A FATAL CASE OF SECONDARY SYPHILITIC NEPHRITIS: WITH REMARKS.*

BY

ARTHUR J. HALL, M.A., M.D., F.R.C.P.,

LECTURER ON PRACTICAL MEDICINE, UNIVERSITY OF SHEFFIELD;
PHYSICIAN, SHEFFIELD ROYAL HOSPITAL,

AND

J. M. BEATTIE, M.A., M.D.,

PROFESSOR OF PATHOLOGY, UNIVERSITY OF SHEFFIELD.

THE case which forms the subject of this paper was admitted to the Sheffield Royal Hospital on May 12th, 1910. The history of his illness may be divided into two parts. For the first of these, relating to the beginning of his illness, our thanks are due to Dr. A. McPhedran, Physician to the Toronto Hospital, for the very complete record so promptly and courteously sent in reply to our inquiry.

P., a chauffeur, aged 23, whilst on a visit to Canada in September, 1909, acquired a primary venereal infection. He was told that these were "soft sores." They healed completely, but he continued to feel ill. What treatment, if any, he then had is unknown.

On December 1st, 1909, his throat began to be sore. On January 4th, 1910, the legs began to swell, followed by swelling of the scrotum, and on January 16th his hair began to fall out. The same day he was admitted to the Toronto Hospital, under Dr. McPhedran. His condition then was, briefly, as follows: Temperature, 101° F.; enlargement of all the superficial lymph glands; general oedema of the whole surface; deep serpiginous ulcers on the fauces; a discrete macular rash; (?) mucous tubercle on the lower lip; urine 1014, albumen 0.2 per cent., no sugar, hyaline and granular casts abundant.

Treatment consisted of: (1) Free purgation; (2) intramuscular injections of mercury salicylate (1 grain) once a week; (3) potassium iodide, 5 grains thrice daily, increased by 5 grains per dose per week. On January 25th the oedema had almost disappeared, likewise the rash. He continued to improve, and on February 21st—that is to say, five weeks after admission—he left hospital against the advice of his physician. At that date the urine still contained 0.17 per cent. of albumen with a few hyaline and granular casts.

He returned to England in March, 1910. Soon after his arrival the dropsy returned, and he suffered from time to time from headache and vomiting.

On May 12th, 1910, he was admitted to the Sheffield Royal Hospital, suffering from general oedema, anaemia, oliguria, vomiting, and headache. Urine, specific gravity 1012, much albumen and considerable blood, many casts. He stayed in hospital until his death, twelve weeks later, and though the severity of individual symptoms varied from time to time, he steadily got worse.

Necropsy.

A post-mortem examination was made by one of us (J. M. B.) on August 10th, 1910.

Naked-eye Appearances.—The kidneys enlarged, the capsules strip easily, leaving a smooth surface, colour pale, stellate veins marked. The superficial cortex increased, being in the proportion to medulla of 1 to 1. On section a uniform yellowish colour, vascular markings obliterated; no amyloid change, no pelvic dilatation; no cysts; tissue firm and oedematous. Vessels slightly thickened at places. The lungs: Slight pleurisy at left base. Heart: Recent pericarditis; left ventricle hypertrophied; pale and fatty. Liver friable; slight atheroma of aorta; no gummata anywhere.

Microscopical Examination.

Kidney.—There are very extensive fibrotic changes both in the glomeruli and between the tubules.

Glomeruli.—The tuft in some of these appears to be hypertrophied, shows marked lobulation, and the space between it

and Bowman's capsule is more evident than usual. The majority of the glomeruli, however, show various degrees of fibrosis, the fibrous overgrowth affecting particularly the glomerular tuft and converting it eventually into a homogeneous fibrous nodule. Various stages in this process can be made out, the earliest forms showing an affection of the part of the tuft adjacent to the afferent arteriole. In a few of the glomeruli there is definite fibrous thickening of Bowman's capsule, this thickening gradually encroaching on and obliterating the capsular space and then extending to the tuft. This process, however, is not the common change, Bowman's capsule in most of the glomeruli showing little or no evidence of proliferation. The capsular space is usually well-marked, though irregular in shape, and often not completely surrounding the fibroid tuft.

Interstitial Tissue.—The fibrous tissue between the tubules, etc., is widely spread, irregular in its distribution, and specially marked in the periglomerular tissues. At some parts fairly cellular it is, however, on the whole well and fully developed fibrous tissue. Accumulations of small round (lymphoid) cells are found at places in the interstitial fibrous tissue, but this is not a marked feature of the condition.

Tubules.—These show very marked and irregular dilatation. The cells lining the tubules have assumed a cubical shape and show well-marked degenerative changes, mostly of the nature of cloudy swelling. A few tubules exhibit catarrhal changes, and in some casts are present.

Vessels.—Apart from the fibrosis in the glomerular capillaries, there are no marked changes in the vessels.

No amyloid degeneration could be detected. No spirochaetes were found in the liver or kidneys.

The following is a brief summary of his symptoms:

(a) **Vomiting.**—This was almost constant, and a troublesome feature of the case. Nothing seemed to give any relief. He thought at first it was due to the milk diet, and eventually solid food was tried, but it made little or no difference.

(b) **Headache.**—Was chiefly frontal and almost constant.

(c) **Dropsy.**—This remained considerable at all times, and increased towards the latter part of his life. The pitting over the thorax and abdomen was always great.

(d) **Urine.**—Specific gravity varied from 1010 to 1019. The quantity was always considerably below normal, but he sweated very profusely, not only in the hot-air baths but often at other times also.

(e) **Blood pressure** usually about 160 (max. systolic).

(f) **Temperature** normal throughout.

(g) **Fundi oculorum** normal.

It will be seen from the accompanying table that for the first seven weeks the daily quantity of urine remained much about the same—never quite regaining the height during the first week. During these weeks the pulse did not alter very much, and yet the rate was steadily and almost regularly rising by one beat per minute each week. This point comes out very clearly when an average for the week is taken in this way, and a slight quickening of the pulse, which can hardly be detected on looking at an oscillating chart, becomes by this means at once evident. About the eighth week the quantity of urine began to fall and the pulse to rise considerably. These were associated with the appearance of various local inflammations of the skin. In the ninth week the urine reached its lowest quantity and the pulse its highest rate. From then onwards the level of each, though slightly improving, never got back to its previous position. During the last week of life urine was passed unconsciously, and could not be examined or estimated quantitatively. The percentage of albumen shows no evident relationship to his quantity of urine or general condition. Blood was almost always present in the urine in variable small amounts. Hyaline and granular casts were always found, but there is no statement as to their quantity.

* Read before the Yorkshire Branch, British Medical Association, at Huddersfield, March, 1911.

Table showing the Daily Average (a) Quantity of Urine in c.cm., (b) Percentage of Albumen (Esbach's Albuminometer), (c) Total Albumen, (d) Pulse-rate, during the Patient's stay in Hospital.

Weeks:	1	2	3	4	5	6	7	8	9	10	11	12	13
<i>Daily Average.</i>													
Urine, c.cm.	700	650	485	510	510	650	610	478	275	425	364	385	(?)
Albumen, per cent.	(?)	0.58	0.72	0.75	0.52	0.53	0.75	0.74	0.71	0.82	0.65	0.50	(?)
Albumen, grams	(?)	3.75	3.55	3.79	3.18	3.46	4.75	3.51	1.89	3.53	2.41	1.56	(?)
Pulse-rate	78	79	80	81	83	82	88	107	110	108	101	101	107

The urine quantities were carefully measured daily and the daily estimation of albumen made from a sample of the mixed twenty-four hours' urine. The pulse-rate is from an average of four-hourly readings night and day.

General Progress.—Early in June a papulo-erythematous rash appeared in the axillae, elbow hollows, and groins, the sites of mercurial inunction. This spread over the trunk and limbs, was very irritable and peeled freely. A month later he became much worse, the dropsy increased, the tongue and lips became sore. The hands became tremulous, later the ears were sore and painful, conjunctivitis and inflammation of the nail-beds followed. On August 6th he became noisy and delirious, with insomnia, and he died comatose on August 9th, 1910.

TREATMENT.

Reference has been made in the history to the course of treatment adopted at the Toronto Hospital, which included five weekly injections of mercury salicylate and the daily administration of potassium iodide to the extent of 15 grains the first week and increasing by 15 grains daily in successive weeks. Between that date—namely, February, 1910, and his admission to the Sheffield Hospital in May, 1910—there is no information as to what, if any, treatment he had. Whilst in hospital he had (1) free purgation, (2) hot-air baths which produced free sweating and gave him considerable relief, (3) diuretics of various kinds, (4) medicines to allay vomiting, (5) mercury for considerable periods in the form of liquor hydrargyri perchloridi, inunctions, and intramuscular injections of sozoidal mercury.

Potassium iodide was tried but it increased the vomiting. This latter symptom was exceedingly troublesome throughout.

As regards diet, he was at first put on milk alone, but after a few days declined to tolerate this, and gradually various solids had to be added.

Amongst the renal complications which arise in connexion with syphilis one is the so-called nephritis syphilitica praecox. This is a severe nephritis of the early secondary stage, accompanying other secondary manifestations of a more common kind. Karvonen,¹ in an exhaustive study of renal syphilis, was only able to collect records of 20 cases of acute syphilitic nephritis in the secondary stage up to the time of his paper in 1900, and we have been able to find references to between 20 and 30 other cases published since that time. Of the 20 cases recorded by Karvonen 17 recovered completely, whilst 3 died. In those which recovered the beneficial effect of mercurial treatment was usually very quickly and strikingly apparent. Of the 3 fatal cases tabulated by Karvonen was one recorded by Engel-Reimers:²

A female, aged 23, who had been infected nine months before. She had oedema of the legs and albuminuria, and under anti-syphilitic treatment these diminished very rapidly. Uraemia set in four weeks after the beginning of treatment, of which she died. The kidneys were pale and large, with many punctate haemorrhages; cloudy swelling and fatty degeneration of the cortical epithelium; glomerulitis; thickening of capsule epithelium; round cells about capsules; in a few places complete destruction of glomeruli.

The second fatal case, recorded by Döderlein,³ was

A male, aged 19. Infected in spring, 1895; secondary symptoms six months later. Treated by calomel injections and mercurial pills. On December 4th, 1895: Pyrexia, papulo-pustulo-squamous syphilide, adenitis, ulcers of cheek and palate. Nine days later universal scarlet rash over whole body, jaundice; three weeks after, exfoliation and albuminuria; four weeks later, gastric pain, vomiting, anuria, drowsiness. Death six weeks after. *Autopsy:* Lungs interstitial pneumonia, liver hard, granular, with thickened capsule; spleen enlarged, indurated lymph glands, kidneys swollen with a subacute interstitial nephritis.

The third case, recorded by Dieulafoy and Sireday⁴:

A male, aged 26. Infection six months before. Treatment had been intermittent. Headache, nausea, albumen (30 per cent.). He was put on a milk diet, but this was followed by rapid development of oedema, ascites, oedema of lungs, and diarrhoea. With mercury inunction there was improvement for two weeks: The uraemic symptoms disappeared. Urine increased to 3,000 to 4,000 c.c.m. daily; albumen reduced to 3 per cent. Then the uraemic and other symptoms recurred, and proved fatal. *Post mortem,* large white kidneys with degeneration of epithelium and small-celled infiltration of tubules and glomeruli.

Of the cases which have been published since 1900, we have, unfortunately, been unable to refer to many of the original papers, but in the cases recorded by Courmont and Cade,⁵ Bonnamour,⁶ and Nordmann and Wies,⁷ it is stated that they were rapidly cured by mercury—in one of them (Courmont and Cade's case) "in spite of a period

of intoxication." In another case, published by Chauffard and Gouvaud,⁸ the title is "hyperacute secondary syphilitic nephritis, with fatal outcome in spite of mercurial treatment." Of the other cases, the title gives no clue as to details of treatment or result.

The term "nephritis syphilitica praecox" has been given to these cases. They may arise at any time from two months to two years or more after infection. In our case the interval was about three months. Osler and Gibson⁹ refer to cold as a possible exciting factor in some cases, and our patient himself attributed his attack to cold, for it began during the height of winter in Canada, where he had never wintered before, and he stated that he felt the extreme cold very severely.

The same authors¹⁰ give the following points as distinguishing an acute syphilitic nephritis, namely: "(1) The amount of urine is not diminished to the same extent as in other forms with the same amount of albumen; (2) that, in proportion to the amount of albumen, casts are rare; (3) that the general type of the disease affects the patient as a rule less than the other types."

We have given above a table showing the respective quantities of urine and albumen (by Esbach's method), and it certainly appeared that in this patient the quantity of urine was greater than one would have expected in an ordinary case with the same amount of dropsy.

As regards the relative quantity of casts there is no reliable information in this case, except that when in Toronto Hospital they were stated to be abundant.

The striking feature about this case seemed to be its obstinacy and the persistence of dropsy in spite of rest, diet, and active treatment.

As regards the question of specific treatment, the possibility of using salvarsan* did not arise, as the drug was not at that time on the market. Mercury and iodide of potassium were therefore alone available. Of these the latter could not be tolerated, as it produced troublesome vomiting, and the former, though administered by intramuscular injection, inunction, and by the mouth, failed to produce any evident improvement. It is possible that larger doses might have succeeded, as in Chauffard and Gouvaud's case, where it was given to intoxication; but, seeing that such a heroic therapeutics is not usually beneficial or desirable, but rather the reverse, in ordinary cases of syphilis, it seemed of even more doubtful value where the kidneys were already in a state of advanced disease.

It is probable that the fatal result was contributed to by the patient's own action in leaving the Toronto Hospital and travelling to England whilst still incompletely cured. The exposure which such a journey at such time of year must have entailed upon one in his condition no doubt made his prospect of recovery more remote. So clearly was this danger foreseen by Dr. McPhedran at Toronto, that the patient was required to sign a paper before leaving that institution, to say that he did so at his own request and against the strongly expressed advice of his physician.

In conclusion it may be asked: Was this a case of syphilitic nephritis at all? or, Was it merely a case of nephritis in a person suffering from secondary syphilis?

It is not possible to make any dogmatic statement from the data before us. There is no reason why a person suffering from secondary syphilis should not, just as much as any one else, suffer from a nephritis of non-syphilitic origin. The two conditions occurring together may be a coincidence. On the other hand, as we can see from the number of recorded cases, this coincidence is of by no means infrequent occurrence; moreover, such cases frequently recover completely on anti-syphilitic treatment when ordinary methods have failed. It is possible that a person suffering from syphilitic poisoning is more susceptible than a normal person to those unknown factors which determine a nephritis from "cold," and that therefore the syphilis does not act directly but only indirectly. A further possibility is to suppose that there was previously existing kidney disease, and that this was merely aggravated by the syphilitic infection. One can only say, in answer to this, that the patient was quite unaware of any previous kidney trouble of any kind, and that he was a young man. Moreover, in the records of Karvonen's cases this point is particularly inquired into, with negative results.

* A case has since then been referred to by Treupel, *Deutsch. med. Woch.*, No. 39, 1910, p. 1787, in which uraemia in a case of syphilitic nephritis was improved by salvarsan.

On the whole, therefore, we may fairly conclude that whatever its cause the kidney disease in our case began at or about the time the symptoms showed themselves, that is, within a few weeks of becoming infected. Whether syphilis was the actual or only the predisposing cause cannot be with certainty decided, but the fact that similar cases have from time to time been recorded, and have completely recovered under antisyphilitic treatment, suggests that the relationship between the two conditions is a close one.

List of Cases Reported since 1903.

1903. Colmayer: *Giorn. internaz. d. sc. med.*, Napoli, 1903, N.S. xxv, 22-24.
Mühlig: *Muench. med. Woch.*, 1903, 505.
Lauterbach: *Med. Bl.*, Wien, 1903, xxvi, 499.
Mantoux: *Bull. et mém. Soc. Anat. de Paris*, 1903, lxxviii, 500.
1904. Pousson: *Ann. méd. chir. du centre*, Tours, 1904, iv, 203.
Cléroutx: *Union méd. de Canada*, Montreal, 1904, xxxiii, 251.
1905. Malherbe: *Journ. des mal. cutan. et syph.*, Paris, 1905, xvii, 321.
Thiemann: *Muench. med. Woch.*, 1905, lii, 214.
de Rezende: *Brazil. med.*, Rio de Janeiro, 1905, xix, 486.
1906. Smith, H. J.: Two cases, *Med. Bull.*, Philadelphia, 1906, xxviii, 248.
Verrotti: Case with Hydropericardium, *Giorn. internaz. d. sc. med.*, Napoli, 1906, N.S. xxviii, 49.
1907. Verger and Lautier: *Journ. de méd. de Bordeaux*, 1907, xxxvii, 185.
1908. Ballagi: *New York Med. Journ.*, 1908, lxxxvii, 1240.
Bourignon: *Limousin méd.*, Limoges, 1908, xxxii, 4.
1909. Signorini: *Cesalpino Arrezo*, 1909, v, 152.

REFERENCES.

- ¹Karvonen: Die Nierensyphilis, *Dermatolog. Zeitschrift*, Band VII, 1900, p. 37, et seq. ²Engel-Reimers: *Monatsschr. f. prakt. Dermat.*, 1892, vol. xv, p. 485. ³Döderlein: *Munch. med. Woch.*, 1896, p. 976. ⁴Dieulafoy and Siredey: *Manuel de pathol. interne*, vol. ii, 1897, p. 139. ⁵Courmont and Cade: Nephritis Syphilitica Praecox Grave; Cured by Mercurial Treatment in Spite of a Period of Intoxication. *Bulletin Soc. Méd. des Hôp. de Lyon*, 1904, vol. iii, p. 289. ⁶Bonnamour: Néphrite syphilitique guérie par le traitement spécifique. *Lyon méd.*, 1904, vol. ciii, p. 830. ⁷Nordmann et Wies: Néphrite syphilitique secondaire guérison rapide par traitement mercurielle intensif. *Loire Médicale*, St. Étienne, 1908, vol. xxvii, pp. 273-278. (Discussion.) ⁸Chauffard and Gouvard: Hyperacute Secondary Syphilitic Nephritis with Fatal Outcome in Spite of Mercurial Treatment. *Internat. Clinic*, Philadelphia, 1904, 14, 8, iii, pp. 53-61. ⁹Power and Keogh Murphy: *System of Syphilis*, vol. iii. Visceral Syphilis, Osler and Gibson. ¹⁰Loc. cit.

THE VASOMOTOR SYSTEM IN TABES.

BY

HORATIO MATTHEWS, M.D.,

LATE HOUSE-PHYSICIAN SEAMEN'S HOSPITAL, S.E.

It is commonly recognized that the cerebro-spinal reflexes in tabes are always considerably impaired, but it is less generally known that similar perversions of functions are frequently present in the sympathetic system.

In investigating the functions of the sympathetic system it will be found convenient, if not physiologically accurate, to view this system as tripartite. (I) The pontine, which may be regarded as equivalent to the cerebral; (II) the spinal sympathetic chain equivalent to the spinal cord; and (III) the visceral terminations corresponding to the peripheral endings of the cerebro-spinal system.

I. The Pontine.

An interesting case is recorded¹ in which a condition of generalized capillary extravasation of blood in a tabetic was present, while it is worthy of mention that Professor Pal claims that the gastric crises of tabes are, as a rule, pontine vasomotor phenomena. He says the crises are invariably associated with a rise of arterial tension due to spasm of the peripheral vessels of the viscera. The heart also beats rapidly.²

II. Spinal Sympathetic.

As would be expected, the areas of the body involved in pathological changes in these regions are extensive. The following are the chief:

(a) *Oedema*.—The extremities are chiefly affected, either symmetrically or otherwise. It sometimes strongly suggests renal or cardiac disease; it may recur in the morning after disappearing at night, and is of variable duration, often only a week or two. R. Birnbaum records a case in which enormous oedema of the lower limbs and vulva, with extreme distension of the bladder (175 oz.),

complicated a four months pregnancy without obvious reason, until tabes was discovered.

(b) *Extravasations of Blood*.—Spontaneous bruise-like marks are not uncommonly observed, usually of a greenish-yellow colour and about the size of a shilling-piece. Straus describes them as "beginning with a bright red colour, passing through the various shades of brown, green, and yellow, until they finally fade altogether."³ But one would only expect this classical sequence of events with a superficial bruise.

(c) *Vaso-constriction*, as evidenced by anaemia, or blanching of the part, may affect merely the extremity of the limb, as in the case of "dead fingers," or actually the whole limb, sometimes producing a most alarming deadly-white appearance, lasting several minutes, to perhaps hours. Also the feeling of coldness in a part, and the "shiverings down the back" indicate the presence of vasomotor constriction, inasmuch as heat and cold sense disturbances are not present. Pembrey writes:

Shivering appears to be a response to the cooling of the sensory nerve endings produced by the marked constriction of the cutaneous arterioles, for external heat will abolish it.⁴

Coldness of the extremities is a common feature of tabes, even in warm climates. Capillary stasis, resembling senile peripheral endarteritis, or the condition termed erythromelalgia, precedes the occurrence of lightning pains in the vicinity at times. Indeed M. M. G. Guillan and J. Troisier record a case in which practically the whole surface of the body was involved in a manner typical of cadaveric lividity. Compression of the affected cutaneous areas induced a zone of "white asphyxia," gravity exerted a marked influence. The patient suffered constantly from cold extremities.⁵

III. Peripheral Vasomotor Disturbances.

(a) The application of cutaneous warmth. Merely enveloping the limbs in the bedclothes is often sufficient to produce a high degree of vaso-dilatation; a feeling of heat and distension is hence especially complained of after first getting into bed. In others immersion in a warm bath would produce a red suffusion of the whole skin.

(b) The application of cold produces the reverse effect. Merely exposing the chest will frequently induce an extensive cutis anserina.

(c) Since the vascular reactions consequent on stroking the skin with the finger-nail, which in certain instances produce the familiar *tache cérébrale*, are somewhat indefinite even normally, it would be unsafe to attribute any but the most striking results to a pathological condition. Persistent, intensely anaemic streaks result in tabes at times; while, on the contrary, in some instances hyperaemia is rapidly induced with the slightest stimulation. Indeed, numerous differences are presented; sometimes alternating hyperaemic and anaemic areas bound the streak, at other times dermatographia, and sometimes, but rarely, oscillatory vascularization. At the meeting of the Société Médicale des Hôpitaux de Paris, February 8th, 1909, M. C. Tinel called attention to the phenomenon known to French clinicians as the "white line" in the diagnosis of pathological conditions of the suprarenal bodies. M. Sergent, who first described it in 1903, found it also in septicaemia, the septic fevers, influenza, etc. At that time it was thought to be of important clinical significance in Addison's disease. Its presence in tabes and other conditions must undoubtedly modify these conclusions.

(d) The effect of trauma also on the peripheral vasomotor system is well illustrated in those numerous cases of spontaneous fracture or fragmentation in a joint which are so often associated with an otherwise alarming and bewildering state of oedema. A case is quoted by M. Touche in which an unguarded diagnosis led to a deep and extensive incision for pus.⁶ Such violent oedematous reactions also arise from toxic conditions, and should not be allowed too much scope in the prognosis, inasmuch as considerable subsidence follows immediately on rest.

Cases.

The following are notes of two cases out of an extensive series of cases from which the above conclusions are drawn:

A. K., seaman, aged 41, was subject habitually to cold feet and general coldness at night, and often could not keep warm