lactin. In 42% of the patients prolactin concentrations were high when blood was first taken. To investigate the cause of this, repeat samples were obtained either at random or after 2 h following the insertion of an intravenous cannula, to obviate the stress of venepuncture. In 10 of the patients prolactin levels had fallen to normal, suggesting that the previous high concentrations could have been due to stress. In our experience "stress" hyperprolactinæmia is much more common in women than in men. Thus, the high incidence of apparently stress-related hyperprolactinæmia in this group of men is atypical of other male patients. Unlike Dr Horning, we would take the view that it would have been positively misleading not to have included this group in our hyperprolactinæmic series. Clearly, most investigators are not going to take serial samples. Also, the ready increase of prolactin in response to venepuncture may not be just a clinical artefact but represent an abnormal response to other environmental stimuli.

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L-CARNITINE ADDITION TO HÆMODIALYSIS FLUID PREVENTS PLASMA-CARNITINE DEFICIENCY DURING DIALYSIS

SIR,—It has been reported that during hæmodialysis there is a marked depletion of blood carnitine,[1-3] an aminoacid important for the utilisation of fatty acids in the mitochondria.[4] It was also shown that the restoration to normal of the blood-carnitine concentration after dialysis can be quickened by oral administration of the aminoacid.[5] Avoiding depletion of carnitine may be important in preventing a fall in tissue carnitine which in turn has been suggested as the cause of a number of undesirable symptoms such as muscular weakness and cramps,[2] which are frequent in patients on hæmodialysis. We report here a simple method of preventing the blood-carnitine falling during dialysis.

PLASMA-L-CARNITINE CONCENTRATIONS (μMOL/L) IN FOUR HÆMODIALYSED PATIENTS

Additions to dialysate:	Total			Free		
	Before	End	6h	Before	End	6h
None	45±3	21±1*	40±2	28±2	7±1*	24±1
L-carnitine (65 μmol/l)	50±3	47±7	49±4	33±5	32±3	35±2

*P <0·01 compared to the level before treatment.

Four patients had dialysis three times a week on a coil kidney dialyser '5 Dialyx SP1052' (Dasco, Modena). L-carnitine (provided by Sigma-Tau, Rome) was added to the dialysate to a final concentration of 65 μmol/l, corresponding to the average pre-dialysis plasma-carnitine (65±7 for 10 patients).

Plasma L-carnitine was measured[6] before, at the end of, and 6 h after dialysis. The results were compared with those of the same patients treated exactly the same way but with no added L-carnitine. Addition of L-carnitine to the dialysate completely prevented the fall of plasma-carnitine during hæmodialysis (table). In this and in a previous study[5] the prevention of the fall in plasma-carnitine led to occasional spontaneous reports from patients of better tolerance of dialysis. This prompted us to begin a clinical trial which is now in progress.

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LITHIUM-INDUCED URÆMIA?

SIR,—Dr Vestergaard (March 3, p. 491) criticises our case-report of probable lithium-induced uræmia (Jan. 27, p. 212). Vestergaard seems to have misunderstood our communication since he argues that our patient was not well controlled. We state clearly that lithium concentrations were measured every one to two months, and we do claim that our patient was well controlled. Even if monitoring is rigorous the patient may, over the years, have episodes of increased lithium values which may damage the kidney in the long run. The therapeutic index of lithium may be less than anticipated.

Vestergaard also misunderstands our description of the progress of the kidney damage, which developed during 1977. When lithium treatment was finally stopped, severe kidney damage was present and of course it took some time before the interstitial nephritis calmed down, so kidney function also decreased in the first month of 1978. Since then, renal function has been stable and last month (a year after the biopsy was done), the clearance value was 23 ml/min at a plasma-creatinine of 350 μmol/l. It is encouraging that the renal function has improved a little and that the rapid progression of renal insufficiency stopped when lithium treatment was withdrawn.

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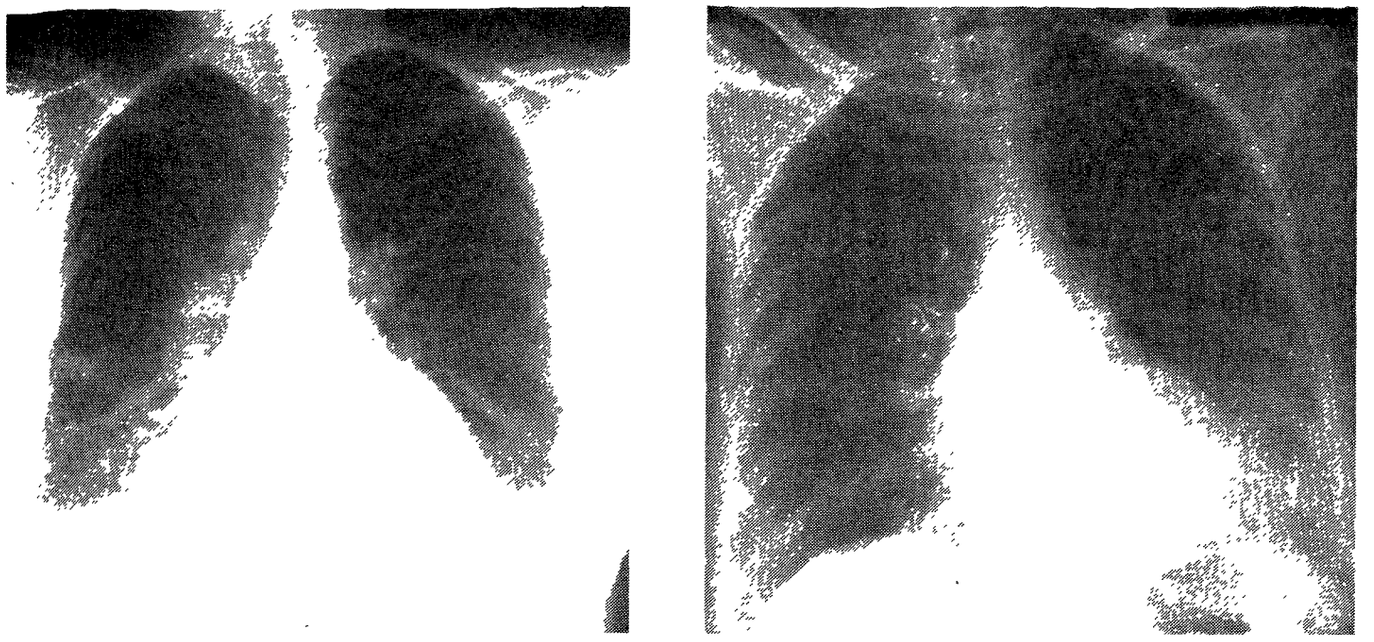
ANTITUMOUR EFFECT OF CIMETIDINE?

SIR,—Two patients with metastatic carcinoma, one of proven and one of suspected bronchogenic origin, received cimetidine for gastrointestinal complaints. With no other additions to their treatment and while receiving no specific antitumour therapy, both had significant regressions of pulmonary lesions.

Case 1

A 52-year-old woman sought advice on July 20, 1978, because of increasingly severe headaches and loss of weight (15 lb) over two months. Her family had noted increasing forgetfulness. She had insulin-dependent diabetes and she had smoked cigarettes daily for 30 years. Examination revealed early papilloedema, a left 7th cranial-nerve palsy, and decreased strength and coordination in the left arm and leg. Chest X-ray showed a large right hilar mass and a computerised-axial-tomography brain scan displayed a 4·5 cm mass involving the basal ganglia on the right. Bronchoscopy failed to yield a diagnosis. Open lung biopsy disclosed a mucin-positive large-cell anaplastic carcinoma. Treatment began with dexamethasone (16 mg daily) and whole-brain irradiation between Aug. 4 and Sept. 13. Because the chest lesion was believed to be producing no symptoms it received no treatment. X-ray on Sept. 14 (figure) showed a slight increase in the size of the right hilar mass and peripheral infiltrate. On Sept. 27 she complained of increasing headache and epigastric symptoms suggest-



Case 1: chest X-rays (left) before and (right) after administration of cimetidine, showing regression of right hilar mass.

ing œsophageal reflux. A repeat brain scan was arranged. She continued on prednisone (20 mg daily) and cimetidine (300 mg twice daily) was added. Other drugs continued included insulin, diazepam, meperidine, and aspirin. The repeat CAT scan showed no change in the large cerebral metastasis. The dose of glucocorticoid was increased to 8 mg daily of dexamethasone. Because of increasing headache and somnolence she was readmitted on Oct. 26 and the cerebral tumour was removed on Nov. 1. Histological examination showed viable carcinoma similar to that from the lung biopsy. Chest X-ray on readmission indicated that the right hilar mass had decreased by about half and the peripheral infiltrate had resolved. The postoperative course was uncomplicated and she was discharged on cimetidine (300 mg twice daily) and on a tapering dose of glucocorticoid. Subsequent chest X-rays have shown persistence of the regression in the chest mass (figure).

Case 2

A 71-year-old man sought advice on March 21, 1977, for a mass in the right side of the neck, which he had first noticed one month earlier. Except for discomfort associated with the mass he had no complaints. He had had a partial gastrectomy for peptic ulcer many years before; and a lung abscess had been successfully treated with antibiotics five years previously. He had smoked cigarettes daily for at least 50 years. A firm, fixed mass of 4·5 cm diameter was found in the right mid-sternocleidomastoid. A chest X-ray was unchanged from one taken a year earlier and showed only residual scarring from the lung abscess. Incisional biopsy revealed squamous-cell carcinoma, and on March 29 treatment began, including adriamycin, cyclophosphamide, 5-flurouracil, and methotrexate. Because of nausea, he refused further treatment after one cycle. The neck mass progressively enlarged over three months and became painful. Because of increasing symptoms, he agreed to further treatment. On May 7 procarbazine (100 mg daily) was started, but he discontined the drug five days later because of nausea. On Nov. 8 the mass was beginning to ulcerate and he was referred for local radiotherapy. Over the next six weeks 6000 rad was delivered to the mass from a cobalt-60 source and regression was almost complete. On Dec. 27 he begun to take cimetidine (300 mg four times daily) because of epigastric distress and œsophageal reflux. Symptoms abated and the dose was cut to 300 mg twice daily on Jan. 26, 1978. On that day chest X-ray showed for the first time pulmonary nodules. They had increased in size by March 23. He refused further antitumour therapy. Because abdominal complaints had not recurred cimetidine (300 mg each evening) was continued but he received no other treatment. Chest X-rays on April 24 and June 22 showed progressive decrease in the size of the pulmonary nodules persisting to the last X-ray on Oct. 10, 1978. The patient is now free of symptoms and continues on cimetidine.

The use of cimetidine, a histamine H_2-receptor antagonist widely given for acid peptic disease, in hæmatological and neoplastic diseases has been associated with amelioration of symptoms in systemic mast-cell disease and basophilic leukæmia,[1] the elimination of pruritis in polycythæmia vera,[2] and the accentuation of hæmatological toxicity in patients treated with lomustine for brain tumours.[3] There have been no reports of a direct anti-neoplastic effect of the drug.

If cimetidine was the cause of tumour regression in these patients, the mechanism is unclear. Possibilities include a direct cytotoxic action (not previously reported), interaction with "receptors" in the tumour cells in a way analagous to œstrogen therapy in breast cancer (not demonstrated), and an immune potentiating effect. Only the latter has been previously proposed as an action of the drug.[4]

There are other plausible explanations besides an antitumour effect of cimetidine, the simplest being spontaneous regression. Conceivably the patients were surreptitiously taking other drugs that caused the responses.

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SEASON VARIATION IN SERUM-THYROXINE

SIR,—An effect of climate or seasonal change on indices of thyroid function has been sporadically reported. For example, Smals et al.[5] have described a marked seasonal variation in T_3 and T_4 levels in healthy men: mean T_4 levels fell from 100 nmol/l to 89 nmol/l when mean ambient temperatures rose from 9°C to 15°C.

We have observed a similar difference in the reference range for T_4 in two series of healthy adult blood-donors attending the Red Cross Blood Transfusion Service to make routine donations. During May, 1977, when the mean daily maximum temperature was 21·7°C and the mean daily minimum was 11·6°C, the T_4 distribution was approximately gaussian with a mean ± S.D. of 104·8±15·7 nmol/l. In December, 1978 (mean daily maximum 28·8°C, mean daily minimum 18·5°C) the distribution was again approximately gaussian but the mean was 87·0±15·5 nmol/l. The difference between means was highly significant (t=8·79, $P<0·0001$).

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