INTOXICATION. Dizziness, headaches, nausea, with treatment and the in developing these side effects on carbamazepine do so because of a fall in the plasma osmolality. When untoward symptoms develop during treatment and subside after the dose is reduced the mechanism of production of the side effect is usually not investigated.

Water retention may itself have an adverse effect on epilepsy, and, as a result of our experience, we wonder whether this may account for the apparent failure of carbamazepine to improve the control of epilepsy in some patients. Measurement of serum drug levels now has a recognised place in the management of epilepsy, and if the serum carbamazepine level is high, as in our second case, the plasma sodium should be measured. If the sodium concentration is low the dose of carbamazepine should be reduced or stopped. Special care should be exercised when carbamazepine is given to elderly patients and those with cardiovascular disease. If symptoms consistent with water intoxication occur the plasma sodium and osmolality should be checked. Hyponatraemia is, then, another indication to reduce or stop carbamazepine.

We are grateful to Dr Geoffrey Walker, chemical pathologist, Nottingham General Hospital, for helpful advice.

ADDENDUM—Since this paper was submitted the potential dangers of carbamazepine have been emphasised by the finding of Henry et al.4 that symptomless hyponatraemia occurred in five out of 16 patients on carbamazepine. Although most of their patients were taking the drug for epilepsy, the cardiovascular consequences are likely to be more severe in elderly patients taking carbamazepine for trigeminal neuralgia.

5. Meinders, A. E., Cejka, V., and Robertson, G. L., Clinical Science and Molecular Medicine, 1974, 47, 289.

(Accepted 16 December 1976)

SHORT REPORTS

Emergency treatment with calcitonin of hypercalcaemia associated with multiple myeloma

Hypercalcaemia is a frequent complication of multiple myeloma. In an analysis of prognostic features1 hypercalcaemia had no adverse effect on prognosis provided that the reduction in calcium concentrations was prompt and associated with a reversal of renal impairment. Such hypercalcaemia usually responds to treatment with steroids and cytotoxic drugs. Nevertheless, more severe hypercalcaemia may be immediately life-threatening and require emergency treatment. There have been reports on single cases of hypercalcaemia in multiple myeloma treated with calcitonin.2 We describe two patients in whom additional treatment with calcitonin appeared to produce a useful hypocalcaemic response.

Case reports

Case 1—A 50-year-old woman presented in March 1970 with a one-month history of chest pain. Multiple myeloma was diagnosed on the basis of Bence Jones proteinuria, radiographic skeletal survey showing multiple osteolytic lesions, and an excess of plasma cells in the bone marrow. She became drowsy and nauseated. The serum calcium concentration was 4.55 mmol/l (18.2 mg/100 ml) and blood urea was 13-6 mmol/l (81 mg/100 ml). Initial treatment of the hypercalcaemia with intravenous saline, intravenous sodium phosphates, and prednisone (60 mg daily) was ineffective. After an initial intravenous infusion of porcine calcitonin (140 MRC units for one hour followed by 280 MRC units hourly for three hours) the serum calcium concentration fell to 3.8 mmol/l (15-6 mg/100 ml) and her clinical condition improved. She was started on melphalan, 8 mg daily, but further fall in serum calcium concentration was seen only in intramuscular calcitonin (640 MRC units six-hourly) was started 36 hours later. The serum calcium concentration then fell to 3 mmol/l (12 mg/100 ml). Blood urea and serum calcium concentrations were normal three weeks later.

Case 2—A 64-year-old woman presented with back pain in 1974. Diagnosis of multiple myeloma was made on the basis of free kappa light chains in serum and urine, excess of plasma cells in the bone marrow, and radiographic skeletal survey showing multiple osteolytic lesions. The serum calcium concentration was 3.15 mmol/l (12.6 mg/100 ml) but fell to normal within 12 days on treatment with melphalan and prednisone. In 1976 she developed symptomatic hypercalcaemia—with a serum calcium concentration of 3.89 mmol/l (15.6 mg/100 ml)—and had a blood urea concentration of 16.3 mmol/l (106 mg/100 ml). Salmon calcitonin, 200 MRC units subcutaneously eight-hourly, had no effect on serum calcium concentration and the dose was increased to 400 MRC units eight-hourly. The serum calcium concentration fell to 2.62 mmol/l (10.48 mg/100 ml) over the next six days.
Discussion

In both cases simultaneous administration of other potentially hypocalcaemic treatment makes it more difficult to assess additional treatment with calcitonin. Nevertheless, in case 1 intravenous calcitonin appears to have had an immediate effect followed by 36 hours without a further fall in the calcium concentration until the addition of intramuscular calcitonin. In case 2 a previous episode of hypercalcemia (serum calcium concentration of 3-85 mmol/l (15-4 mg/100 ml) was treated with steroids and rehydration alone with a fall in the serum calcium concentration to 3-05 mmol/l (12.2 mg/100 ml) taking 19 days. No side effects attributable to calcitonin were observed.

Supernatants from tissue culture of bone marrow cells from patients with multiple myeloma have been found to secrete a calcium mobilising factor and parathyroid-hormone or prostaglandin-mediated osteolytic activity has not been shown. Calcitonin lowers the plasma calcium concentration principally by reducing osteoclastic resorption, although it does have a small calciuric effect.

Use of intravenous phosphate in hypercalcemia is not always successful and may be complicated by soft tissue calcification. The use of intravenous sodium chloride or sulphate depends on good renal function. Mithramycin has been used successfully in small doses, although toxicity would theoretically be a problem if doses were repeated. Calcitonin offers a means of rapidly correcting hypercalcemia associated with multiple myeloma, giving time for treatment of the primary condition to take effect.

We thank Dr C W Bartley for permission to report on both patients.

Methods and results

Selection of children—Ten obese boys and ten obese girls born in 1961 and a similar number of control children were studied at the age of 12 years. The weights for height of the obese children had been >75th centile at the age of 10 years and were still >90th centile at the age of 12. The control children had weights for height between the 25th and 75th centiles and were individually matched with the obese children for sex, age, and school.

Dietary study—Energy intake was measured over one weekend (Friday teatime to Monday breakfast inclusive). The mother of each child recorded every item of food eaten by the child during the study. To help her assess the weight or volume of the food eaten she was given a standard cup and spoon and a diagram of a slice of meat, a chop, and a piece of cheese of known weight. The children themselves kept a diary record of food eaten between meals. The entries were discussed with the family within a day or two of the study period. The weights and volumes of the foods recorded were converted to units of energy using Department of Health Food Tables.

Exercise study—This was done on the same children within three months of the dietary study with a pedometer (HB, Paris), firmly attached at the waist in a wide belt. The children wore the belt during the waking hours on a school day except when swimming (two in each group). They were told that they could wear it without harm for other games and were asked not to modify their behaviour because of the study. The pedometer was set at zero before it was put on the child, and the final reading taken 24 hours later. The setting on the pedometer was the same for each child and no attempt was made to change the units of activity to units of work.

The results showed that there was no significant difference between the energy intake or the measured activity of the obese and control children, although the obese boys tended to take less exercise than did their controls. The ranges of energy intake and exercise were wide but there was a tendency, not significant, for above average intake to be associated with above average activity. In all groups one-sixth of the energy intake was eaten between main meals.

Discussion

The findings of this study indicate that children who are already obese have usually reached a state of equilibrium in which food intake and pattern of exercise are little different from those of children of normal weight. Although treatment will involve reducing intake and increasing activity it seems that it is usually unjust to accuse obese children of overeating. Although the eating pattern during a weekend may differ from that during the week, the large proportion of energy taken between major meals indicates one easy way for children to reduce energy intake.

Energy intake and physical activity in obese children

It is commonly believed that obese children overeat. Nevertheless, energy intake in these children is not excessive and decreased physical activity is a more constant characteristic. Few studies have measured both energy intake and exercise in the same obese individuals. Therefore, as part of a community study of obese children we re-examined this relationship.

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Diet and exercise study of ten obese boys, ten obese girls, and their controls

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