diagnosis of gastric cancer; for these reasons we believe that endoscopy should still be undertaken in all cases where gastric ulceration is demonstrated or suspected radiologically. The thrust of the argument of Dr Salter and his colleagues should have been towards radiologists and not endoscopists.

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Women and duodenal ulcer

SIR,—In their article (14 March, p 866) Dr Norman R Peden and colleagues have examined their case list of patients affected by duodenal ulcer who, in past years, had been treated with H₂-receptor antagonist drugs. Their results show that there have been a higher incidence of duodenal ulcer formation, a lower healing rate, and a higher pepsin output in the female population in the past two years (1979-80) than in preceding years (1975-7). The lower healing rate after one month of treatment with H₂-receptor-antagonist drugs has been related to an increased maximal pepsin secretion, on the grounds that the H₂-receptor antagonists inhibit pepsin secretion less than they inhibit acid secretion.¹

At our gastrointestinal unit we have re-examined the files of 203 consecutive patients with active duodenal ulcer. They were all submitted to endoscopy and treated for one month with H₂-receptor antagonists or placebo in double-blind studies from 1976 to 1977 and from 1979 to 1980. In our experience the incidence of duodenal ulcer formation appeared always higher in men than in women, and no significant difference was observed either between the two periods in which patients were observed (79% v 21% in both periods) or between patients treated with placebo and those treated with the active drug. With regard to the healing rate, no difference was observed in the male group either between the two periods of examination or between the two treatments, whereas in women a higher healing rate was observed in the 1979-80 period than in the preceding period, the difference being significant (39%; $p < 0.01$).

Our findings therefore differ strongly from those of the Dundee group. Regarding age of patients at the time of observation, both men and women in either treatment groups had matching average ages, although in men the average duration of the illness was longer (men 8.6 years, women 5.1 years); moreover, the age at presentation was always lower in men than in women (men 33.7 years; women 40.6 years).

Determination of basal acid output (BAO) and maximal acid output (after intravenous pentagastrin, 6 µg/kg) (MAO) yielded similar results in both treatment groups and both periods of observation. Both mean BAO and mean MAO were greater in men than in women (BAO: men, 7.6 mmol (277 mg)/h; women, 4.03 mmol (147 mg)/h; MAO: men, 36.99 mmol (1.35 g)/h; women, 24.02 mmol (877 mg)/h). Further analysis of acid secretion levels revealed non-significant differences between healed and not-healed patients.

In our opinion, however, the most interesting aspect of these observations was the relationship observed between smoking and duodenal ulcer healing rate (table). In both treatment groups in the two observation periods, there was a lower healing rate in smokers of both sexes than in non-smokers. The difference was statistically significant in all the various comparisons made, except in the case of the women treated with H₂-receptor antagonist drugs in the last years; this is probably due, in our opinion, to the small number of patients.

Duodenal ulcer: smoking and healing rate. Results are numbers of patients (and percentages)

Healing rate	Placebo	H ₂ -receptor antagonists
Men:		
Smokers	15/57 (30)	43/66 (65)
Non-smokers	5/8 (63)	19/21 (90)
p Value	<0.01	<0.01
Women:		
Smokers	0/5	7/10 (70)
Non-smokers	5/12 (42)	12/15 (80)
p Value	<0.01	NS

In conclusion, we believe that, apart from the problem of duodenal ulcer pathogenesis and independently of the treatment selected, smoking should be considered an important factor in the duodenal ulcer healing rate, especially since sex, age, duration of illness, and acid secretion output cannot be considered, at this stage of our knowledge, decisive factors.

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Toxicity of interferon

SIR,—With reference to the paper by Dr G M Scott and others on the toxicity of interferon (25 April, p 1345), we believe that some unknown contaminants may represent the possible factors involved in the side effects and in the variable responses associated with interferon therapy of malignancies. We would like to suggest the endotoxin lipopolysaccharide as an unsuspected candidate: in fact, on account of its ubiquitous diffusion and physicochemical stability, the endotoxin is the contaminant that most concerns the producers of biological products.¹

We²—like others^{3,4}—have demonstrated that some interferon preparations (HuIFN α) are contaminated with different amounts of endotoxin: contaminating endotoxin may cause some side effects and could alter the results of experimental research and clinical observations. In fact, the myriad of biological properties of endotoxin includes inflammatory effects⁵ and in addition a beneficial effect on the area of the tumour⁶ and an increase in interferon production.⁷ In view of these well-known properties, the endotoxin content of processed materials should be tested by investigators or certified by producers before the study, with the purpose of avoiding confusion of the findings with the effect of the material in which it is present. In this way, the *Limulus* lysate gelation test is extensively used

as providing an in-vitro correlation of endotoxin potential.⁸

Endotoxin, however, is only one of the possible contaminants. Detailed investigations will be necessary to determine the profile and the exact role of other ambiguous representatives of the catalogue of such substances.

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Present use of five-day wards

SIR,—We were very interested in the article from Southampton describing the present use of "five-day wards" by Mr R Davies and others (27 June, p 2118) and are in full agreement with the authors' conclusions. The efficient use of these units and, we would add, the safety of the patients require that they should be accommodated in the inpatient area used by the acute services; we have recently experienced a very large increase in invasive investigations requiring not only intensive nursing supervision but also close proximity to the doctors. The following points apply particularly to the medical investigation units.

(1) We are aware that in many hospitals physicians are using the principles of "programmed investigations" without the facilities offered by a special unit and this might not have been revealed to the Southampton inquiry. Of course, this does not achieve the advantages of a five-day unit but the patients profit nevertheless. Programmed investigation was an idea to protect the patient's interests before it evolved into a system benefiting both patients and hospitals. This primary purpose may have spread more widely than the article suggests.

(2) Five-day investigation units are also suitable for certain therapies—for example, preliminary stabilisation of diabetes and cytotoxic therapy.

(3) Medical investigation units offer an opportunity to improve the quality of performance of a wide range of procedures; the rarer ones are performed more commonly than elsewhere, and the staff are constantly practised; non-clinicians have the chance of suggesting changes in protocols to staff who are particularly interested and likely to put them into practice very soon; the nurses have no other duties which might clash with the precise performance of a test. Presumably our colleagues would agree with this claim because not only is the Manchester unit working to maximum capacity according to its advertised function but it is also performing a very large number of investigations on day patients and on patients referred from other wards and hospitals. There is also a clinical research role, since several research protocols in this hospital stipulate a sequence of agreed observations in the unit.