Observations

ON

TRENCH NEPHRITIS, ITS LATER STAGES
AND TREATMENT.

BY

J. MICHELL CLARKE, M.D., F.R.C.P.,

LIEUT.-COLONEL R.A.M.C.(T.),

SOUTHMEAD SECTION, 2ND SOUTHERN GENERAL HOSPITAL;
PROFESSOR OF MEDICINE, UNIVERSITY OF BRISTOL.

This paper deals with cases of nephritis in a base hospital, the initial stage being over. All the patients came from France, except about six from Salonica, who showed no special features. The cases were taken in order of admission without selection. They were all under my immediate observation, and eighty cases seemed a sufficiently large number to represent the chief features of the disease.

The occurrence of nephritis on the large scale of the present war has afforded an opportunity of studying the first attack of the primary disease in young adults, which rarely occurs in civil hospitals, because in them the majority of cases of nephritis are exacerbations of a pre-existing disease. One would therefore be prepared for possible variations in the course and symptoms of the disease from those met with in civil practice, and possibly even for a new clinical type of nephritis, either as the result of the unprecedented physical conditions under which the men were placed and of a diet which mostly contained a relative excess of protein, or as the result of infection by a specific micro-organism. At the stage in which these cases were seen it seemed too late to make it worth while to carry out bacteriological investigations. The general result seems to point to a diffuse nephritis, chiefly affecting the convoluted tubules, focal in distribution in the kidney, and presenting a corresponding clinical syndrome with some special but no absolutely distinctive features.

In view of the youth of most of the patients, it might be expected that some cases classed as nephritis would in reality turn out to be examples of "functional albuminuria" or "albuminuria of adolescents," but this was not the case, and, speaking generally, this form of albuminuria has hardly been seen at this hospital throughout the war.

Taking the 80 cases admitted to the hospital with the label "nephritis," there were only 6 in which the diagnosis was at fault, and in which the patient was suffering from some disease with secondary albuminuria.

The remaining 74, for convenience of reference, are placed in four groups:

I. Thirteen cases in which there was either a distinct history of a previous attack of nephritis or definite signs of an affection of the kidneys of some standing.

II. Ten cases in which the nephritis was found to have cleared up on admission, though the symptoms of an attack before admission were quite definite.

III. Nineteen cases which completely recovered in hospital and were discharged cured.

IV. Thirty-two cases which left this hospital not cured, though the majority were greatly improved.

CAUSATION.

With regard to causation: In Group I, five, probably six, patients had had attacks of nephritis at some antecedent time, and one gave a family history of Bright's disease; four patients had had scarlet fever severely, two recently, one diphtheria followed by general anasarca, and four were either painters or plumbers before the war. In Group II, two had had scarlet fever, one recently, one trench fever shortly before, and one diphtheria three years before. In Group III, one had had scarlet fever, three bronchitis, and two malaria shortly before. In Group IV, three had scarlet fever in childhood, two diphtheria, four had recently suffered from malaria, but not severely, and in one the affection of the kidneys followed pneumonia eighteen months before. Twelve patients attributed the illness to standing in cold water, and four admitted alcoholism.

In three the illness began with a sharp attack of bronchitis, in two with pneumonia, in one with pleurisy and bronchitis, and in two with an attack of malaria.

There was no case in which the nephritis came on directly after being "gassed," and very few of the patients had been "gassed" at any time.

AGE.

The average age of the patients in Group I was 31.8 years; in II, 24.9; in III, 27; and in IV, 31.7 years. Those in Groups II and III, with early recovery, were thus decidedly younger than the others. Length of service appeared immaterial both to the incidence of disease and to its severity.

ONSET.

The onset in nearly all appears to have been sudden, and oedema of the face and limbs, with pains in the back, and dyspnoea the chief symptoms; the latter was only partly accounted for by the frequency of bronchitis. Oedema at onset was present in 57 out of 74 patients. Haematuria, generally slight, occurred in many.

LATER SYMPTOMS.

The chief symptoms of the disease whilst in hospital were oedema, most often of the face and limbs, much less often general anasarca; as a general rule oedema showed a disposition to clear up fairly quickly, but in bad cases was, of course, persistent, sometimes for many weeks, and in a few attended with ascites and pleural effusion; dyspnoea, often but not always associated with some bronchial or pulmonary complication; pains in the limbs and back, headache, less frequently vomiting, only occasionally diarrhoea, a feeling of great prostration, and sometimes mild cyanosis; anaemia was only present in the more severe cases and uraemic fits in one only.

Changes in the Cardio-Vascular Apparatus.

The changes in the cardio-vascular apparatus are summarized in the table. The greater frequency of all cardio-vascular changes in Group I, where there was evidence of past kidney trouble, is to be noted, also that the blood pressure affords a fair index of the severity of the case. The pulse pressure seems a little large in all, and especially in the severe cases.

Table showing Changes in Cardio-Vascular System.

	Hypertrophy of Left Ventricle.	Thickened Arteries.	Alteration in Heart Sounds.	Retinal Changes.	Average Blood Pressure in mm. Hg.		
					Systolic.	Diastolic.	Pulse Pressure.
Group I (13 cases) ...	5	5	11	5	147.9	90.8	57.1
Group II (10 cases) ...	0	0	5	0	123	76	47
Group III (19 cases) ...	0	0	9	2 (14)	131	83.7	47.3
Group IV (32 cases) ...	8	7	23	8 (29)	143	91.2	52
Total (74 cases) ...	13	12	48	15 (66)			

In most cases several observations on blood pressure were made. The highest systolic pressure taken was 198 mm. Hg. and the lowest diastolic 65 mm Hg. The figures in brackets indicate the number of cases in which the particular symptom referred to was investigated. The blood pressure was taken in 10 cases in Group I; in 6 cases in Group II; in 13 cases in Group III; and in 29 cases in Group IV.

The blood pressure was estimated by the auscultatory method with French's sphygmomanometer, and the diastolic pressure was taken as the point of disappearance of the loud third sound. The changes in the heart sounds consisted of a ringing or accentuated aortic second sound, with occasionally a systolic murmur or reduplicated first sound at the apex, and except in Group I displacement of the apex-beat outwards, when present, was never great.

The retinal changes comprised two cases with intense retinitis, optic neuritis, numerous haemorrhages and yellow-spot changes—both died; one of mild optic neuritis, who also died; three of mild oedema of the optic disc; two of pallor or oedema around the disc, and five of decided thickening of retinal arteries (one "silver wire" in a painter at 41). No other instance of retinal haemorrhage was noted.

Urinary Changes.

The quantity of urine was generally small for some days after admission; in severe cases 10 to 20 oz. a day.

Later the quantity varied from 30 to 60 oz. a day, and was sometimes larger. Exceptionally the amount passed was small throughout, and some of these cases did quite well. Quite apart from treatment, there were periods of increased diuresis, as occurs in most forms of nephritis. An increased quantity of water did not always carry with it any considerable increase in the daily amount of urea.

The specific gravity of the urine was, generally speaking, low, the average being from 1015 to 1018, often below 1015, rarely over 1025, and fixation of specific gravity was seen in the more severe cases.

The quantity of albumin was often very large on admission, but in most soon diminished. In Group I on admission the average amount in 9 cases was 0.89 per cent., and in 3 a trace, and on discharge in 4 a trace, in the rest 0.26 per cent.; in Group IV the average quantity of albumin on admission in 22 cases was 0.46 per cent., in others a large to a small trace, and on discharge from 0.1 per cent. to a faint trace (Esbach's tubes).

Urinary casts were numerous on admission in most cases, except the mildest, and very abundant in the severe ones. They consisted generally of the epithelial, hyaline, and granular varieties, and fatty casts were rarely seen. In cases that recovered, the casts rapidly diminished, but were very persistent in small numbers. These statements apply to centrifugized urine.

Decided haematuria in hospital was exceptional; in many cases the urine was smoky on admission and for a short time afterwards, and this condition was apt to recur occasionally; in still more the only evidence of blood was microscopic.

With regard to the nitrogenous excretion, in 4 cases in Group I, several estimations in each, the nitrogen excreted as urea was 53 per cent. of the total nitrogenous intake; and in 10 cases in Groups III and IV, several estimations in each, the average excretion was 67 per cent. of the intake. Urea was estimated by the hypobromite method, as more exact methods were not available. These cases may be taken as typical examples of varying degrees of severity.

As to excretion of NaCl, the amount in the food would vary from 4.5 to 6 grams a day; on the whole there was a deficiency in excretion of NaCl, but not to any great degree; it was most marked in severe cases and on admission, and improved as the case improved.

Thus in Group I the average excretion of NaCl was 4.9 grams a day (average of 5 cases with several estimations in each), whilst in a fatal case it was only 3 grams a day, and in Group IV the average excretion in 5 severe cases was nearly the same, 4.7 grams; and in 7 less severe cases it was 7.9 grams a day. In 3 of these it was at first as low as 1.5 to 2.2 grams.

Before estimations of urea and NaCl were made, the patients had been on a fixed diet of known quantity for some days. Three teaspoonfuls of salt were given in water to two cases of average severity and the excretion in the subsequent twenty-four hours was 10 and 12 grams respectively.

Phenol-sulpho-naphthalein tests were made on several occasions, and although in severe cases elimination was practically *nil*, unfortunately I can make no positive statement on this point, as the drug used was afterwards found by control tests to have deteriorated.

DURATION OF ILLNESS.

The average duration before admission to this hospital was two to three weeks, and that of the whole illness until the cases were sufficiently recovered for discharge was, in Group I, 9.6 weeks, in Group II (convalescent on admission) three weeks, in Group III (recovered in hospital) 6.8 weeks, and in Group IV, 8.1 weeks.

RESULTS.

The results were far worst in Group I; of these 13 cases, 1 died, 5 were discharged *in statu quo*, 5 showed some improvement, and in 2 only had the albumin and casts disappeared, and they might be considered well. Groups II and III are composed of cured cases. Of 30 cases in Group IV, 2 died, 3 were discharged not improved, 5 with casts and a considerable amount of albumin in the urine, and 12 with only a faint trace of albumin, or on some days none, and with a few casts present at intervals. The last 17 patients were sent to auxiliary hospitals and subse-

quent inquiry has elicited that 5 have fully recovered, 6 are much better and doing light work, and 2 unchanged.

To sum up: Of 68 patients, 3 died, 8 were discharged slightly improved as permanently unfit, 11 much improved but the urine contained casts and more than a trace of albumin, 6 fairly well and able to do light work, and 32 recovered completely; of 8 patients I have not sufficient information. It has already been pointed out that the younger patients gave the highest proportion of recoveries. It may also be noted that the only two cases in which there was intense retinitis and the only one with distinct optic neuritis died.

Ultimate Prognosis.

I think that in those cases who left the hospital with urine free from albumin and casts, with a kidney functioning well, with a normal blood pressure and without signs of any cardio-vascular impairment, it is reasonable to expect a permanent cure, provided they are not placed under too unfavourable conditions. Probably the same may be said for those in whom the above conditions obtained, with the exception of a faint trace of albumin, and results of inquiry as to the subsequent condition of several of them support this view. If, as is probable, the nephritis is of focal distribution in the kidneys, persistence of a trace of albumin and a few casts in the urine may be attributed to the slow healing of a focal patch, the rest of the kidney being unimpaired, and the condition may be expected to clear up in time, though for this it is obviously essential that the patient should lead a careful life.

If there have been previous attacks of nephritis or evidence of pre-existing (to the attack) cardio-vascular-renal changes, then it is unlikely that the patient will completely recover.

With regard to cases in which, after a first attack, moderate or considerable albuminuria remains after three months, or there is evidence of cardio-vascular changes, further lapse of time is required to show the result, but the prognosis may be regarded as unfavourable; especially in men over thirty-five years of age.

TREATMENT.

Rest in bed was insisted upon at first, and in all cases until either the albuminuria and casts had cleared up and there was a fair balance between the intake of nitrogenous foods and salt and the output by the kidney, or until it seemed that there was no prospect of the albumin and casts disappearing. The presence of blood in the urine was a further reason for complete rest, and also for great caution in increasing the amount of food, especially as to the addition of egg-yolk, fish, and chicken to the diet.

Diet.

Severe cases were placed on milk only on admission. The large majority were on a fixed diet of milk 2½ pints, bread 6 oz., rice 1 oz., butter ½ oz., potatoes 4 oz., greens 4 oz., jam 1 oz., and fruit occasionally. As improvement took place the bread was increased to 8 oz. and the yolk of one or two eggs was added. Later on, 4 oz. of cooked fish or chicken were added and sometimes more bread and butter. Salt was not used as a condiment, nor added by the cook, except in cooking green vegetables. The amount of water was not restricted when once the kidney began to secrete freely. It is essential to know the amount of food by weight that a patient with nephritis is taking, and reliance cannot be placed on the ordinary hospital dietary unchecked, as the amount taken by individual patients varies greatly.

Drugs.

Many of the patients had only a simple diaphoretic mixture with a saline or other purgative when required. Hot-air baths were used when free diaphoresis was necessary. Nitroglycerin was given when the blood pressure was raised. Iron was given in the later stages if there was anaemia.

In many cases with deficient urinary excretion on admission, the treatment with sodium carbonate, suggested by Dr. Martin H. Fischer, was used with very satisfactory results in establishing a free flow of urine. Dr. Fischer attributes nephritis to an abnormal production and accumulation of acid in the kidneys, and the oedema, anasarca,

and other symptoms of nephritis to a similar process occurring in the tissues, and the object of his treatment is to diminish the concentration of acid by giving water freely and to neutralize it by an alkali. This may be given by mouth, or if not absorbed thus, by rectal or intravenous injection. The treatment is not suitable for chronic interstitial nephritis, which has a different origin.

alkaline treatment with digitalis and caffeine is efficient when they fail singly as diuretics.

Although the excretion of urea was also increased to a varying extent in different cases—for instance, in the foregoing case, on one day with 90 oz. urine, specific gravity 1010, urea excreted was 28.5 grams, or N 12.38 grams (with intake of N about 10 grams), albumin 12.75 grams

CHART 1.—Illustrating the rapid and free diuresis produced by administration of sodium carbonate (see also Chart 2). A—A, Sod. carb. gr. xv hourly; bowels moved once daily. B, Trinitrin m j of 1 per cent. solution four-hourly.

CHART 2.—From the 24th to the 29th day of illness sod. carb. gr. xij was administered every hour, and from the 29th to the 35th day every three hours. Bowels moved twice daily.

CHART 3.—Shows a slower effect of sodium carbonate. A—A, Adrenalin, 1 in 1,000, m ij t.i.d. B—B, Sod. carb. gr. xv hourly; bowels moved once daily. C—C, Tr. digitalis m xx twice daily. Patient had had scarlet fever twelve months before.

Whatever view be taken of this explanation of the pathology of nephritis, there is no doubt that the treatment is often most efficient in producing free diuresis in about forty-eight to seventy-two hours with disappearance of oedema and relief of accompanying symptoms, such as dyspnoea, headache, etc.

Pure crystallized sodium carbonate ($\text{Na}_2\text{CO}_3 \cdot 10 \text{H}_2\text{O}$) was given in doses of gr. x-xv in 8 oz. of water every hour during the daytime; the interval was increased to two to three hours after free diuresis had lasted two to three days. In two cases where administration per os was not feasible the rectal injections advised by Fischer (sod. carb. 10 grams, sod. chlor. 14 grams, water to 1 litre) were given every six to eight hours, but without success.

Most patients took this large quantity of fluid well, without special discomfort; two or three objected to it, and in three cases it had to be stopped because of nausea or vomiting. No other outward effects were observed. Reference can only be made to a few cases typical of many treated in this way. Charts 1 and 2 illustrate the rapid and free diuresis produced. Chart 3 shows a slower effect, the urinary excretion rising gradually with some fluctuation during four to five days and then maintaining a level of 80 to 110 oz. for eighteen days. The diuresis was followed by disappearance of oedema and amelioration of symptoms.

Chart 4 illustrates a very severe case in a patient, aged 20, with uraemic symptoms and extreme general anasarca. The effect of the alkaline treatment was remarkable; as the chart shows, in ten days the anasarca had disappeared, and from an apparently hopeless case he had become convalescent. In this case and in one or two others it has seemed to me that the combination of the

NaCl 28 grams—the chief effect was on the excretion of water and salts.

In a few cases the treatment failed for no ascertained reason.

In one case uraemic fits, the only instance in the whole series of cases, occurred on the sixth day of treatment, but they did not recur; free diuresis set in next day, dropsy disappeared gradually, and he made a good recovery.

Adrenalin.

One other point in treatment may be mentioned.

Several patients complained of feelings of great prostration, attended with a low blood pressure. Relief was given by the administration of adrenalin chloride (1 in 1,000) m ij to m v every four hours.

PATHOLOGY.

With regard to the pathology I have little to say. Of the three fatal cases, a *post mortem* was allowed in one only. This was a patient in Group IV, of 23 years of age, with no history of previous illness except bronchitis as a child. He had never had scarlet fever, nor been "gassed." He was admitted with oedema of the face and legs and general bronchitis,

with coarse, moist râles over both lungs, slight enlargement of the left ventricle of the heart, and a systolic apex murmur. The systolic blood pressure was 198 mm. Hg, and the diastolic 140. Liver and spleen not enlarged. He had double optic neuritis and intense retinitis, with numerous haemorrhages. The urine was scanty, specific gravity 1013 to 1016, contained a large quantity of albumin, no blood, and abundant hyaline, epithelial, granular, and fatty casts. He died of diffuse bronchopneumonia, with some haemoptysis. The sputum contained pneumococci.

CHART 4.—A very severe case of trench nephritis. A—A, Sod. carb. gr. vij hourly. x x x Saline enemata every six to eight hours on these days. B—B, Tr. digitalis m xv every six hours. C—C, Sod. carb. gr. xij hourly from the ninetieth to the ninety-fifth day, every two hours for the remainder. D—D, Tr. digitalis m xv , caffeine gr. v. every six to eight hours; twice daily after the 103rd day of illness; anasarca and dropsy disappeared.

The following is the report of the condition of the kidney:

This shows a condition of focal nephritis with evidence of several acute attacks recent in date.

Capsule thickened in patches. Blood vessels do not show arterio-sclerotic changes. Glomeruli normal in places; in others they show capsular fibrosis and fibrosis or atrophy of glomeruli; elsewhere there are intracapsular exudation, cell proliferation, and fibrosis. The interstitial tissue is increased in patches, and contains many areas of lymphatic spaces laden with fat.

The convoluted tubules are almost normal here and there, but to a great extent show cellular degeneration, especially fatty desquamation and degradation of the lining cells and granular debris in the lumen. Some show dilatation, and a few cystic spaces are present in the subcortical area.

The heart shows interstitial myocarditis in some areas.

The spleen, suprarenal, and pancreas are normal.

So far as this case goes it would confirm the clinical evidence, which points to this form of nephritis as being a diffuse nephritis, affecting chiefly the convoluted tubules, but not especially the vascular elements of the kidneys. The characters of the urine, with its rather low specific gravity, excretion scanty at first and later as a rule abundant, moderate or large amount of albumin, and with numerous hyaline, epithelial and granular casts in the early stages, correspond to a change of this kind.

To sum up, in cases of nephritis at a base hospital, the general clinical features perhaps especially characteristic are the benign character of the nephritis in the large majority, the frequency of pulmonary complications, especially bronchitis, oedema of lungs, and broncho-pneumonia, apart from these complications a not infrequent dyspnoea, the generally good appetite, clean tongue, and maintenance of fair nutrition, and, on the other hand, infrequency of anaemia, of marked uraemic symptoms, and of a high blood pressure or cardio-vascular changes. The short duration of the illness in most cases would explain some of these latter departures from the usual symptoms of other types of nephritis. Severe retinitis or optic neuritis is uncommon—3 out of 80 cases.

I regret that more thorough investigations on the blood and on the excretion of uric acid, creatinin, etc., could not be carried out, and in conclusion it is my pleasing duty to thank the resident medical officers at Southmead Hospital, especially Captain H. H. Carleton, R.A.M.C., for much help in taking blood pressures and other investigations, and Professor Walker Hall, of the University of Bristol, for pathological reports, and to express our great indebtedness to the Medical Research Committee for their help in maintaining the pathological laboratory at Southmead Hospital, in which the urinary examinations were carried out.

REFERENCE.

¹ Davies and Weldon: *Lancet*, 1917, vol. ii, p. 118.

REAMPUTATION.

BY

W. A. CHAPPLE, M.D., CH.B., M.R.C.S., D.P.H.,
MAJOR R.A.M.C.,

OPERATING SURGEON, PAVILION MILITARY HOSPITAL
FOR LIMBLESS MEN.

ASSUMING that a reamputation of a limb has to be done, at what period after the primary amputation should it be undertaken?

The practice of surgeons differs widely. Some wait for healing and a "clean" operation which often takes months. But an experience of the use of button-sutures threaded through vulcanite boat-shaped buttons or india-rubber tubing acting as a support for the flaps and taking all the tension off the skin stitches shows that it is possible to reamputate in the presence of suppurating surfaces with almost complete certainty of union either by first intention or a kind of second intention, with preservation of the apposition of the flaps and the covering of the end of the bone.

Men upon whom an urgent amputation has been done in France arrive at hospitals in Britain after an interval varying from several days to a week or two.

If the amputation has been of the guillotine variety, the incision in the skin has been clean and circular, the skin is retracted up the limb, the muscle surfaces have retracted to a lesser degree, the end of the bone is exposed and protruding, and all the surfaces are bathed in pus.

Sometimes flaps have been attempted and a similar

condition exists, with the addition that the flaps may be large, hanging, and ragged at the edges from stitches which have cut through owing to suppuration.

My own invariable practice ever since the commencement of the war has been to allow these cases to settle down in hospital for a few days and then to reamputate, stitching the skin edges together as for a clean operation. During the waiting days the exposed surfaces are dressed with moist antiseptics, and when the general condition (usually disturbed by the journey and the necessary handling) has improved, the resistance has reached its maximum and the temperature has become steady, though slightly elevated, the patient is considered ready for operation.

When there was nothing other than the condition of the stump to consider reamputation has, as a rule, been done within a week or ten days of the patient coming in.

In no case have the skin and soft tissues failed to heal over the end of the bone by either first or second intention, with at worst, and rarely, a small granulation area at the point where the drainage tube was left in for the first twenty-four or forty-eight hours; or where some pus had formed at a skin stitch or between two stitches. Even when this pus has formed it has not interfered with the complete healing of the soft tissues over the end of the bone and the union of the skin, usually within twenty-one days. In no case has the end of the bone appeared or been exposed even to the probe after a reamputation. That this is not the general rule there is abundant evidence at the Pavilion Military Hospital for Limbless Men. It would appear that reamputations have been done and the bone shortened, but that the condition of the stump has reverted to its original state, the skin and other soft tissues retracted, and the bone exposed, the only difference being that the limb is shorter.

The secret of healing by primary or by secondary, or rather delayed primary, union in septic cases is the relief given to the skin stitches by the "button-sutures" planted well back from the incision, and arranged staple-wise in such a way and position as to bear the whole weight of the flaps and keep them in apposition.

The "second intention" to which I have referred is a union in the presence of or following suppuration affecting the skin edges, but not sufficient to separate those edges from each other (either by the stitches cutting through or by sloughing) to such a distance as to prevent the epithelial margins from uniting without the intervention of a granulation area.

As the button-sutures carry all the weight of the flaps and bear all the tension, the skin stitches have no other function than to keep the skin edges opposite one another and prevent bulging of subcutaneous tissues. In short stumps the loss of another inch of bone by reamputation may seriously curtail locomotion. With button-sutures less provision has to be made for long flaps to meet contraction, and therefore valuable length is saved. These button-sutures tend also to keep the severed tendinous ends and muscle edges in apposition over the end of the bone. This either gives attachment between the two groups of locomotor muscles over, or it gives attachment to, the end of the bone. If it unites by close fibrous intervention over the end of the bone the result is a greater muscle purchase, and therefore a greater power of movement of the stump than would follow an attachment higher up the shaft, which is usual when muscles are allowed to retract after amputation. Moreover, a muscle shortened by contraction and attachment higher up suffers the disadvantage in "pull" that a rower does at the end of his stroke, as compared with the advantage at the commencement, when his arms are fully stretched and the point of "attachment" to the oars most distant from the base to which they have to be drawn. It should never be forgotten that a stump is a locomotive organ as well as a weight-carrying organ, and will have to swing and control an artificial limb often as heavy as 7 lb. It is also of advantage to get a substantial boss of soft tissue over the end of the bone. Even if atrophy takes place under muscle pull or from the pressure on an end-bearing stump the residuum is something to the good. In my opinion an effort should always be made to get a stump that will stand the pressure of the body weight. Even if this may not be urgently required, as in a short thigh stump, it has certainly two advantages—it shares the body weight with the tuber ischii, and, from the sense of firmness and