months three patients with severe hyperthyroidism accompanied by hypercalcaemia. In two of these anorexia and vomiting were conspicuous symptoms. This caused some puzzlement and was responsible for considerable delay in diagnosis. Thus in the only two cases I have seen of vomiting with hyperthyroidism hypercalcaemia was present, and I have always assumed since then that this combination should prompt a request for a serum calcium determination.

It would be interesting to know if any such determinations were made in the case of the patients described.

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*We sent a copy of the above letter to Dr Rosenthal, whose reply is printed below.—Ed, *BMJ*.

SIR,—In answer to Dr Sanderson's inquiry, in the discussion on p 210 of our paper, at the start of the fifth paragraph, we state: "There was no evidence of any serious metabolic disorder other than thyrotoxicosis in our patients." For lack of space we could not include all negative findings in the case histories. However, in all our patients the serum calcium was within our normal range of 2.2-2.6 mmol/l (8.8-10.4 mg/100 ml).

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Histamine H₂ antagonists and cluster headache

SIR,—Although histamine has been implicated in the pathogenesis of cluster headache,¹ conventional antihistamine preparations (H₁ receptor antagonists) have so far proved to be inefficient in its treatment. Recent reports showing that the carotid vessels seem to possess histamine H₂ receptors^{2,3} and the fact that a histamine H₂ receptor antagonist (cimetidine; SK&F92334) is currently undergoing clinical trials have led us to examine the possibility of histamine involvement in cluster headache via histamine H₂ receptor sites.

Our preliminary data are derived from 10 male patients suffering from cluster headache who took part in a double-blind study. Each was allocated to one of four schedules in which cimetidine and placebo were interchanged at weekly or two-weekly intervals. The dosage of cimetidine was 400 mg four times a day and the study was continued for a six-week period. The patients recorded the incidence, duration, and intensity of attacks on a diary card and they were assessed weekly in this department, when haematological, biochemical, and urine analyses were also carried out. Analgesic drugs were restricted as much as possible during the trial, their eventual use being noted on the diary cards. One patient discontinued the study owing to the development of nausea and vomiting; otherwise no significant side effects have so far been observed. The mean number of attacks ranged from 2 to 17 per week during cimetidine and from 2 to 13 during placebo medication.

Four of the nine patients improved on cimetidine medication compared with placebo, whereas one remained unchanged and four deteriorated. Statistical analysis of the results has so far not shown cimetidine to be superior to placebo ($P < 0.2$, null hypothesis).

From these preliminary results it therefore seems unlikely that histamine H₂ receptors alone are responsible for the symptomatology of cluster headache. Confirmation of these findings, however, will not exclude a possible therapeutic role for a combined H₁-H₂ receptor antagonist preparation in the treatment of cluster headache.

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¹ Sjaastad, O, in *Vasoactive Substances Relevant to Migraine*, (ed S Diamond *et al*), p 45. Springfield, Thomas, 1975.

² Edvinsson, L, and Ownam, C, in *Proceedings of the Bergen Migraine Symposium, Sandoz-Information*, 1975, suppl. 1, p 32.

³ Saxena, P R, in *Proceedings of the Bergen Migraine Symposium, Sandoz-Information*, 1975, suppl. 1, p 68.

Economy in prescribing

SIR,—The Department of Health and Social Security has requested that general practitioners should prune their prescribing in such a way as to ensure a reduction of £70m in the next year. How is this to be achieved? The majority of doctors realise that in keeping with every commodity the cost of the drugs tends to rise. There are few cheap medicines, only the expensive and the very costly.

I feel sure that substantial sums could be saved if patients were made to respect drugs at a financial level. The majority regard their medicines as costing from nothing to 20p per item whatever the nature or amount supplied, and as a consequence abuses are numerous and varied. One answer to the problem would be for all patients to pay a percentage of the cost of the retail price of the drugs dispensed, the percentage varying to cater for the elderly and the young. Scaled on the percentage basis the patients' outlay need not be excessive, but realisation of the actual cost of the drug would possibly breed a greater respect in many ways.

The method could be employed easily as the dispensing chemist with a pocket calculator could work out the arithmetic, and in view of the fact that most modern widely used drugs are so very easily dispensed, often by an electronic tablet counting machine, the pharmacist could really earn the dispensing fee, which in itself is a percentage based on the prescription cost.

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Nicotine chewing gum

SIR,—Dr M A H Russell and his colleagues (14 August, p 391) have attempted to ascertain to what extent, if any, nicotine gum can be substituted for cigarette smoking with satisfaction to the smoker.

Chewing nicotine gum doubtless results in buccal and alimentary absorption of nicotine dissolved in saliva—as did chewing tobacco,

which was common at the beginning of the century. Some 66% of cigarette smokers, however, inhale the smoke, as I did myself for 12 years. Inhalation of cigarette smoke results in almost immediate appeasement of the inhaler's usually urgent craving for nicotine. Here, *vaporised* nicotine is inhaled and absorption through the pulmonary alveoli is almost immediate. Buccal and alimentary absorption of nicotine *in solution*, on the other hand, is very much slower and much less satisfying to the craving cigarette inhaler. This, I suggest, explains why Dr Russell and his colleagues found merely a "modest inhibitory effect on smoking behaviour" when nicotine was introduced "from another source."

Slowness of absorption doubtless also explains the absence of any pleasure when nicotine is absorbed through unbroken skin. I painted an area 3 × 2 in of the flexor surface of my forearm, previously washed with hot soapy water and dried, with 5% nicotine solution at a time when I was partially addicted to nicotine. No pleasure was experienced, but seven minutes after the painting I experienced nausea, headache, and faintness which persisted for over an hour.^{1,2}

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9 Julian Road,
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Douglas, Isle of Man

¹ Johnston, L M, *Lancet*, 1942, 2, 742.

² Johnston, L M, *The Disease of Tobacco Smoking and Its Cure*, pp 29-35. London, Johnson Publications, 1957. (Copies available from the author at the above address.)

Requests for references

SIR,—In the context of the recent correspondence about the security of references (24 July, p 236, and 14 August, p 424) another aspect that has slipped badly lately is the casual photocopying and distribution of confidential references. I protested to the personnel department of a London teaching hospital about this in April. This week I was handed an uncovered sheaf of information about the two vocational training scheme doctors who are rotating to this hospital next month. This included confidential references from consultants which had been photocopied.

In former times a request for a reference would be accompanied by an assurance that it would *not* be copied or distributed but would simply be read out at the appointments committee. Please could this admirable practice be reinstated?

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Development of RhD antibodies after kidney transplantation

SIR,—Mr M G Kenwright and others (17 July, p 151) report a case in which anti-RhD developed after kidney transplantation. It was thought to be a case of primary response due to "residual" red cells in the kidney. An earlier communication¹ in 1973 reported three cases of anti-RhD production after renal transplantation, but each of these was thought to be a secondary response. These grafts survived for quite lengthy periods in spite of the presence of anti-RhD, the longest being for seven years, when the patient died.