On admission a voided specimen of urine was acid and contained protein, acetone, a large amount of sugar, and a very large number of yeasts with numerous pus cells. Aerobic culture of the urine gave a heavy growth of *Candida albicans* and also a few colonies of *Streptococcus faecalis* and *E. coli*. The blood sugar was 457 mg./100 ml. All other relevant investigations were normal.

A diagnosis of diabetes mellitus and retention with overflow was made. After micturition the patient was catheterized and a jet of 40 oz. (1,140 ml.) of foaming turbid urine was expelled. This settled into three approximately equal layers: first a deposit of pus cells and yeasts, secondly, a supernatant urine, and thirdly foam. Continuous bladder-drainage and washouts were started, initially with a magnesium citrate mixture and later with dequalinium (decamethylene-bis-4-aminoquinaldinium). The urine was made alkaline with mist. pot. cit. (N.F.) and she was stabilized on insulin. A cystoscopy and an examination under anaesthesia performed three weeks after admission were normal. After six weeks the catheter was removed, but she still had occasional urgency of micturition.

Two months later cystometry was performed, and this showed a mild sensory neuropathy of the bladder. *C. albicans* could not be isolated from the urine, vulva, vagina, sputum, or faeces. An intravenous pyelogram showed no significant abnormality apart from a poorly emptying bladder.

DISCUSSION

It was thought that the *C. albicans* was fermenting the sugar in the urine, with the production of gas.

Of the various fungistatic agents available, dequalinium was chosen for bladder irrigation. It is soluble (Wilkinson, 1959), known to be effective against *C. albicans*, is not inhibited by serum (Babbs *et al.*, 1956), and is well tolerated by abraded surfaces (Coles *et al.*, 1958).

Dequalinium in a concentration of 0.01% in N saline was used as a twice-daily bladder washout for seven days. This produced a dramatic improvement and after four days *C. albicans* was never again isolated.

There are a few reported cases of possible *C. albicans* infection of the urethra (Harkness, 1950), of the bladder (Moulder, 1946), and of the kidney (Lundquist, 1931), but in the present case only the urine was infected.

C. albicans will grow most profusely between pH 5.1 and 6.4 (Benham, 1957). It ferments glucose anaerobically at pH 7.2 or lower to produce acid and carbon dioxide (Martin *et al.*, 1937), while a rise of pH will inhibit fermentation. The rate of growth of *C. albicans* rises in proportion to the concentration of glucose present, when this is above 150 mg./100 ml. (Johnson, 1954).

C. albicans is a normal commensal of the mucosae, and in diabetics with vulval irritation may be found in large numbers throughout the external genitalia. These profuse numbers might colonize the glucose-containing urine and ferment it if it were acid. During micturition a patient with normal bladder function would empty the bladder of urine and any *C. albicans* present. However, if there were a residual urine, due to a diabetic vesical neuropathy, *C. albicans* would increase to much higher numbers and the effect of any fermentation would then become more apparent. A large residual urine has been reported in most cases of pneumaturia associated with glycosuria. It is surprising that pneumaturia is not found more commonly in diabetic patients, among whom infections and a vesical neuropathy may occur.

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Pseudohyperparathyroidism with Carcinoma of Bronchus

Hypercalcaemia associated with malignant disease is well recognized in the presence of bone metastases. However, there have been only 16 reported cases of hypercalcaemia in malignant disease without demonstrable bone metastases (case records of Massachusetts General Hospital, 1953; Connor *et al.*, 1956; Myers, 1956; Plimpton and Gellhorn, 1956; Schatten *et al.*, 1958; Lucas, 1960). The present report concerns a patient with the chemical characteristics of hyperparathyroidism with a bronchial carcinoma but no enlargement of the parathyroid tissue and no bone metastases.

CASE REPORT

The patient was a retired architect aged 73. Apart from a partial thyroidectomy and tracheostomy (on account of a goitre) at the age of 23, he had been well all his life. His complaints were loss of weight (6.5 kg. in four months), anorexia, nausea, epigastric discomfort, and constipation for two months, and for the last month he complained of general weakness, and his wife said he was becoming drowsy.

On examination his temperature was 99° F. (37.2° C.) and blood pressure 130/70. He had a dry scaling skin. He was drowsy, inattentive, and disorientated in time and space. His liver was palpable 8 cm. below the right costal margin and had an irregular surface. His sigmoid and transverse colon was easily palpable and was felt to be full of hard faeces. Rectal examination revealed a slightly enlarged prostate with a smooth surface. All tendon reflexes were present but sluggish.

Investigations.—Hb, 12.3 g./100 ml.; W.B.C., 14,000/c.mm., neutrophil leucocytosis; E.S.R., 70 mm. in first hour; blood urea, 51 mg./100 ml.; serum cholesterol, 190 mg./100 ml.; serum sodium, 132 mEq/l.; potassium, 3.7 mEq/l.; chloride, 100 mEq/l.; alkali reserve, 25 mEq/l.; serum acid phosphatase, 4 units/100 ml. Chest x-ray examination: opacity 2.5 cm. in diameter in left mid-zone. Gastro-intestinal studies: barium-meal, N.A.D.; barium enema, patient was unable to retain barium; stools for occult blood $\times 3$ were

negative. E.C.G.: QTc 0.365 second; flat T waves and prominent U waves in the precordial leads. C.S.F.: clear; protein, 30 mg./100 ml.; W.B.C. 4/c.mm.; calcium 7 mg./100 ml. Serum calcium, phosphorus, and alkaline phosphatase (see Chart). Urinary calcium, 700 mg. in a 24-hour period. Concentration of calcium was 36 mg./100 ml. in one specimen and 42 mg./100 ml. in another. X-ray examination of lumbar and thoracic spine showed spondylosis and slight osteoporosis but no evidence of metastasis.

Serum calcium, serum alkaline phosphatase, and plasma phosphorus levels during patient's stay in hospital. Effect of cortisone is shown.

X-ray examination of hands, N.A.D. Renal function studies: glomerulo-filtration rate, 44 ml./min. Average TmP (maximal tubular capacity to reabsorb phosphorus), 0.91 mg./min. With the above G.F.R. the TmP was expected to be 1.75 mg./min., suggesting a loss of 45% in the TmP in this patient.

The initial diagnosis on the history and clinical findings was carcinoma of the colon, but after investigations it was thought that his symptoms were probably explained by the hypercalcaemia. In view of the combination of a raised calcium and relatively low serum phosphorus the possibility of primary hyperparathyroidism was seriously entertained. However, the finding of a shadow resembling that of a bronchial carcinoma in the chest radiograph suggested a more likely diagnosis of bronchial carcinoma with metastases to the liver, so it was thought unjustifiable to explore the patient.

He was given 100 mg. of cortisone a day in an attempt to lower his serum calcium, but this had little effect (after four days' treatment the serum calcium was 14 mg./100 ml.). His clinical condition gradually deteriorated; he would sleep most of the day and was only just rousable. His mental state was poor. After 10 days on cortisone his serum calcium was 16 mg./100 ml. and his blood urea 61 mg./100 ml. He declined still further and died one month after admission.

At necropsy he was found to have a squamous-cell carcinoma (Broder's grade III) of the bronchus with metastases in the liver and pericardium. The whole of the skeleton was examined macroscopically and there was no obvious bone metastasis. Histology from the vertebral strip, sternum, and iliac crest showed moderate osteoporosis only. The haemopoietic marrow was normal. The neck and thorax were carefully explored for the parathyroid glands and any abnormality of them, but with negative result. It is possible that the high serum calcium tended to cause atrophy of the parathyroids. Kidneys were normal macroscopically and section showed only occasional obliterated glomeruli. No evidence of metastases or encephalopathy was found in the brain.

DISCUSSION

This patient's symptoms could all be accounted for by hypercalcaemia: the mental changes could be associated with the raised C.S.F. calcium. Plimpton and Gellhorn (1956), who reported C.S.F. findings in three of their cases, found raised calcium levels in two patients with mental change, but a normal C.S.F. calcium was found in a patient with no mental symptoms.

There was no evidence for multiple myelomatosis, Hodgkin's disease, overdose of vitamin D, sarcoidosis, berylliosis, Paget's disease, thyrotoxicosis, or excessive immobilization, which are conditions that may cause hypercalcaemia. Primary hyperparathyroidism was thought unlikely because no tumour or hyperplasia of the parathyroids was found despite careful search, and there were no other histological changes in favour of the diagnosis.

The raised alkaline phosphatase also made it unlikely that this patient had primary hyperparathyroidism as a whole diagnosis, for if the high alkaline phosphatase were due to this condition one would have expected x-ray and post-mortem changes in the bones compatible with this diagnosis, but these were not found. The high alkaline phosphatase was thought to be due to liver secondaries. Hypercalcaemia due to bone metastases was discounted because there was no evidence of them either radiologically or at necropsy.

It is therefore suggested that this patient's tumour was secreting a substance with an action similar to that of "parathormone." It appears that such tumours can play an active metabolic part, for when they are removed or when cytotoxic drugs are given, the serum calcium suddenly falls and the phosphate tends to rise (Plimpton and Gellhorn, 1956; Myers, 1956; Connor *et al.*, 1956; Schatten *et al.*, 1958). In support of this hypothesis our patient had a Tm for phosphate which was reduced out of proportion, which is compatible with a parathormone-like action on the secretion of phosphate by the distal tube.

I thank Dr. P. Hugh-Jones for permission to publish this case and for his advice and criticism. I also thank Dr. V. Parsons for estimations on phosphate excretion.

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Outlining the development of medical services in Nyasaland, Mr. B. D. Goldberg, Minister of Health for the Federation, said that there were now nearly 5,000 beds for the sick of all races in Government hospitals and Government-aided mission hospitals. This is an increase of 3,000 on the figure for 1955. In the year before Federation £200,000 had been spent on health services in the territory. This year the Federal Government will spend £1,100,000. The grant to missions in 1953 had been £10,000; this year it would be £56,000. Mr. Goldberg went on to say that in the Federation approximately £1 per head was spent on health services—some 13% of the Federal budget.