Percentage incidences of toxic effects of chemotherapy

Symptoms		Marrow depression	
Nausea or vomiting or both	Mild 38, Severe 5	WBC 2·5–4·0 × 10⁹/l	46
Oral ulceration	4	WBC <2·5 × 10⁹/l	2
Hepatotoxicity	2	Platelets 75–100 × 10⁹/l	6
Alopecia	3	Platelets <75 × 10⁹/l	2
Diarrhoea	6		
Gastrointestinal bleeding	2		
Dermatitis	2		

toxicity with the two agents have stimulated us to progress to a three-drug regimen of melphalan, methotrexate, and 5-fluorouracil in a further attempt to devise a treatment with high acceptability and low toxicity. The findings will be reported.

Advancing the management of early breast cancer is so complex that progress can be made only by multicentre studies. Evidence on toxicity with the moderate drug regimen should encourage other clinicians to participate.

We thank all the clinicians in the trial for their help and support in this preliminary study.

[1] *British Medical Journal*, 1976, **1**, 414.
[2] Fisher, B, *et al*, *Cancer*, 1977, **39**, 2883.
[3] Bonadonna, G, *et al*, *Cancer*, 1977, **39**, 2904.

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Cimetidine and serum prolactin

The evolution of H_2 (gastroselective histaminergic) receptor antagonists (burimamide, metiamide, cimetidine) as healing drugs has ushered in a new and unique approach to the therapeutics of peptic ulcer disease. Raised plasma prolactin concentrations have, however, recently been reported in all of six patients under treatment with cimetidine.[1]

We report here five cases where there was neither biochemical nor clinical evidence of hyperprolactinaemia after treatment with cimetidine.

Patients, methods, and results

Five male patients aged 30–55 years (mean age 43·6) were investigated (see table). All had received 200 mg of cimetidine thrice daily, with 400 mg every night. The serum prolactin concentration was measured by the supra-regional assay service for south-east London.

Serum prolactin concentrations in patients studied

Case No	Age	Sex	Diagnosis	Duration of treatment (months)	Serum prolactin concentration (n = up to 360 mU/l)
1	30	M	Duodenal ulcer	2	170
2	41	M	Post partial gastrectomy	3	98
3	40	M	Duodenitis	1½	280
4	55	M	Reflux oesophagitis	1	250
5	52	M	Reflux oesophagitis	6	370
Mean ± SE of mean	43·6 ±4·5	—	—	—	167·0 ±45·5

Comment

Hyperprolactinaemia may lead to impotence, hypogonadism, and gynaecomastia in men and cause galactorrhoea or amenorrhoea in women. Delle Fave *et al*[1] have reported significantly raised concentrations of plasma prolactin in six patients with various gastrointestinal conditions (duodenal ulcer, anastomotic ulcer, and Zollinger-Ellison syndrome) being treated with cimetidine. Of these, one patient had gynaecomastia and a young woman had galactorrhoea. Bateson *et al*[2] have reported progressively increasing hyperprolactinaemia with sustained galactorrhoea in a middle-aged woman with an endoscopically confirmed peptic ulcer under treatment with cimetidine. This patient was also concurrently being treated with chlorpromazine and metoclopramide, both of which block dopaminergic receptors in the hypothalamus—while dopamine is related to prolactin inhibitory factor or may itself be this factor.[3] These drugs may, therefore, have played a part in the developing hyperprolactinaemia.

Hall[4] reported breast pain and gynaecomastia in two patients with the Zollinger-Ellison syndrome and peptic ulcer disease under treatment with cimetidine: in both cases the plasma prolactin concentration was found to be normal. Our patients had no evidence of mastitis or gynaecomastia, or a history of taking other drugs which might have interfered with prolactin secretion.[3] Their serum prolactin concentrations were within normal limits except in one case, the longest treated, where it was just higher than the normal limit. Hence our findings agree with those of Hall.[4]

As yet we have insufficient and conflicting information to allow any evaluation of the association between hyperprolactinaemia and treatment with cimetidine.

We thank the supraregional assay service for south-east London for measuring serum prolactin concentrations in our patients.

[1] Delle Fave, G F, *et al*, *Lancet*, 1977, **1**, 1319.
[2] Bateson, M C, *et al*, *Lancet*, 1977, **2**, 247.
[3] Thorner, M O, *Lancet*, 1975, **1**, 662.
[4] Hall, W H, *New England Journal of Medicine*, 1975, **295**, 841.

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Apparent spontaneous rupture of the spleen

Since Atkinson[1] first reported spontaneous rupture of the spleen in 1874 several cases have been described. The term "spontaneous rupture" has often been misleading, however, and Wright and Prigot[2] stated, "there is no such clinical entity as spontaneous rupture of the normal spleen." Johnson[3] suggested that careful questioning of the patient and relatives will always elicit a history of injury. Nevertheless, as Orloff and Peskin[4] pointed out, there are a few cases that even after careful scrutiny can only be instances of spontaneous rupture of the normal spleen. The following is apparently such a case, though there may be an explanation for the aetiology—namely, that it was a traction tear of the spleen caused by severe retching and vomiting.

Case history

A 72-year-old retired bank director presented in coma as an emergency case. He was pale, cold, sweating, and in obvious shock, with an unrecordable blood pressure and a rapid, thready pulse. He had been well until the