agrees with the often recorded observation that an accident may prolong the emptying time of the stomach. In the light of this experience, it would seem that if a general anaesthetic must be given to a patient who has suffered an accident shortly after eating a large meal the safest course would be to postpone the operation until the next morning and instruct the patient not to have breakfast that day. If this does not prove acceptable to the surgeon then the risk must be faced that in about 1 in 18 accident cases the patient can bring up a dangerous quantity of vomitus four hours or more after the last meal. But, of course, the longer the interval between the meal and the accident the less likely is the stomach to be full.

When by force of circumstance a patient who may not have an empty stomach must be anaesthetized we regard it as sound practice to fill his lungs with oxygen as soon as the nitrous oxide is turned off. This will tide the patient over the brief but dangerous post-operative period when emergence vomiting may occur; if there is breath-holding or momentary obstruction, hypoxia may be avoided.

Summary

Vomiting occurred in 14.7% of 3,000 consecutive out-patients to whom nitrous oxide was administered. Children were more prone to vomit than adults; the longer the anaesthetic the higher the incidence of vomiting; some types of operation carried a much higher vomiting rate than others. The rate was as high as 45.5% or as low as 2.6%, depending on the presence or absence of these factors. Comparative studies are likely to be misleading unless such variability is taken into account.

About 1 in every 18 out-patients undergoing an operation for an injury sustained the same day brought up a potentially dangerous quantity of vomitus, despite an interval of over four hours between the last meal and the anaesthetic.

ACUTE HYPERCALCAEMIA FROM CARCINOMATOSIS WITHOUT BONE METASTASIS

BY

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Hypercalcaemia was for many years linked mainly with hyperparathyroidism, and the effects of the hypercalcaemia *per se* have been overshadowed by the bizarre bone disorder, renal stones, and nephrocalcinosis. In recent years hypercalcaemia has been demonstrated in a number of other disorders and its direct clinical effects have been recognized.

The objects of this case record are to stress the importance of the clinical syndrome of hypercalcaemia and its treatment, and to describe its occurrence with unusual acuteness in carcinomatosis without demonstrable bone secondaries.

Case Report

The patient, a man aged 49, had been perfectly well until six weeks before admission to hospital. For three weeks he was vaguely unwell but able to work; he then became increasingly drowsy, so that he would sleep all day, and, in the last fortnight, complained of abdominal discomfort, constipation, polyuria, polydipsia, and vomiting so severe that he could not keep even fluids down in the previous 48 hours. He had lost 2 stone (12.7 kg.) in this time.

On admission his weight was 14 stone (88.9 kg.), temperature normal, and pulse 90. He appeared pallid but not anaemic. The most striking clinical feature was drowsiness, so marked that he would drop off to sleep while talking. General examination was normal; blood-pressure 150/80.

Investigations on Day of Admission.—Hb, 96%; W.B.C., 7,200/c.mm., normal differential; E.S.R., 6 mm. in 1 hour. Urine: trace of albumin, scanty R.B.C. and W.B.C., no casts, no Bence Jones protein. Fasting blood sugar 95 mg., blood urea 34 mg., serum calcium 16 mg., inorganic phosphate 2.2 mg./100 ml.; alkaline phosphatase 20 K.A. units; serum sodium 138, potassium 2.6, chloride 106 mEq/l.; electrophoresis, slight rise in gamma-globulin; *x*-ray examination showed chest, skull, spine, pelvis, and femur to be normal; electrocardiogram showed features consistent with hypercalcaemia.

A diagnosis of hyperparathyroidism was made and the patient was put on a high fluid intake with glucose and potassium supplements. During the next 10 days vomiting almost ceased and abdominal discomfort subsided. There was no spontaneous bowel action. His drowsiness gradually increased. The serum calcium rose steadily to 18 mg./100 ml., the phosphate remaining below 3 mg./100 ml. The urine output fell and the blood urea rose to 90 mg./100 ml. Urinary calcium excretion was 350 and 550 mg. in 24-hour periods. The hypokalaemia persisted. W.R. was negative.

It was felt to be unsafe to delay any longer, and exploration of his neck was undertaken by Mr. W. H. G. Jessop on the 11th day after admission. A small swelling in the thyroid proved to be a cyst; no other abnormality was found.

He remained unconscious for 36 hours after operation and his condition appeared terminal. The day after operation 100 mg. of hydrocortisone was put in the drip, followed by 100 mg. of cortisone intramuscularly twice daily. Within six hours he began to improve, and next day was able to recognize his relatives, talk, and take fluids. Serum calcium had fallen to 14 mg./100 ml. from a maximum of 18 mg.; blood urea was 77 mg./100 ml. Six days after operation his calcium was 11.5 mg./100 ml., phosphate 3.4 mg./100 ml., and sodium, potassium, and chloride were within normal limits. There was considerable difficulty in maintaining electrolyte balance, particularly in keeping up the serum potassium, and he became increasingly drowsy and the blood urea rose to 158 mg./100 ml. This fell to 105 mg., but the calcium rose again to 16.2 mg./100 ml. in spite of continued cortisone. He died nine days after exploration. Sodium E.D.T.A. had no effect on this terminal rise in calcium.

Necropsy showed widespread abdominal carcinomatosis, the primary being thought to be in the tail of the pancreas, histologically an adenocarcinoma. There was also marked fat necrosis in the omentum, and pancreatitis. Macroscopic examination of several bones failed to show any metastasis.

Discussion

It seems that all this man's symptoms were the direct result of the hypercalcaemia. He never complained of abdominal pain, and such discomfort as he had subsided on admission, when the vomiting also ceased; it seems likely on this history that the pancreatitis found at necropsy was of a few days' duration at most, and unlikely that it caused the hypercalcaemia. The cardinal features of hypercalcaemia are thirst, polyuria, vomiting, lassitude, and loss of weight, mental disorder and drowsiness being particularly marked in acute cases. Other important symptoms are hypotonia, constipation,

and anorexia; calcium deposits or band keratitis may be seen in the eye; isosthenuria, albuminuria, and renal failure are the inevitable outcome, irrespective of the cause.

This clinical syndrome occurs in hyperparathyroidism (Mellgren, 1943; Albright and Reifenstein, 1948). Bradlow and Segel (1956) collected seven cases with acute onset, of which only their patient survived; it was their paper which led us to the exploration of the neck, as delay has been fatal in a potentially curable disease. All these cases had long-standing symptoms of bone or renal disease and may be regarded as "acute on chronic." The syndrome also occurs in myelomatosis (Albright and Reifenstein, 1948), carcinomatosis (Gutman *et al.*, 1936), vitamin D, calciferol, or "A.T. 10" overdosage or sensitivity (Tumulty and Howard, 1942; Danowski *et al.*, 1945), sarcoid (Anderson *et al.*, 1954), the milk-alkali syndrome (Burnett *et al.*, 1949), idiopathic hypercalcaemia of children (Schlesinger *et al.*, 1956), and on immobilization, especially of children, with poliomyelitis (Albright *et al.*, 1941), and fractures (*Ann. intern. Med.*, 1942); it has also been produced by accidental "parathormone" overdosage (Lowenburg and Ginsburg, 1932) and experimentally in animals (Collip, 1925). All these cases show similar features.

In malignant disease, it is thought that bone destruction releases calcium into the circulation. This is only a partial explanation, as the presence of hypercalcaemia does not depend on the extent of the metastases (Gutman *et al.*, 1936; Baker, 1956). Such cases are likely to be seen more often because hormone treatment of carcinoma of the breast may raise the serum calcium (Herrmann *et al.*, 1949; Baker, 1956). Furthermore, cases have now been described in which there is hypercalcaemia when careful post-mortem examination has shown no secondaries in bone (Connor *et al.*, 1956; Plimpton and Gellhorn, 1956). In all these malignant conditions the inorganic phosphate is usually normal or high, but a number of cases have been described in which, as in this case, it was low. Diagnosis may be very difficult, but it seems that the cortisone test is a valuable and rapid means of distinction from hyperparathyroidism, which is the most important differential diagnosis; it has proved ineffective in some cases of carcinomatosis (Plimpton and Gellhorn, 1956). A survey of reported cases suggests that a rapid onset of the syndrome of hypercalcaemia is especially common in malignant disease (Swyer *et al.*, 1950).

The treatment is that of the underlying disease, but Albright and Reifenstein point out that a calcium of 17 mg./100 ml. is the danger point, and, in hyperparathyroidism at least, treatment to prevent death from calcium intoxication before operation is vitally important. In the main, restriction of calcium in the diet and high fluid intake, intravenously if necessary, are all that are required or, indeed, possible. This is an urgent matter and to delay may prove fatal. Symptoms of calcium intoxication can be relieved in most cases of myelomatosis, carcinomatosis (Plimpton and Gellhorn, 1956), sarcoid (Anderson *et al.*, 1954), and hypercalcaemia of children (Creery and McNeill, 1954), by cortisone, and this drug is a valuable form of symptomatic treatment in these circumstances, as well as prolonging life and providing a useful diagnostic test. Sodium citrate and sodium "versenate" (E.D.T.A.) are generally ineffective.

Summary

The clinical course is described of a man aged 49 who presented with features of hypercalcaemia of rapid onset. Necropsy showed carcinomatosis, but there was no sign of bone metastases. The hypercalcaemia was temporarily controlled with cortisone.

I thank Dr. D. Stern for carrying out the necropsy; the resident staff and nurses for their untiring efforts in the care of this patient; and Professor Dent for valuable advice in his management.

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MUCORMYCOTIC GRANULOMA POSSIBLY DUE TO *BASIDIOBOLUS RANARUM*

BY

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This paper is about an unusual case in which biopsy of a subcutaneous mass showed a granuloma containing mycelium of a fungus which, though cultures were not obtained, was thought possibly to be *Basidiobolus ranarum*, one of the rarest causes of mucormycosis. This interpretation was made because of the similar findings by Joe, Eng, Pohan, van der Meulen, and Emmons (1956) in Djakarta in specimens from comparable but more extensive granulomas in two Indonesian children: in one of their cases they isolated a fungus which Emmons identified as *B. ranarum*. The patient whose case is recorded below seems also to have acquired her infection in Indonesia, and this common geographical factor, together with the similarity of the clinical observations and the apparently identical histological findings, is thought to justify the conclusion that the three cases may be of the same nature.

Joe *et al.* (1956) appear to be the only authors who have identified *B. ranarum* with certainty as the cause of human infection. They mentioned two other reports in which infection had been attributed to this organism. One, from the East Indies, concerned a horse (van Overeem, 1925), and the other, from Istria, a gastric