and may be conditioned by micronutrient deficiencies in food plants grown on soils of high organic content; and that populations whose diets include vegetable foods grown on such soils may be subjected to the action of carcinogens, or may be deprived of protective substances.

I thank Mr. G. C. Worters for the original suggestion that total cancer mortality might be at a maximum on soils of high reducing power and at a minimum on well-oxygenated soils; and the General Register Office for granting access to unpublished statistical data. Most of the work on which the paper is based has been done during the tenure of a research studentship of the London School of Economics.

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BILATERAL GIANT RENAL CALCULI

BY

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Giant renal calculi have not infrequently been described in the literature, but only four weighing over 1 kg. have been reported, Pohl's (quoted by Legueu, 1921) being 2,005 g. Although such calculi have been reported in one kidney, accompanied by a small calculus in the other, bilateral giant renal calculi are rare. Morrison (1921) described the case of a man aged 50 who had a left renal calculus weighing 1,130 g., together with a smaller one on the right side. Everett (1934) described an example in a woman aged 59, in whom the right kidney contained a calculus weighing 622 g., while the left contained one weighing 329 g. Gutierrez (1939) described three cases. A further case is reported below. It demonstrates the extraordinary adaptation of which the kidneys are capable, and seems to be the largest example of bilateral renal calculi yet recorded.

Case History

The subject was one of a family of eight children, of whom one died in infancy, another of pulmonary tuberculosis at 25 years, while the other five are alive and well. His father was a small farmer who died of old age at 88. His mother died at 83 from a fractured femur. He was apparently well and free from illness until 15, when he began to experience recurrent attacks of pain in the abdomen and back, occurring at intervals of three to five weeks and lasting sometimes up to 24 hours. He developed an aversion to sitting down, as this tended to bring on the pain. His preference for spending his time engaged in some such pursuit as carpentry, instead of performing his milking duties with the other sons, for a time earned him the disapproval of his family and the reputation of a malingerer. Eventually a doctor was consulted. He was admitted to hospital for a month, during which time he was symptom-free. On returning home his symptoms recurred. He learnt to ease his pain during attacks by riding on a bicycle over rough ground as hard as he could. He became a butcher and also kept a smallholding.

At the age of 27 a large stone and some smaller ones were removed from one kidney at Guy's Hospital. To his great disappointment, however, the symptoms recurred as soon as he returned home. Thereafter he eschewed medical advice as much as possible. As time went by the attacks of pain became less frequent, but he experienced bouts of haematuria, and episodes when his urine became foul-smelling and offensive, presumably being heavily infected. A constant dull aching pain in the back developed. From the age of 45 onwards he attended his doctor infrequently for episodes of haematuria and urinary infection. Further operative treatment was advised but refused. At the age of 61 his doctor attended him for a severe bout of haematuria and found him to have easily palpable and very hard kidneys. His blood pressure was 210/100; he was obviously anaemic, yet managed to do his work. X-ray examination revealed enormous bilateral renal calculi. He would consent to no

FIG. 1.—Radiograph showing large bilateral renal calculi.

further investigations, yet offered his kidneys for examination after his death. He experienced periods of sickness and headache, and usually had a brown furred tongue. He continued his work, smoking heavily and consuming a pint of beer daily until May, 1949, when, during a local influenza epidemic, he became ill with headache and a cough. After initial improvement he became drowsy and began to vomit; his urinary output fell, and he died 10 days after going off sick.

Specimens

The right kidney weighed 1,680 g. (see Fig. 2). It consisted of a thin shell of renal tissue covering an enormous coralliform calculus measuring approximately 19 by 10 cm. On hemisection, septa of renal tissue only 2 to 4 mm. in thickness were seen to extend down in between the stout processes of the stone. The renal tissue covering the stone varied from 1 to 3 mm. in thickness, except at those places from which the septa arose, where triangular areas of renal tissue were present, each having a base of approximately 1 cm. One ureter appeared to be a little thickened. The calculus was mostly white, was very hard, and resembled marble in appearance. In the lower part of what had once been the renal pelvis a central yellow and brown stone was present which appeared older than the rest. When freshly cut, laminations running parallel to the convex surfaces were visible throughout the calculus and fine radial markings were also apparent. Until cut the calculus was in one piece. The kidney (unfrozen) was clamped in a vice for cutting, a process which took about one hour with a hacksaw.

FIG. 2.—The calculus of the right kidney.

The left kidney weighed 720 g. and contained one main calculus measuring approximately 18.5 by 8 cm., together with several smaller calculi. The lower end of the main calculus extended down into an elongated portion of the renal pelvis and contained a laminated brown oval stone appearing older than the rest. The remainder of the main calculus extended in a coralliform fashion into dilated calices, leaving a narrow rim of renal tissue. The main portion of the stone was composed of a hard white laminated material possessing radial markings. A natural joint was present between the main calculus and another at the upper pole of the kidney. The surfaces of the joint were convex and concave, and were covered by a smooth thin layer which was denser and whiter than the subjacent stone. Several other smaller calculi were present in some calices. The rim of renal tissue varied in thickness from 2 to 10 mm. At the upper pole and on the lateral border were moderately sized areas of renal tissue 10 mm. in thickness. The ureter was only slightly thickened.

The calculi of both kidneys were composed of carbonates and phosphates. No trace of urates or oxalates was found even in the denser pelvic stones.

Microscopical sections from the recognizable areas of kidney substance in each kidney showed a flattened single layer of pelvic epithelium, separated by a layer of fibrous granulation tissue from functioning renal tissue. Most of the glomeruli showed thickening of the capillary basement membrane; a few were shrunken, but none were obliterated. In some areas the tubules were dilated. There was moderate interstitial fibrosis. The arteries were narrowed by thickening of the intimal connective tissue and by medial hypertrophy.

Summary

A case of bilateral renal calculi of exceptional size is recorded. Despite the distortion of the kidneys into mere rims of renal tissue thinly covering the calculi (a state which was shown by x-ray examination to have been present for at least three years), renal function had been adequate until the subject contracted a terminal acute respiratory infection.

Reference is made to other giant renal calculi recorded in the literature.

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PETHIDINE AND LIVER DAMAGE

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Detoxication of pethidine by the liver has been proved by the animal experiments of Bernheim and Bernheim (1945). This has been verified by Way, Swanson, and Gimble (1947), who suggested that in patients with severe hepatic impairment the desired therapeutic effect of pethidine might be obtained with smaller dosage. A review of the literature has failed to reveal any case report to substantiate this view, and it is therefore felt that the following cases will prove of interest in support of the hypothesis.

Case Reports

Case 1.—The patient, a man aged 40, had a history of repeated haematemesis. Laparotomy in November, 1950, revealed a cirrhotic liver and splenomegaly. Liver biopsy showed early multilobular cirrhosis. Liver-function tests on April 19, 1951, gave the following results: van den Bergh, direct reaction, very feeble, delayed; serum bilirubin, 1.6 mg. per 100 ml.; serum alkaline phosphatase, 8.3 units per 100 ml.; serum colloidal gold, 5; zinc turbidity, 10 units; thymol turbidity, 5 units; thymol flocculation, ++++; cephalin cholesterol, ++++. Hippuric acid excretion was impaired. Urinary urobilinogen was present in dilution 1:40.

On May 1 splenectomy was performed under D-tubocurarine chloride, thiopentone, nitrous oxide, oxygen, and pethidine anaesthesia. The patient's condition was satisfactory at the end of operation, and morphine, 10 mg., was given on three occasions for post-operative sedation. Pethidine was administered in divided doses as follows: during operation, 100 mg.; first post-operative day, 100 mg.; second day, 200 mg.; third day, 400 mg.; fourth day, 200 mg. Up to the third post-operative day the patient's progress was satisfactory. That evening he became delirious and disorientated, a condition which was attributed to uraemia. The blood urea, however, was 39 mg. per 100 ml. His condition remained unchanged during the fourth day, when, on bearing in mind the possibility of drug intoxication, the pethidine was discontinued. The following morning he was much improved and was quite lucid. He had complete amnesia for the second to fourth post-operative days. His subsequent progress was uneventful.

Case 2.—A woman aged 25 had a history of subacute hepatic necrosis in 1943, and haematemesis on two subsequent occasions. Clinical examination revealed marked ascites, enlarged spleen, but palpable liver. On May 16, 1951, liver-function tests showed: van den Bergh, direct reaction, feeble, prompt; serum bilirubin, 1.6 mg. per 100 ml.; serum alkaline phosphatase, 15 units per 100 ml.; serum colloidal gold, 5; zinc turbidity, 9 units; thymol turbidity, 7 units; thymol flocculation, ++++; cephalin cholesterol, ++. Urinary urobilinogen was present in dilution 1:40. The A/G ratio (Howe's technique) was 1.05:1. On May 25 splenectomy and spleno-renal anastomosis were performed under D-tubocurarine chloride, thiopentone, nitrous oxide, oxygen, and pethidine anaesthesia. The operation lasted four hours, during which time 0.45 g. of thiopentone, 50 mg. of D-tubocurarine chloride, and 50 mg. of pethidine were administered. A frozen section of the liver showed a nodule of excellently regenerated liver tissue