SYPHILITIC NEPHRITIS.

BY

G. B. DOWLING, M.D., M.R.C.P.,

DERMATOLOGIST, WEST LONDON HOSPITAL; PHYSICIAN IN CHARGE OF
SKIN DEPARTMENT, MILLER GENERAL HOSPITAL; MEDICAL OFFICER,
VENEREAL DISEASE DEPARTMENT, GUY'S HOSPITAL.

WHEN the patient whose case is about to be described first presented himself for treatment the renal condition was not fully investigated. The results of such investigations might have been of interest in the light of his subsequent history, but even without them the facts are sufficiently striking to make them worth recording.

A watchman, aged 56, came to the venereal disease department in 1922, suffering from tertiary ulceration of the soft palate and fauces and from chronic nephritis. He stated that he had been discharged from the police force some four years previously on account of chronic Bright's disease, which had started in 1917, when he was 51 years of age. He had remained in the police force for about a year after the onset, but having been laid up for three months during that period, and being chronically unfit the whole time, he was ultimately discharged. After leaving the police force he was able to do light work, but was never really well. He suffered from intermittent oedema of the legs and ankles, and backache as well as giddiness. In 1922 he was laid up for three months with an exacerbation, and the tertiary ulceration of his palate developed at this time. On the day he first attended the department he presented fairly extensive ulceration of the soft palate and fauces. He looked grey and ill; the legs were moderately oedematous and the urine contained a heavy cloud of albumin. A note of his name and address was made on this occasion with a view to having him admitted to the hospital in order to have the renal efficiency investigated and to try and estimate whether he would be likely to tolerate a course of antisyphilitic treatment. Fortunately, in a sense, this turned out to be unnecessary. The Wassermann reaction was strongly positive.

It was decided to start gentle treatment for syphilis immediately and to observe the condition of the urine at each attendance. He returned a fortnight after the first dose (0.3 gram of silver salvarsan) to say that he felt much better in every way. The oedema had practically gone and the urine contained only a trace of albumin. After the second dose he returned to work feeling quite well. That was two years ago. He has never looked back, and has not had another day's illness.

He has had two full unit courses of antisyphilitic treatment—the first consisting of ten doses of 0.3 gram of silver salvarsan, the second of four doses of sulphoxyl salvarsan; the treatment was given in combination with iodide, but not with mercury. When I examined him recently he looked a healthy man, and had a ruddy complexion. The heart was not enlarged and there were no murmurs. The arteries were not unduly thickened for his age. The blood pressure was 130 (systolic); the lungs were emphysematous to a degree compatible with his age and build. The urine contained neither albumin nor casts. The blood urea was 0.25 per 1,000—a normal figure. The Wassermann reaction was still strongly positive.

But for the circumstance that this patient developed tertiary syphilitic ulceration of the fauces, the true nature of the renal affection would never have been diagnosed. Acute syphilitic nephritis occurring in the secondary stage presents well defined clinical features. It is a rare accident of syphilis. Fournier¹ in his treatise (1906 edition) mentions twenty-six cases. Since our clinic was established (1917) only one case has been recognized. It was published by Rawlins² in 1919.

Several isolated cases of acute syphilitic nephritis have been published from time to time. All bear a striking resemblance to one another. The usual time for the appearance of the condition is the second month. More than a third of the cases, according to Fournier, occur during this month, and later observers state that it almost invariably accompanies the acute exanthematous stage of the disease, but may occur earlier or later. Talamon's case, quoted by Fournier, occurred a few days after the appearance of the chancre in a woman of 21. The albumin content of the urine was 32 parts per 1,000; it disappeared without treatment in a few weeks. Fournier quotes a case of his own in the pre-roseola stage; the albumin disappeared quickly under mercurial treatment. Cases may occur as late as the second half of the first year of infection. Fournier had two fatal cases in this period.

The symptoms do not differ from those of nephritis due to other causes; the patients have oedema and backache, but little or no headache as a rule; occasionally early uraemia is observed. The most striking feature, however, is the very abundant albumin. Fournier quotes a case of his own with 110 grams of albumin per litre. Other observers

have found amounts varying from 10 to 100 parts per 1,000. Casts of all kinds may be present—epithelial, granular, and waxy, and some with fatty droplets. Munk described doubly refractile lipid granules in the casts. Other observers¹³ have confirmed this, but Munk stated that he found similar droplets in cases of nephritis due to causes other than syphilis, though less constantly, and it is doubtful whether the observation is of much importance from a diagnostic point of view. Bernard and Widai found that renal permeability was not much impaired according to the methylene blue test. This has been confirmed by other observers, especially in America; with the phenol-sulphonaphthalein test almost normal figures were obtained, even when the damage to the kidneys, to judge by the symptoms and the condition of the urine, must have been severe.

Fournier states that besides the more serious cases of acute parenchymatous nephritis, benign cases, without general symptoms and of short duration, occur; albuminuria may be the only symptom even when it amounts to 10, 20, or 30 grams per litre. In other cases albuminuria is accompanied by facial oedema, or a little oedema of the ankles. These cases yield easily to treatment, but there may be recurrences. Such cases are not to be confused with the slight transient albuminuria often found in the acute secondary stage of syphilis. Fatal cases, according to Fournier, are rare if the mild cases are counted with the grave ones. Many of them clear up, like the rash, without treatment, and many of them must pass unnoticed. But some of them pass on to the chronic stage or recur in later years.

The most striking feature of the later cases published is the remarkable effect of a single dose of salvarsan or of its substitutes. The effect is instantaneous. The case that attended this clinic in 1917 was a young woman under the care of Dr. Morna Rawlins.² She was pregnant and was in the florid stage of secondary syphilis. The urine contained 7 parts per 1,000 of albumin. After one injection of disodoluargol the albumin rapidly disappeared. She has been seen from time to time and her recovery has proved to be complete.

Elliott and Todd³ published a case in a man, aged 30, with 7 per cent. of albumin in the urine, with comparatively few casts and almost efficient permeability according to the phenolsulphonaphthalein test. This case responded promptly to treatment with arsphenamin. Day⁴ reports the following very typical case.

A man, aged 20, presenting a secondary syphilitic eruption. His symptoms were anorexia and occasional vomiting, followed a week later by extensive oedema. The urine was scanty, and contained 15 parts of albumin per 1,000 and numerous casts. Improvement began within a few hours of a dose of 0.45 gram of novarsenobillon. It was accompanied by diuresis; this continued for a fortnight, during which time the patient lost 3 st. in weight.

Cole⁵ records the case of a man, aged 26, in the secondary stage. The urine became solid on boiling; it contained many granular and hyaline casts, but, he states, few compared to the amount of albumin. The excretion of phenol-sulphonaphthalein was 40 per cent. in the first hour, 20 per cent. in the second. The albumin practically disappeared the day following a dose of arsphenamin and totally disappeared on the second day.

Fournier¹ describes the *post-mortem* and histological appearances in his two fatal cases.

The kidneys were large, being increased both in volume and weight. The capsule stripped easily; the surface was a little granular. The cortex was thickened, pinkish-grey, and of firmer consistence than normal. The pyramids were enlarged and congested. The changes were more marked in one kidney than in the other. Both cases presented the appearance commonly known as large white kidney. The histological changes were purely epithelial, with fatty degeneration of the lining cells of the tubules. He quotes from Dieulafoy a case with purely epithelial changes, swelling, and loss of nuclear staining, and degeneration of epithelial cells obstructing the lumen of the tubes; the lesions predominated throughout in the convoluted tubules.

Le Play and Sézary⁶ demonstrated *Spirochaeta pallida* in acute secondary syphilitic nephritis.

The patient was a man, aged 45, who in the first months of syphilitic infection presented anasarca, headache, digestive trouble, and a large amount of albumin in the urine (12 grams per litre). Mercurial medication brought about amelioration of the condition

and a notable diminution of the albumin. At the end of a month, however, treatment failed, and the patient died of uraemia. At the autopsy the large white kidney was found. Histological examination showed lesions of nephritis predominating in the convoluted tubules. The cells were partly or totally destroyed, and the lumen of the uriniferous tubules obstructed by cellular or granular casts, or with albuminous coagulum. By silver impregnation numerous spirochaetes were demonstrated, most often in the casts or albuminous coagulum, but some also in the cells of the convoluted tubules not yet desquamated.

It is clear that in acute secondary syphilitic nephritis we have a well defined condition, with constant urinary and clinical symptoms, affording a definite pathological and histological picture. It may, I think, be described as an allergic phenomenon, the intensity of the reaction of the kidney being part of the supersensitive condition of the patient's tissues at this stage of syphilis, so well illustrated by the exanthematous response of the skin.

The well defined clinical and urinary symptoms presented by acute syphilitic nephritis occurring in the secondary stage are altogether lacking in nephritis due to syphilis of the tertiary period. The symptoms and condition of the urine give no hint that the renal condition is syphilitic in origin. Although numerous statistics are on record showing the incidence of clinical tertiary syphilis or of a positive Wassermann reaction only, without clinical evidence of syphilis, in chronic nephritis, no absolute test can be applied to prove the syphilitic origin of the renal condition. Most of the statistics were made out before salvarsan came into use.

Fournier, in 5,335 cases of syphilis, records 54 with renal affections. Lian and Vernes,⁷ in 8 cases of chronic nephritis, found a positive Wassermann reaction in 2 out of 5 cases under 50 years of age. Letulle and Bergeron,⁸ out of 46 cases of chronic nephritis, found 12 with a positive Wassermann reaction. Various series of autopsies are quoted by Fournier; Bamberger, out of 2,430 autopsies, found 49 with renal syphilis. Lancereaux, in autopsies on 24 syphilitics, found diseased kidneys in 8. Spiers, in 220 autopsies, 123. These figures include amyloid disease of the kidney, which no doubt was commoner in those days than at the present time.

Fournier was of opinion that with the exception of gumma, which is decidedly rare, there is nothing specific about the pathological anatomy of chronic nephritis due to syphilis. He points out that, though a gumma may be recognizable as such, the sclerotic changes resulting from a gumma may often be indistinguishable from interstitial changes due to other causes. He describes two main types of anatomical change.

(1) A chronic diffuse parenchymatous nephritis resembling the common large white kidney. Histologically this kidney shows granular and fatty epithelial degeneration (most marked in the convoluted tubules), glomerulitis with proliferation of the epithelial lining of Bowman's capsule, and cellular infiltration in the interstitial connective tissue. Such cases later show more marked glomerular and interstitial changes and a late atrophic stage.

(2) A chronic nephritis with atrophy, sclerous induration, and scars. This condition has its origin in specific arteritis, and cannot be regarded as a primary disease of the kidney.

Amyloid disease of the kidney is often combined with chronic nephritis.

Faroy⁹ succeeded in demonstrating spirochaetes in a kidney of this kind.

He examined the kidneys of a woman, aged 34, who died of amyloid disease of the kidneys and intestine. At the autopsy gummatous cirrhosis of the liver, amyloid kidneys, and a gumma of the stomach were found. Microscopical examination of the kidneys showed, besides amyloid degeneration, the presence of *Spirochaeta pallida*, few in number, and localized in the secretory tubules, generally in granular or hyaline casts which occupied their interior.

It is extremely probable that these late cases of the parenchymatous type owe their origin to an infection of the kidney about the end of the second incubation period. At this stage, as is well known, nests of spirochaetes may be deposited in almost every organ in the body. After this no further invasion of the tissues from the blood stream takes place. The immediate result of this invasion of the tissue is usually the allergic response of the skin in the form of the rash, occasionally of other organs, such as the central nervous system, in the form of acute cerebro-

spinal syphilis, rarely of the kidney in the form of acute syphilitic nephritis. During the latent period which follows, the spirochaetes that have survived the first explosive reaction of the tissues lie dormant, often for many years. Where they light up, the response is of a different kind: the reaction of the tissues is not so explosive. The spirochaete is destroyed more slowly, the skin macule or papule of the secondary stage gives place to the gumma. In the same way lighting up of dormant infection in the kidney evokes now a less explosive response. There is less albumin, less oedema, fewer casts, and the clinical condition of the patient can in no way be distinguished from that present in chronic nephritis due to some other cause. The patient's age only may suggest the possibility of syphilitic origin, for such cases occur most commonly between the ages of 30 and 50.

It is evident that the crucial test must often rest upon the result of salvarsan treatment. I have succeeded in finding only two other cases in the literature that responded to treatment in the same way as that I have here described. Both were found to be syphilitic in origin by accident.

Schnabel's¹⁰ patient was a negro, aged 36, admitted as an in-patient with nephritis. The urine contained a heavy cloud of albumin and numerous hyaline and granular casts; there was a history of chronic illness for a year. The symptoms complained of were vomiting, abdominal pain, and nocturnal frequency. It was not suspected that this case was syphilitic, but the Wassermann test was applied as a routine procedure. The result was strongly positive. Arspenamin treatment produced immediate relief, and after three doses the urine yielded only the faintest trace of albumin.

The other case was reported recently by Barbosa.¹¹

The patient was a man of 62, in whom irreparable damage appeared to have been done to the kidney parenchyma; the symptoms cleared up immediately on being treated for syphilis.

On the other hand, Merklen and Heuyer¹² reported three cases of chronic nephritis in syphilitics in whom treatment with small doses of salvarsan produced no improvement. One of them died of cerebral haemorrhage.

Treatment, then, may not be successful in all cases. We may look for success in the chronic diffuse parenchymatous type, but hardly in the atrophic interstitial type due primarily to disease of the arteries. At all events, as Fournier and others have pointed out, syphilis is probably a far commoner cause of chronic nephritis than is generally believed.

REFERENCES.

- ¹ Fournier: *Traité de Syphilis*, 1906, p. 21. ² Rawlins: Ante-natal Treatment of Syphilis and Gonorrhoea, *Proc. Nat. Conf. on Infant Welfare*, 1919. ³ Elliott and Todd: Acute Syphilitic Nephritis, *Arch. Derm. and Syph.*, Chicago, 1921, N.S. 3, p. 534. ⁴ Day: A Case of Syphilitic Nephritis, *Lancet*, 1920, i, p. 1009. ⁵ Cole: Acute Syphilis of Kidney, *Amer. Journ. Syphilis*, 1920, 4, p. 46. ⁶ Le Play et Sézary: Constataion du Tréponème dans la Néphrite Syphilitique Secondaire, *Sem. Méd.*, 1911, 31, p. 523. ⁷ Lian et Vernes: Du Rôle Étiologique de la Syphilis dans les Aortites Chroniques avec ou sans Insuffisance Aortique et dans la Néphrite Hydrurique, *Presse Médicale*, 1914, 22, p. 204. ⁸ Letulle et Bergeron: Réaction de Wassermann et Syphilis Latente au cours des Cirrhoses et de Néphrite Chronique, *Presse Médicale*, 1912, 20, p. 777. ⁹ Faroy: Constataion de Tréponème Pâle dans la Syphilis Tertiaire du Rein, avec Dégénérescence Amyloïde, *Sem. Méd.*, 1911, 31, p. 238. ¹⁰ Schnabel: Syphilis of the Kidney, *Med. Clin. N. Amer.*, Phila., 1922-23, 6, p. 985. ¹¹ Barbosa: Syphilitic Chronic Nephritis, *Brazil Med.*, 1923, 2, p. 384; *Abstract Journ. Amer. Med. Assoc.*, 1924, 82, p. 504. ¹² Merklen et Heuyer: Néphrite Sèche et Syphilis, *Presse Médicale*, 1917, 25, p. 44. ¹³ Stengel and Austin: Syphilitic Nephritis, *Amer. Journ. Med. Sci.*, 1915, 12, p. 149.

TREATMENT OF DIABETES BY RAW FRESH GLAND (PANCREAS).

BY

R. CARRASCO-FORMIGUERA, M.D.,
BARCELONA (CATALONIA).

WHEN I read Dr. Hollins's paper¹ I planned to verify his contentions concerning the efficiency of raw fresh-pancreas in the treatment of diabetes. As soon as possible I conducted a clinical trial on a boy aged 7, who had been receiving insulin for some weeks. On account of some minute incidents—which occurrence, by the way, is illustrative of the numerous sources of error which, if not carefully looked for and eliminated, may vitiate any conclusions drawn from such experiments—it took a rather