classified as lobar pneumonia and four as bronchopneumonia. The predominating organisms were pneumococci and a mixed catarrhal flora. The patients' ages ranged from 16 to 87 years (two cases), with an average of 50 years. There were fifteen recoveries and two deaths. One of the two fatal cases, a man of 45, was admitted in a semi-conscious condition with severe toxæmia and congestive cardiac failure. He died within eighteen hours of admission after receiving two injections of 250,000 units of penicillin. The second fatal case, a man of 87, died on the seventh day of treatment from congestive cardiac failure, with auricular fibrillation and arteriosclerotic myocardial degeneration, after an initial apparent response to therapy. The fifteen patients who recovered all showed an excellent response to penicillin treatment. The temperature and pulse fell by crisis, and there was a great improvement in the clinical condition with loss of toxæmia in an average of thirty-six hours from the beginning of treatment. The average duration of stay in hospital of these patients was fourteen days.

My thanks are due to Dr. B. Gottlieb, senior resident physician at St. Alfege's Hospital, for the invaluable help he has given me in preparing this paper, and to many other members of the medical staff who have assisted in the treatment of these patients. I am grateful to Dr. E. N. Allott, of the Lewisham Group Laboratory, for his generous co-operation and advice, which have meant so much to us in developing penicillin treatment. Finally, I would thank Mr. White, the chief pharmacist, whose skill and ingenuity in dispensing this new and labile substance in all its forms have been a stimulating example of the high pharmaceutical technique we now expect from our pharmacists.

THE PLACE OF UNILATERAL RENAL DISEASE IN HYPERTENSION

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Until recently hypertension has been the province of the physician and, apart from blood-letting, its treatment has been mainly rest and a restriction of activity. Now, however, there is a surgical approach to this very great problem, and attacks have been made along both direct and indirect lines. *Direct*: In cases in which unilateral renal disease has been found it may be assumed that this plays some part in the genesis of the hypertension, and the offending organ may be excised in an endeavour to remove this cause. *Indirect*: By interruption of the sympathetic nervous system a lowering of the blood pressure has been obtained. All operations of this type have their effect irrespective of the aetiology of the hypertension, and do not attempt to remove its cause.

This paper is concerned with the direct line of attack. It has been our routine to perform excretion pyelography in every case of severe or considerable hypertension which has come under investigation. If at this examination both kidneys do not show a normal contour of pelvis and calices, then further investigation by cystoscopy and retrograde pyelogram has been undertaken. The following cases of hypertension occurring in association with renal disease have been encountered, and it is desired to put them on record.

Case 1

A flight-lieutenant aged 38 noticed puffiness of the eyelids and swelling of the ankles in June, 1943. This persisted and became gradually worse. In September, 1944, he had an attack of acute tonsillitis, and at a medical board was found to have a raised blood pressure and albuminuria. For some years he had had frequency of micturition. He was admitted to an R.A.F. hospital on Jan. 12, 1945, and was seen to be a well-nourished man with no demonstrable oedema. The blood pressure was 215/140. The heart sounds were normal. Nothing abnormal was found in chest and abdomen. The blood urea was 33 mg. per 100 ml. Van Slyke: first hour 85%, second hour 92%. There was no albumin or deposit in the urine. A radiograph showed a calculus in the pelvis of the left kidney. He was given 21 days' leave, and returned to hospital on Feb. 13. A radiograph showed the calculus to be in the same position. Blood urea, 38 mg. per 100 ml. Blood pressure, 190/130.

On Feb. 18 the left kidney was exposed through a curved loin incision. It appeared normal in size and consistency, but was rather adherent to the perinephric fat. The pelvis was cleared and opened posteriorly, and the stone was removed. A bougie was passed down the ureter easily, and the opening in the pelvis was sutured. The wound was closed and a rubber drain inserted. He passed some blood-stained urine the following day, and there was a slight leakage from the drainage-tube for the first three days after operation. Convalescence was satisfactory. On March 14 the blood pressure was 180/120.

Case 2

A wireless operator aged 25, with 4½ years' service, began to have headaches about June, 1944. These became more frequent, and about the beginning of May, 1945, he noticed that the left side of his field of vision was blurred. His appetite was good, weight steady, and bowels regular. There were no urinary symptoms. Past history revealed nothing relevant.

On May 30 he was admitted to an R.A.F. general hospital overseas. His right vision was 6/6, left vision 6/6. The fundus of the right eye showed a cotton-wool-like horseshoe-shaped area, enclosing the macula nasally, and the disk was oedematous. There were one or two small haemorrhages and a patch of exudate in relation to the superior nasal vessel. The left fundus showed similar changes. The urine contained albumin +. The blood pressure was 210/160. Urea concentration was 78% of average normal. Two years previously he had been rejected for flying duties because his blood pressure was raised (amount not stated). On June 18 he was transferred to an R.A.F. hospital in England with a diagnosis of malignant hypertension.

On admission his general condition was good. The tongue was clean, pulse 100, blood pressure 260/180. The apex beat was in the fifth space, outside the mid-clavicular line, with a thrusting impulse but no bruits, and the artery walls were thickened. The lungs were normal. The liver, spleen, and kidneys were not palpable. Examination of the central nervous system revealed nothing abnormal; the jerks were brisk. The disks were substantially as above, with commencing papilloedema of the right eye. There was defect in the left upper outer quadrant of the visual fields.

Investigations.—Urine specific gravity 1020, albumin +. Urea clearance: first hour 2.26 g.; Van Slyke 133%. Second hour 2.3 g.; Van Slyke 129%. Blood urea: 33 mg. per 100 ml. Midstream specimen urine showed a moderate number of red blood cells, calcium oxalate crystals, epithelial cells, and several granular casts; culture was sterile. Blood count: R.B.C., 4,800,000; haemoglobin, 94%. Excretion urography showed a slight degree of hydronephrosis of the left side, with no excretion on the right side up to 60 minutes. (See Fig. 1.) Cystoscopy showed the bladder mucosa to be normal. Both ureteric orifices were normal. A catheter was passed up the right side without obstruction to 20 cm. and 35 ml. of sodium iodide 12% was injected. Radiographs revealed a small kidney with a marked hydronephrosis, and a diagnosis of hypoplastic kidney was made. (See Fig. 2.) Despite continued rest in bed the blood pressure remained raised; the lowest recorded was on June 29, when it was 235/145.

On July 10 the right kidney was exposed through a curved loin incision. It was represented by a shell of tissue only,

and there was a fair-sized funnel-shaped hydronephrosis. The kidney was removed. (See Figs. 3 and 4.) The next day the blood pressure was 118/76. Apart from a little blood-stained urine, the patient had passed nothing since the operation. He

of urine. On the 13th the blood urea was 100 mg. per 100 ml., and from then onwards it gradually fell until on July 24 it was 34 mg. per 100 ml., and the output and intake were normal. The blood pressure was 140/80.

On Sept. 4 the headaches were much better. The sole complaint was of slight vertigo on getting up suddenly and some discomfort over the nephrectomy scar. Urine: n.a.d., no deposit, culture sterile. The blood pressure was 140/100. Ophthalmic report: There is some sheathing of the vessels where the exudates have been and a scotoma of the left eye but no signs of active retinopathy.

FIG. 1.—Case 2.—Excretion urography, 15 minutes; showing slight degree of hydronephrosis on the left side. No excretion on the right. Calcified glands at level of transverse process of third lumbar vertebra, right.

FIG. 3.—Case 2. Photograph of removed kidney. There was no mechanical obstruction of the ureter.

FIG. 2.—Case 2. Retrograde pyelogram on right side. Tip of catheter to level of second sacral segment. Bizarre pelvis with small renal shadow.

FIG. 4.—Case 2. Specimen cut open. Practically no renal parenchyma left.

Case 3

L.A.C.W. aged 27, with 4 years' service, reported sick on July 13, 1945, complaining of blurring of vision and headaches; she was admitted to hospital. For some two years she had had bilious attacks consisting of violent headaches and vomiting. The attacks lasted about 12 hours, and then cleared up for a period of from two weeks to two months. The present attack had begun 7 days before, and in 4 days the vision had become blurred. There was nothing in her past medical history of significance.

On examination her general condition was fair. The left vision was 6/8, the right vision 6/24. Nothing abnormal was seen in the lungs and abdomen. Neither kidney was palpable. The pulse was 100, and blood pressure 260/210. Heart

was given 2 pints (1.14 litres) of sodium sulphate, followed by glucose-saline. On July 12 he began to pass some urine. The blood urea was raised to 120 on the 11th, on the 12th it was 160 and the blood pressure 140/92. He passed 71 oz. (2 litres)

sounds: triple rhythm at apex, aortic second ++. Urine: albumin, faint trace; centrifuged deposit—epithelial cells only; culture sterile. Urea clearance: first hour, 76%, second hour, 74%. The blood urea was 39 mg. per 100 ml.

Ophthalmic report: Bilateral swelling of the nerve head with scattered patches of exudate. No haemorrhages seen. The vessels appear somewhat attenuated. The fundus appearances are those of malignant hypertension.

An intravenous pyelogram revealed no function on the left side. The outline of the right kidney pelvis and calices was normal. On cystoscopy the right ureteric orifice was normal; no orifice was seen on the left side.

At operation on Aug. 8, 1945, the left loin was explored. A curved loin incision was made and the renal space opened and examined. There was no evidence of a kidney. The suprarenal gland was identified. The extraperitoneal space on the left side was explored down to the pelvis: no evidence of kidney. The wound was closed, with drainage. The blood pressure on Oct. 16 was 260/200. On Oct. 31 the patient proceeded on sick leave, pending discharge from the Service, and died suddenly in the street three weeks later.

Discussion

When a new treatment or a new conception of an old condition is introduced it has at least a temporary vogue, and unilateral renal disease as a cause of hypertension has been no exception. A number of papers have appeared, some with an extensive series of cases, describing hypertension relieved after nephrectomy for unilateral renal disease. On analysing these cases the majority are seen to fall into the group of mild hypertension, and success has been claimed for the treatment if the blood pressure has been reduced by as little as 20 mm. Hg. It is well established that a period of complete rest in bed, with appropriate dietary care, especially if accompanied by a major operation, will be followed for a time by some fall in blood pressure. Most of the published cases fall into this class. Often there has not been a clear-cut urological indication for the nephrectomy, and its performance has had only a slight temporary effect on the hypertension.

In our first case the patient had a relatively mild hypertension. On excretion urography and on indigo-carmin excretion at cystoscopy both kidneys appeared to be functioning normally. It was therefore not considered justifiable to remove the kidney. The blood pressure fell slightly after operation, and from the time the patient was first seen it had been reduced from 215/140 to 180/120. It is not considered that this was in any way attributable to the removal of the stone from the kidney, for the fall is not more than would have been expected from the combined effect of rest in bed and a major operation.

In Case 2 there was a dramatic fall in the blood pressure after nephrectomy. In addition symptoms subsided completely and there was a remarkable clearing of an advanced retinopathy. In view of this there would seem to be no doubt that the hypoplastic kidney was intimately concerned with the production of the malignant hypertension. A case of hypertension was described by Schwarz (1924) in which a hypoplastic kidney was found post mortem. Higbee (1944) reported two cases of congenital renal hypoplasia with hypertension, and both of these were relieved after nephrectomy.

In renal hyperplasia there is an immature or rudimentary kidney. It must be differentiated from renal agenesis, as in Case 3, where no kidney tissue is present, and from renal aplasia in which rudimentary kidney tissue exists without any collecting system. There is a thin rim of parenchyma which secretes urine of varying amount and quality. The calices may be normal or bizarre, and the pelvis may be hydronephrotic or quite small and bulbous in shape. The ureter is usually normal. As a general rule

the kidney is too poor in function to excrete dye in sufficient concentration to give a picture after an intravenous pyelogram, so that a retrograde pyelogram is necessary to show the configuration of the pelvis and calices.

The hypoplastic kidney, like all other congenital abnormalities, is liable to become infected, and there may be repeated attacks of infection or a chronic infection which both macroscopically and microscopically alter the kidney. Histologically, the glomeruli are usually small and scanty; some may be hyalinized. The epithelial lining of the tubes is degenerated, and it may be difficult to distinguish the appearance from the atrophic changes brought about by pyelonephritis in a normally formed kidney. Lowsley (1944) states that almost every hypoplastic kidney causes pain and that nephrectomy is necessary to relieve it. In our case there were no renal symptoms, nor was there anything in the previous medical history to suggest that there had been.

The most widely accepted explanation of the cause of hypoplasia is that the foetal kidney, during some stage of its development, receives an inadequate blood supply. There is, in effect, an embryological ischaemia. The resulting peculiarity of formation is, of course, dependent on the time of development at which the deficiency in blood supply occurs.

In Case 3 the patient had malignant hypertension, and no evidence of a left kidney was found. It was considered just possible that the case might be one of renal aplasia, and, if so, that the rudimentary kidney could be responsible for the hypertension. After full discussion with the patient and her parents, and without offering other than a possible chance of relief, an exploratory operation was advised and undertaken, with negative result.

These cases illustrate the necessity for renal investigation in hypertension. In Case 1 the stone which was found could only have done harm to the kidney, and would have adversely affected the hypertension had it not been removed. The renal lesion was not the cause of the hypertension, and therefore surgical treatment directed to the calculus could be expected to be followed by only a temporary lowering of the blood pressure.

In Case 2 there was a dramatic fall in blood pressure after the removal of the affected kidney. So much so that the remaining kidney was temporarily thrown off its balance and failed to excrete for a period of 36 hours. Although the case was followed up for only a few months, after which time the patient returned to Argentina, there was no doubt as to the immediate effect of the surgical treatment. In the third case the exploratory operation was purely speculative and entirely unproductive.

It would appear that unilateral renal disease is not a common cause of malignant hypertension, but it does undoubtedly occur. Investigation of the renal tract must therefore always be considered. If a unilateral disease of the kidney is found it should be treated according to accepted urological standards, and operation should be performed with a view to treating the renal lesion rather than the hypertension. Treatment should not be refused because of high blood pressure or advanced cardiovascular disease. In some cases the dramatic beneficial effect of a nephrectomy will undoubtedly make justifiable surgical intervention in a poor-risk subject, and may prolong life or even effect a cure in an otherwise fatal disease.

Summary

Three cases of unilateral renal disease—calculus, hypoplasia, and agenesis—associated with hypertension are described.

Removal of the calculus did not materially affect the blood pressure.

Removal of the hypoplastic kidney produced a dramatic fall in blood pressure, and this remained low over the period of some months during which the patient was observed post-operatively.

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ARSENICAL ENCEPHALOPATHY

AN UNUSUAL CASE OCCURRING IN THE TREATMENT OF CONGENITAL SYPHILIS

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The onset of acute cerebral symptoms occurring during, and attributable to, organic arsenical therapy is a well-recognized but rare clinical condition.

Arsenical encephalopathy was first described by Almkvist (1911), Fischer (1912), and Kannengiesser (1912). Its incidence is given by various authorities as follows. Only 8 cases are recorded from 800,000 intravenous injections of organic arsenicals given to the British Army in the 1914-18 war (*Brit. Encyc. med. Pract.*, 1939). Glaser, Imerman, and Imerman (1935) estimate the mortality secondary to neurological involvement in standard arsenical therapy as 1 in 5,398. The incidence of arsenical encephalopathy is increased in the intensive treatment of syphilis; Stokes, Beerman, and Wammock (1943) estimate the mortality in the five-day treatment of syphilis as between 1 in 200/300. Rattner (1943) describes 481 cases of syphilis treated with 0.24 g. mapharside by intravenous drip given daily for 5 days, in which 3 cases developed cerebral symptoms without fatal result. Craige and Sadusk (1944) report 74 cases of early syphilis in which no cerebral complications occurred following the same course of therapy. However, Goldstein, Stolman, and Goldfarb (1943) give the incidence of arsenical encephalopathy as 1.3% in intensive mapharside therapy.

We should like to present a case of arsenical encephalopathy occurring in a young adult with congenital syphilis, in whom we adopted the treatment suggested, and used with much success, by Ransome, Paterson, and Gupta (1945).

Case Report

The patient, a soldier with no overseas service, was admitted to this hospital on March 12, 1946, for surgical treatment of a right inguinal hernia. His age was 20, his general condition and physique were satisfactory. On examination he was found to have a left interstitial keratitis and iridocyclitis, and he gave a history of "inflammation of the eyes" for the past nine years. The Wassermann and Kahn reactions were both positive on two occasions in March, 1946. The hernia was treated successfully by radical surgery, and the following antisyphilitic therapy was adopted.

Local treatment consisted of subconjunctival injections of penicillin (500 units per ml.), penicillin drops, 2% atropine drops, and hot bathings. Systemic treatment was started on March 14 with 3-hourly intramuscular injections of penicillin—a total of 1.7 mega units being given. Arsenical therapy was begun on the 30th, 0.3 g. neoarsphenamine being given twice weekly for 5 weeks, ending on May 10. A second similar course was started on July 5, the fifth injection of 0.3 g. neoarsphenamine being given on the 19th. There had previously been no toxic reaction of any kind, and the eye lesions were slowly improving.

On July 20 he complained of malaise and frontal headache, which lasted until the next day, when he developed epileptiform convulsions. The aura (elicited on later questioning) consisted of "spots before the eyes." He fell on to his back, uttered a cry, and became unconscious. He then developed generalized spasticity with opisthotonos, and became deeply cyanosed. This stage lasted about a minute. It was followed by generalized clonic movements lasting 4 minutes and accompanied by severe tongue-biting and incontinence of urine and faeces. Consciousness was regained after 30 minutes, but he had no recollection of the attack except for the aura. Six similar convulsions occurred during the night, and

between these he remained semicomatose and vomited profusely. He was first seen by us while he was having these fits, and thereafter was under our care.

On examination (July 21) the patient was comatose. All tendon reflexes were absent, and the abdominal reflexes could not be elicited. There was a bilateral extensor Babinski response, but no ankle or knee clonus. There was no neck rigidity or Kernig's sign. He had a conjugate deviation of the eyes to the right; the right pupil reacted to light, but the left pupil was dilated under the therapeutic influence of atropine. The blood pressure was 135/90. No physical signs were found in the other systems. The urine contained no albumin, sugar, or acetone bodies. There was no evidence of purpura, other skin lesions, or jaundice. On lumbar puncture the C.S.F. was under 90 mm. pressure; there was no spinal block and the fluid was clear and colourless; 2 lymphocytes per c.mm., 170 mg. protein per 100 ml., 708 mg. chloride per 100 ml.; Lange curve, 012355544; culture sterile; Wassermann reaction negative. The blood sugar was 117.6 mg. and the blood urea 47.1 mg. per 100 ml. The haemoglobin was 110%, R.B.C. 6,000,000, W.B.C. 11,600 (polymorphonuclears 71%, lymphocytes 23%, monocytes 6%). No malarial parasites were found in the blood on thick and thin films.

A provisional diagnosis of arsenical encephalopathy was made, and treatment was adopted on the lines suggested by Ransome *et al.* (1945). They stress the prevention of cerebral oedema by postural nursing by keeping the patient's spine erect, repeated lumbar puncture, calcium thiosulphate, calcium gluconate, vitamin C, and adequate fluid intake. Our patient was sat up in a vertical position, given 1 ml. of adrenaline (1 in 1,000) and 1 pint (568 ml.) of 20% glucose by slow intravenous drip in an attempt to prevent cerebral oedema. Calcium thiosulphate 0.6 g., 10 ml. of 10% calcium gluconate, and 500 mg. of vitamin C were each given intravenously at 6-hourly intervals for the first day and then daily. Fluids were given *ad lib.* by an intranasal Ryle's tube.

The next day (July 22) the coma gradually deepened and he became cyanosed. There were no signs of congestive heart failure, and venesection was not indicated. Continuous nasal oxygen was given. On the 23rd he was sweating profusely and in deep coma. There were slight neck rigidity and a doubtful Kernig's sign on the right. He had marked twitching of the right arm and leg, and the extensor responses were still present. The temperature had risen to 104° F. (40° C.). One pint (568 ml.) of isotonic glucose-saline was given by slow intravenous drip to combat slight dehydration. Lumbar puncture was repeated. The C.S.F. was clear and colourless, and the pressure was 90 mm. There were 7 cells per c.mm. (equal numbers of polymorphs and lymphocytes), and the protein was 110 mg. per 100 ml.; Lange curve, 0123455433; chlorides, 727.5 mg. per 100 ml.; culture sterile.

On the 24th the coma was much deeper, the cyanosis more marked (despite oxygen therapy), and he was breathing stertorously. The pupils were fixed to light, and there were slight neck rigidity and a bilateral slight Kernig's sign. All deep tendon reflexes were absent, and there was still a bilateral Babinski response. The temperature had risen to 105° F. (40.6° C.), where it remained until his death early on the 25th.

Necropsy was performed by Prof. P. L. Sutherland, who reported that the cerebral convolutions were slightly flattened and the superficial cerebral vessels congested. The ventricles of the brain contained a little blood-stained fluid and the choroid plexuses were deeply congested. Numerous petechial haemorrhages were found on the visceral pleura of both lungs, and there were signs of a terminal bronchopneumonia. The liver and kidneys were normal in appearance and also histologically. Histological examination showed slight thickening of the pia mater. The vessels of the basal ganglia were unduly prominent and some appeared to be thrombosed. There was slight focal demyelination, but no other evidence of cerebral lesions. Obermiller (1913) and Stühmer (1919) state that there may be no pathological changes in arsenical encephalopathy other than cerebral congestion and oedema. The characteristic lesion, however, in this condition is multiple plugged capillaries with petechial haemorrhages and surrounding necrosis and demyelination (Russell, 1937; Strauss and Globus, 1930; Alpers, 1928).

Differential Diagnosis

We consider this case to be one of arsenical encephalopathy, for the following reasons. There was no personal or family history of epilepsy; there was no previous evidence of cerebral syphilis, and it is very unlikely that he would develop the first signs of this after starting treatment with penicillin and arsenic and in the presence of a negative C.S.F. Wassermann reaction. The blood pressure and blood urea were normal and there was no albuminuria, thus eliminating hypertensive encephalopathy and uraemia. The blood sugar was normal, and there was no glycosuria or acetonuria, ruling out diabetic coma or spontaneous hypoglycaemia. The patient did not have any other