

REPORT ON FIFTY-EIGHT CASES OF ACUTE NEPHRITIS
OCCURRING IN SOLDIERS OF THE EXPEDITIONARY
FORCE, INVESTIGATED AT ST. BARTHOLOMEW'S
HOSPITAL FOR THE MEDICAL RESEARCH
COMMITTEE.

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THOUGH in general the health of the Expeditionary Force has been so good, some anxiety has been occasioned by an outbreak of cases of acute nephritis. At the request of the Director-General the Medical Research Committee made arrangements for its immediate investigation and the Committee have defrayed the special expenses connected with it. Arrangements were made for a number of these cases to be placed under my care in wards at the St. Bartholomew's Hospital section of the 1st London (City of London) General Hospital. Dr. Mackenzie Wallis and Dr. Trevan have made the chemical investigations involved. Captain F. W. Andrewes, F.R.S., Professor of Pathology in the Hospital Medical School, has reported on the morbid anatomy of the kidney, and the pathological investigations have been carried out in the pathological department of the hospital of which he is the director. Dr. R. G. Canti has particularly interested himself in carrying out many of these. Mr. Foster Moore has reported on the condition of the eyes in the majority of the cases. Without the cordial co-operation of all these gentlemen this investigation could not have been attempted.

It has been thought advisable to issue this interim report for the information of those medical officers who are engaged in treating these cases of nephritis, before the whole investigation is complete. Observations confirmatory of, additional, or opposed to those herein described would be welcomed. In this way it is hoped that a useful contribution to the medical history of the War may be arrived at.

INCIDENCE.

It appears that 1,062 cases of acute nephritis occurred in the Expeditionary Force up to the end of June. The monthly returns show that very few cases occurred till February, in which month 72 cases were reported, 138 in March, 220 in April, 211 in May and

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326 in June. Of these cases 58 have been investigated at St. Bartholomew's Hospital. These figures differ strikingly from those of the South African War. The late Dr. Washbourn reported that "acute nephritis was singularly infrequent." At Deelfontein there were only six cases of acute Bright's disease in whom the disease was contracted in South Africa. Old standing nephritis with an acute attack superadded was more frequent. Moreover, there can be little doubt that the disease has been much more frequent in this campaign than in civil practice. As acute nephritis is not a notifiable disease it is impossible to provide exact figures, but it may be said that at St. Bartholomew's Hospital, where the number of medical cases admitted in a year averages 7,000, there were in a period of nine years only 166 cases, 120 males and 46 females. In a period of five years only 26 cases were admitted in men between the ages of twenty and forty, which is a better standard of comparison. Again, among the troops serving in the United Kingdom the incidence of nephritis closely approximates to the peace ratio for this disease. We may conclude that ordinarily acute nephritis is a rare disease in men of a military age and that a special explanation must be sought for the present frequency of the disease in the Expeditionary Force.

It was thought by some observers that the condition was commoner in the older soldiers, but the ages of the patients admitted to St. Bartholomew's Hospital do not bear this out. Arranged in hemidecades the age incidence was as follows:—

Under 20	2
20 to 24	14
25 to 29	11
30 to 34	13
35 to 39	10
40 to 44	5
45 or over	3

ETIOLOGY.

In dealing with a comparatively small proportion of the total number of cases it is of not much value to tabulate the places at which the disease was contracted; the cases came chiefly from

Ypres	15
Bethune	12
Boulogne	6
Givenchy	4
Festubert	3
Floubaix	3
Richebourg	3

Exposure to wet and cold has always been held to play an important part in the causation of acute nephritis, but this epidemic goes far to disprove that contention. For during the winter when there was much wet weather the cases were few and far between, and it was not until the weather was better that the disease assumed epidemic proportions. In each case, however, careful inquiry was made into the question of recent exposure to wet; in twenty cases there was a definite history of this, but in thirty-eight cases no history could be obtained.

The water supply has also been suggested as a possible cause; whether by reason of its being obtained from an unwholesome source, or by chlorination or from metallic poison derived from the galvanized water-carts or the water-bottles. It may be said at once that these cases lend no support to any such hypothesis; the sources from which the patients had obtained water were extremely variable, as is shown by the following table:—

Source from which water was obtained	Wholly	Partially
Water carts	17	7
Pumps	13	13
Dug-outs	5	7
Springs	1	4
Ponds	1	0
Wells	1	3
Town water supply	1	1

Moreover in some cases the patients had been careful about boiling the water, in others they had not; in some cases the water had been chlorinated, in others not.

Another suggestion was that the disease was rife amongst the horses. We need not stop to inquire whether they derived it from the same source as the men or whether it was transmitted by or to the horses, since investigation has failed to reveal the existence of the disease among the horses to any extent. Only ten of the patients had had the handling of horses; it is interesting that one of these volunteered the statement that his horses had strangury.

None of the men admitted for acute nephritis had been wounded, and no case of acute nephritis occurred among the wounded men admitted to St. Bartholomew's Hospital. Clearly, if the disease is due to an infection, a wound infection plays no part in it. As respiratory symptoms have been common in this series of cases, it should be mentioned that only two of the men had previously suffered from gas asphyxia.

Excessive protein diet has been suggested as a possible cause.

It seems highly improbable that one hundred and eighty grammes of protein would cause acute nephritis in a number of otherwise healthy men, and that without impairing the health of the others in any way. Moreover, as will appear later, the evidence is in favour of an infective rather than a merely toxic change in the kidneys, and, a more important point, there were no signs of an intestinal toxæmia.

On this point Dr. Mackenzie Wallis's observations appear quite definite. Proteins as such would not exert a toxic influence; they could only do so through their putrefactive products. Among the more striking of these products is indican, which can be readily recognized in the urine. But it is not altogether a safe guide to the total amount of putrefactive change. The putrefactive bodies are largely combined with sulphates and excreted as ethereal sulphates; indican is merely one of these. Normally the ethereal sulphates form about one-tenth of the total sulphates. With intestinal intoxication the ethereal sulphates rise both absolutely and relatively. In the cases investigated the total amount of ethereal sulphates was low, probably because of the relatively low protein intake, and the proportion of ethereal sulphates did not show an increase. Another guide to the amount of intestinal putrefaction is the presence of urobilin in the urine. Urobilin is derived from the bile pigment in the bowel by the reducing action of the bacteria there. In this series of cases urobilinuria was not observed. If fermentative rather than putrefactive changes predominate, oxalates are apt to be formed in considerable quantities and crystals of calcium oxalate are found in the urine. In this series calcium oxalate crystals were only found twice. So that the evidence is all against excess of either putrefactive or fermentative changes in the bowel.

Acidosis has been suggested as a cause, on account of the frequency with which dyspnoea occurred in the early stages of the disease. It is not clear how acidosis could arise on the diet given to the troops, nor is there a general agreement that acidosis can cause nephritis. The cases of dyspnoea investigated did not show acidosis as a constant feature.

In a few cases the disease was evidently an exacerbation of old trouble, there being a clear history of previous attacks in 5, 3 of them being apparently scarlatinal in origin. In 3 others there was a history of scarlet fever but no evidence of previous kidney trouble.

An ætiological factor of some interest was the high percentage

of positive Wassermann reactions. The reaction was done in 56 cases and was positive in 18, being strongly so in 4, and feebly so in 3. That is to say, practically one in three of the cases was positive, and though this is too low to make a specific taint the cause of the disease, it is high enough to make it a probable factor in lowering the patient's resistance. It is noteworthy that in three out of the four instances where the reaction was strongly positive there was evidence of extensive kidney damage, with a tendency to prolonged hæmaturia and to relapse. I gather that an incidence of nearly thirty-three per cent is higher than the incidence of syphilis in the Army in general. It may be added that the majority of the positive reactions were in the long service men, though three out of the four strongly positive reactions were in men who had enlisted for this war.

PATHOLOGY.

That the disease may be considered a form of nephritis is sufficiently shown by the combination of œdema with albuminous urine which also contains blood and casts. But a nephritis may be the result either of an infection or an intoxication. Taking scarlet fever as the classical example of an acute nephritis due to an infection it is generally admitted that the stress of the disease falls especially on the glomeruli, though the tubules are not spared. In a toxic nephritis, on the other hand, such as that produced by corrosive sublimate, the lesion is tubular. It seemed important to determine how far the glomeruli and the tubules were respectively involved in these cases, as the methods of combating an infection and a toxic agent would differ widely.

Certain tests are relied upon to differentiate the parts of the kidney chiefly affected, and I may summarize here the principal results obtained by Dr. Mackenzie Wallis and by Dr. Trevan, which will be published *in extenso* later.

(1) *The Chloride Test.*—That chlorides are often badly excreted in nephritis is well recognized. In 1911 Schlayer went further and attempted to differentiate between tubular and glomerular damage by the reaction of the kidney to ingested chlorides. A kidney that is healthy can get rid of five grammes of salt by merely increasing the concentration of the urine: but if the tubules are damaged it cannot excrete urine of the requisite concentration. If the glomeruli were intact they could come to the assistance of the damaged tubules by excreting more urine of a low concentration and thus

help in the excretion of the salt. It is claimed that in an early stage of glomerular damage there is an exaggerated response on their part producing excessive diuresis, so that more salt is excreted than was administered. But if the damage to the glomeruli is more profound they are unable to respond by increasing the output of water, which may even fall. A rise in the percentage of sodium chloride in the urine, with a fall in the total quantity of this substance excreted, would be evidence that the tubules could respond while the glomeruli could not. The absence of a rise in the percentage of sodium chloride or an inadequate rise would be evidence, on the other hand, that the tubules were damaged.

This line of investigation has been carried out by Dr. Trevan in twenty-three cases. As some of these were getting rid of previously retained chlorides, i.e., were recovering from a tubular lesion, it was necessary to continue observations on the chloride output on a diet of known chloride content for some days before administering the dose of five grammes of salt. The general conclusion reached was that all the cases investigated showed damage to both glomeruli and tubules. In twelve cases, i.e., just over fifty per cent, the glomerular damage was sufficiently severe to produce an actual fall in the quantity of water excreted after the dose of salt.

He confirmed the fact of salt retention in four cases by determining that the chlorides in the blood were higher than normal.

(2) *The Iodide Test.*—According to Schlayer iodide is excreted by the tubules. In eight cases Dr. Trevan estimated the time taken to excrete a dose of two grams of potassium iodide, and also the amount excreted in certain periods of time. A great reduction in the total amount excreted was shown in every case. The evidence as to tubular damage as given by the chloride and iodide tests agreed fairly well in these eight cases. The difficulty in excreting iodide was further evidenced by the intolerance to iodide shown in those cases where it was given therapeutically because of a strongly positive Wassermann reaction.

(3) *The Lactose Test.*—Lactose injected intravenously appears to be excreted by the glomeruli. In three cases where this test was tried, Dr. Trevan obtained marked evidence of extensive glomerular damage, as there was marked delay in excretion. As a rigor occurred after the injection in one case, and hæmaturia in this and one other case, the test was discontinued.

(4) *The Diastase Test.*—Of recent years the amount of diastase

present in the urine has been used in the diagnosis both of pancreatic disease and renal permeability. In the presence of the former the diastase output is greatly increased. Given the absence of this the amount of diastase should vary between 10 and 22.2 units. But if the renal permeability is diminished this amount may fall to 5 units or less, and perhaps to 0. A colloidal substance such as a ferment would probably be excreted by the tubules. Dr. Mackenzie Wallis, who has paid special attention to this test for the last two years, has estimated the urinary diastase in fifty of these cases, in many of them on more than one occasion. The results have been interesting and valuable. In no instance was the diastase output increased, as it often is in toxic processes. In thirty-one cases the diastase value was low, and eight had none at all in the urine. Nineteen cases showed a normal value. Speaking generally, this method agreed with the others in indicating the cases with definite tubular damage. Those with normal values were usually slight cases. But further, this method was of distinct prognostic value, for those cases with a normal value generally recovered quickly, while those with a low value ran a more protracted course and showed a tendency to relapse. As the cases improved the diastase value tended to rise. Again in some cases the low diastase value persisted after the albuminuria had ceased, showing that the kidney had not completely recovered. The test has an important bearing on the prognosis, and a case of acute nephritis cannot be said to have recovered completely until the diastase value has returned to normal.

The Nature of the Proteins Present in the Urine.

Though this does not enable us to distinguish between the glomerular and tubular damage its determination enables us to distinguish an actual inflammatory lesion of the kidney from a functional albuminuria and from the so-called "leaky" kidney, which is not the seat of an inflammatory lesion. Dr. Mackenzie Wallis's investigations on this point show that the ratio of albumin to globulin in these cases ranged from five to one to six to one, which accords with all previous observations upon inflammatory conditions of the kidney.

All these tests taken together point to a nephritis of a diffuse type usually thought to be infective in origin and bearing no relation to that caused by metallic poisons.

MORBID ANATOMY.

Up to the present only one of the cases at St. Bartholomew's Hospital has proved fatal, and a full report on the kidneys is not yet forthcoming. It can be said, however, that they showed extensive glomerular with some tubular change. One case, under the care of Major Calvert, at the First London General Hospital, died, and Captain F. W. Andrewes has furnished a report on the post-mortem examination and the histological appearances of the kidney. He found that all the glomeruli showed some evidence of inflammation, but that some were affected more than others. There was extensive damage in the convoluted tubules. The interstitial tissue of the kidney was œdematous and infiltrated with lymphocytes and polymorphs. The change was apparently recent, for there was no fibrosis. No micro-organisms could be found in stained sections. He concluded that the appearances were those of a fairly recent subacute diffuse nephritis, and that there was nothing to suggest that the nephritis was of any distinct or unusual type.

There is therefore a substantial agreement between all the methods of investigation. The improbability of a simple toxic agent or an intestinal toxæmia has already been shown.

We must next consider the steps that have been taken to detect an infective agency.

(a) *Blood Cultures*.—These were made in three cases, in two because of serious symptoms of a possibly septicæmic nature, and in the other because it was admitted to the hospital in an early stage of the disease. In all cases the blood was sterile.

(b) *Cultures from the Urine*.—Catheter specimens were obtained in twenty-one cases and cultures made. In eighteen of these the urine proved to be sterile. In the remaining three, *Bacillus coli communis* grew, but in two of these only when one cubic centimetre of the urine was taken, while the remaining case was not a typical one being much more of the type of pyelitis, which came on during an attack of typhoid fever.

There is therefore no evidence of the nephritis having been set up by an ascending infection, or by a blood infection, the stress of which fell upon the kidney. This accords with Captain Andrewes's observations on the morbid anatomy of the kidney.

(c) *Throat Cultures*.—Seventeen of the cases complained of a sore throat as an early, if not the initial, symptom. In view of the generally accepted association between tonsillitis and nephritis (see Sir Wilmot Herringham's "Kidney Disease") it seemed important

to investigate this point. Cultures were taken from all the throats where soreness was complained of, and in several in which no such complaint had been made. It was found in every instance that streptococci grew in abundance, and sometimes in practically pure culture. Pneumococci, diphtheroids and *Micrococcus catarrhalis* were also found in some cases. Before it could be concluded that the streptococci were responsible in any way it was necessary that control observations should be made, since streptococci are normal inhabitants of the throat. Dr. R. G. Canti therefore made cultures from the throats of ten soldiers with nephritis, ten wounded soldiers who had not got nephritis, and ten civilian patients suffering from various surgical diseases. His report shows that the throats of the soldiers were, as far as bacteriological examination went, in a healthier condition than the civilians, while the throats of the soldiers with and without nephritis were closely similar. He is engaged in estimating the streptococcal antibodies in the blood of some of these cases. This would afford evidence of a recent streptococcal infection. So far here is no proof of the presence of any excess of these antibodies.

While this points away from a possible streptococcal origin, there remains the possibility of a filter-passing ultramicroscopic organism being the cause. The comparative frequency of sore throat as a symptom and the failure to find a bacterial cause for a disease which is almost certainly of infective origin make it very important that a filter-passer should be looked for. Animal experiments with this object in view are now in progress, but it is too early to speak of results yet. It has been suggested that the cases are due to a suppressed form of scarlet fever, which is also thought to be due to a filter-passer. It is interesting in this connexion to note that so far cases of nephritis have not occurred among the Indian troops, and the natives of India are said to enjoy comparative immunity from scarlet fever. It is also interesting, in view of the frequency of otitis media in scarlet fever to note this occurred in two cases just before the œdema. But as the ordinary incidence of nephritis in scarlet fever is ten to twenty per cent, this view would entail the conclusion that there had been ten to twenty thousand cases of scarlet fever had occurred among the troops up to the end of June. The general health of the troops has been so good as to make such a large number of suppressed cases unlikely. Moreover, even in "scarlatina sine eruptione" desquamation follows, and this has not been observed in these cases.

SIGNS AND SYMPTOMS.

In the majority of cases the first thing noticed was the œdema, which usually started in the face and legs, and was curiously localized in some cases. The swelling became generalized in most cases. In one case admitted on the second day of the disease the legs and scrotum were very œdematous, but the rest of the body escaped. œdema was almost a constant feature, being present in 53 cases, and of the 5 in whom it did not occur 4 gave a history of previous nephritis. In every case it soon cleared up.

Pain in the back was common at the outset, and was sometimes the initial symptom. It was not so common as œdema, however, being experienced in 37 cases. "Biliousness," nausea, vomiting and abdominal pain were given as initial symptoms by 6 patients, while 2 first complained of pains all over. Cough, diarrhœa and headache were occasionally the initial symptoms. Two cases developed an aural discharge just before the onset of the nephritis, again pointing to a possible throat infection. As already stated, 17 patients complained of sore throat at the beginning.

One of the most striking points was the frequency with which shortness of breath occurred as an early symptom. It was present in 49 cases, and only absent in 9. Of these 9, 2 had no œdema, while the œdema was slight in 2 others. œdema occurred without shortness of breath in 3 cases. As a rule this shortness of breath started at the same time as the œdema, but did not last so long, having ceased at the end of two or three days. Only 5 cases had any dyspnœa while in St. Bartholomew's Hospital. The alveolar CO_2 was determined in each of these by Dr. Trevan: in 3 it was normal, while in the remaining 2 it was reduced from the normal five per cent to about three per cent. Dyspnœa due to acidosis is always associated with this reduction of alveolar CO_2 and uræmic dyspnœa is of this type. In three of the cases it would therefore appear that the dyspnœa was not uræmic.

Dyspnœa is not regarded as a common feature of acute nephritis. It may occur from uræmia or cardiac failure, of course, but the majority of these patients were not so ill that either the kidney or the heart was failing, and none of them showed signs of cardiac dilatation. The close agreement between the onset of œdema and dyspnœa suggests that the outpouring of fluid into the lungs or pleural cavities may have been responsible for the shortness of breath. This is supported by the frequency with which a cough

and bronchitis also occurred. Some of the early cases showed well-marked respiratory distress after their journey from France.

A slight and irregular temperature was common in the earlier stages and was sometimes prolonged where recovery was slow. More or less severe headache was common and was sometimes persistent. Anæmia was present in a fair number of cases, especially in those with a positive Wassermann reaction.

The urine was noted by the patients to be altered in most cases, though 11 failed to observe any change, 18 noted that it was scanty, while 8 observed that it was increased in amount. One patient noted great variation in the amount he passed; 8 had increased frequency of micturition, 3 had strangury, and 2 had incontinence; 22 observed that the urine was dark or actually contained blood.

While in hospital the variations in the quantity of urine were often striking, as illustrated by the following five cases, in which the extreme limits are given :—

52 to 140 oz.
60 „ 160 „
30 „ 125 „
35 „ 108 „
42 „ 128 „

The amount of urine was definitely reduced in fourteen cases; in these the output varied between eleven and thirty-seven ounces. But such extreme reductions as are usually seen in acute nephritis were not observed, and most of the above soon excreted larger quantities, while in some the amount was always increased. The highest figures observed were :—

100 to 120 oz. in	8 cases
120 „ 140 „	5 „
140 „ 160 „	2 „

This variability in amount with frequently marked increase is due to what Muller called hyposthenuria; the kidney being unable to excrete a concentrated urine. Herrick says that it occurs not only in chronic interstitial nephritis, but also in acuter forms, especially when there is glomerular involvement. It was certainly a more marked feature of these cases than in the acute nephritis met with in civil practice.

The amount of albumin differed greatly. Usually it varied from a trace to 0.3 per cent as estimated by Esbach's method, but higher readings, such as 0.5 to 0.8 per cent were obtained occasionally. Some were estimated by the more exact Aufrecht method and yielded readings ranging from 0.001 to 0.3 per cent.

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Red blood corpuscles were found in forty-four of the fifty-eight cases. The amount was very variable. Sometimes the urine was bright red with blood, sometimes merely smoky, and often chemical and microscopical tests were needed to detect the blood. A common feature was the settlement of a flocculent reddish-brown precipitate in which alone the blood could be found.

The reaction with tincture of guaiacum and ozonic ether was not found to be a reliable test for the presence of blood.

White blood corpuscles were present in thirty-six cases; sometimes only a few were found, but usually they were more abundant than is the rule in acute nephritis. Isolated renal cells, transitional epithelial cells, squamous cells from the lower urinary tract and cells from the genital tract were commonly found also in the centrifugalized deposit.

Casts were found in all but three cases. By far the commonest thing was to find a mixture of epithelial, granular and hyaline casts. Blood casts and fatty casts, on the other hand, were uncommon. The frequency with which the different forms were found may be tabulated thus:—

Blood casts	2
Epithelial casts	36
Fatty casts	7
Granular casts	51
Hyaline casts	33

Crystals were rare in the urine; calcium oxalate crystals were found twice, and uric acid crystals once. The rarity of organisms in catheter specimens has already been referred to. *Bacillus coli* was found in only three cases; in only one were they abundant, and this case also had pyelitis after enteric fever.

The systolic-blood pressure was estimated in every case, and usually on several occasions. The figures obtained were not very helpful; perhaps at the outset the pressure would have been found to be raised in all cases; it was one hundred and fifty-five in the case admitted on the second day of his disease. The figures obtained as soon as the patient had settled down after his journey may be tabulated thus:—

Blood-pressures				Cases
Under 120	4
120 to 129	13
130 to 139	10
140 to 149	10
150 to 159	9
160 to 169	6
170 to 179	3
180 and over	3

It may be said in general that as the patient improved, the pressure tended to fall to normal. The cases with a history of former attacks gave readings of 130, 148, 152, 155, and 200 respectively, but in a few days the 130 had fallen to 110, and the 200 to 140.

It cannot be said that the blood-pressure had a definite prognostic value. Thus three men were admitted with a pressure of one hundred and twenty-eight. The first had reached the eleventh day of his illness; eight weeks later there were still red corpuscles in his urine. The second was at the seventh day of his disease; ten weeks later he still had hæmaturia. The third had been ill a month, and he died eight weeks after admission. On the other hand, cases admitted with blood-pressures of 165, 168, and 179 have proved obstinate. Probably the best thing is a moderately raised pressure at the outset, falling fairly quickly to normal. Such cases have usually made a good recovery.

The eyes were examined by Mr. Foster Moore in fifty cases. He found--

No changes	37
Retinal hæmorrhages	4
Old iritis	1
Corneal nebula	1
Subconjunctival hæmorrhages	2
Conjunctivitis	1
Choroiditis	2

Of these changes only the retinal hæmorrhages were definitely associated with the nephritis, though the subconjunctival hæmorrhages were probably due to high pressure.

Three patients had fits which were presumably uræmic in origin. One of these had been venesected for fits in Boulogne. The other had a severe fit after reaching England and bit his tongue very badly. He had another epileptiform fit in the ward; yet he had never had fits before or after these two. His Wassermann reaction was negative, and he made a good recovery.¹ These were the only complications observed.

It may be added that the milkiess of the blood serum referred to by Bright in his original account of the disease was not observed in any of the fifty-six cases in which the blood was drawn for

¹Since writing this, one new case had violent uræmic fits immediately after admission. They quickly yielded to free venesection.

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Wassermann's reaction, but was present in the fatal case under Major Calvert's care.

COURSE AND PROGNOSIS.

On the whole it may be said that the disease has run a favourable course. Only one of the fifty-eight cases has died, and in no other case has life appeared to be in danger. It may also be assumed that the cases sent home have been the more protracted ones. The patient who developed the disease immediately after his return from France on leave, and who was admitted to the hospital on the second day of the disease, was free from albuminuria on the fourth day. Most of the cases have felt quite well as soon as the œdema subsided, though some have complained of headache, cough and digestive disturbances for a week or more. Yet many of those who felt and looked quite well were still passing albumin, blood and casts. A curious feature has been the tendency to relapse, in that there has been a return of albuminuria and hæmaturia, generally without ascertainable cause, though in some cases the first motor drive might be held responsible. The fact that they had been permitted to go for a drive shows that they were considered to be convalescent at the time.

Up to the present (August 5), twenty-two have apparently recovered. A considerable number of the remainder are still under treatment. Final statistics are not yet forthcoming, but the following data may prove of interest.

Blood was never found in fourteen cases. It disappeared from the urine in

10 days in	1 case
3 weeks in	2 cases
4	3 "
5	2 "
8	3 "
9	2 "

It was still present at the end of

6 weeks in	2 cases
8	4 "
9	2 "
10	2 "
12	3 "
14	1 "
20	1 "

Albumin disappeared from the urine in

4 days in	1 case
10 "	1 "
2 weeks in	1 "
3 "	4 cases
4 "	3 "
5 "	3 "
6 "	1 "
7 "	1 "
8 "	3 "
9 "	2 "
10 "	1 "
14 "	1 "

It was still present at the end of

6 weeks in	4 cases
7 "	4 "
8 "	7 "
9 "	4 "
10 "	2 "
11 "	1 "
12 "	5 "
14 "	1 "
15 "	1 fatal case
20 "	1 case

Casts have been observed to disappear from the urine at the end of

4 weeks in	2 cases
5 "	2 "
12 "	1 "
16 "	1 "

It has generally been observed in this series of cases, that as improvement occurred the units of diastase present in the urine rose to a normal level. Comparing the diastase reaction with the time of disappearance of the casts, it may be noted that in one case where the casts went in four weeks the diastase reaction was normal, that in another where they went within the same time, the diastase rose to normal as the casts disappeared. Where the casts disappeared in five weeks the diastase steadily rose to normal. On the other hand, where three months elapsed before the casts disappeared the diastase remained very low, and where four months were needed for the casts to go the diastase remained low until about the time this happened. But casts vanished in five weeks in one case where diastase was entirely absent, and it is interesting to note that this man still felt ill; he was one that had a strongly positive Wassermann reaction. In several instances there seemed to be no agreement between a normal diastase reaction and the

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cessation of hæmaturia, but in general it may be said that a normal diastase reaction is of distinctly favourable prognosis, especially in the absence of hæmaturia.

All these dates have been calculated from the onset of symptoms and not from admission to St. Bartholomew's Hospital.

The fatal case suffered throughout from much anorexia, repeated vomiting and irregular temperature. Blood cultures were made on two occasions as a secondary infection was suspected; no growth was obtained, however. He developed more bronchitis, and a doubtful pericardial friction was heard on two days. He gradually became weaker, and passed less urine (on one day only eight ounces) and died at the end of fifteen weeks from the onset of symptoms. He never had any fits; the blood-pressure was only 128, and the Wassermann reaction was positive. Unfortunately, no post-mortem examination was allowed beyond the removal of the kidneys, which will be reported on later.

TREATMENT.

There is unfortunately not very much to be said under this head. Speaking generally, the cases were kept in bed as long as there was any hæmaturia or even marked albuminuria. Otherwise, unless there were some special symptoms the patients were allowed up, and when convalescent went into the square. The hospital milk diet was given in the first instance. This consists of:—

Tea	1 pint
Bread	14 oz.
Milk pudding	8 "
Milk	2 pints
Butter	1 oz.

This diet contains approximately:—

Proteins	86 grm.
Fats	77 "
Carbohydrates	353 "
Calories	2550 "

As improvement occurred, the next step was to add two eggs to the diet, giving it an approximate value of:—

Proteins	100 grm.
Fats.. .. .	90 "
Carbohydrates	353 "
Calories	2,720 "

Cases which did not seem to do well on this were put on a special "Low Nitrogen Diet," on the view that in acute nephritis

a period of comparative nitrogen starvation would afford the most rest to the kidney. This diet was only given for a short time, though occasionally as long as a week if it was well tolerated. It consisted of:—

Bread	6 oz.
Butter	1½ „
Potatoes	10 „
Greens	4 „
Salad	3½ „
Boiled rice	8 „
Milk	½ pint
Stewed fruit and sugar.				

This has a value of:—

Protein	54 gm.
Fats..	50 „
Carbohydrates	290 „
Calories	1,615 „

The chief deficiency in this diet is the lack of fat. In some cases it was improved by the addition of some cream cheese or salad oil with the lettuce. Its advantage was that while reducing the protein intake to about Chittenden's standard, it gave the men a greater variety. The rice was sometimes cooked with a tomato flavouring, which was appreciated. It could easily have been improved by the addition of jam, but the men having had jam constantly in their rations, did not like this. Exceptionally it was improved by the addition of honey, and but for the difficulty of cooking for a number of men, the fat could have been increased by frying the potatoes in fat or mashing them with butter. In this way a diet can be constructed which permits of variety while giving the kidney little work to do. Unless a considerable amount of fat is taken, however, the diet is of low calorie value, and is not suitable for prolonged use. Another drawback is that it requires a fair amount of salt to make it palatable.

It is difficult in a disease of such variable duration to assess the value of any treatment, but my impression is that this low nitrogen diet was a distinct benefit in several cases.

Where salt retention seemed to be a prominent feature, saltless bread and butter were given. While the salt excretion was being determined, a diet of known salt content was given, with saltless bread and butter, and a known weight of salt (one or two grammes, usually the latter) was added.

Drugs.—Potassium citrate was given where the excretion of urine was scanty or painful. Stimulating diuretics were never

given except theocin in some test cases. Theocin sodium acetate belongs, of course, to the caffeine group, but is claimed to have the power of increasing the permeability of the kidney. It occasionally seems to be of definite benefit in chronic nephritis. It was tried in three of these cases. In the first case it had a marked diuretic effect, and also raised the diastase content of the urine from 0 to 20. In the other two cases it had no effect on the diastase, and only a slight diuretic action. One of these cases also had a return of hæmaturia when the theocin was given. Theocin, therefore, like caffeine, diuretin, and theobromine, has an irritant effect as well as a diuretic action. It is an unsuitable drug as long as there is any degree of acuteness of the disease; in the more chronic stages, however, it does definitely increase the permeability of the kidney. When the drug is stopped, the permeability of the kidney returns to its former level. The dose administered was two grains twice a day.

Bicarbonate of soda was given in drachm doses where there was shortness of breath, and with definite benefit when the dyspnœa was accompanied by a low alveolar CO_2 .

Potassium iodide was given where the Wassermann was strongly positive, but it was not well borne, and generally had to be discontinued. In one case its administration was followed by marked œdema of the eyelids, which soon subsided when the drug was discontinued. This is, perhaps, to be expected, considering the evidence given in Dr. Trevan's report as to the difficulty with which iodide was excreted by these patients.

Several drugs were tried for the relief of hæmaturia. Emetine having been tried with some success for various forms of bleeding, such as hæmoptysis, was given a trial in several cases, but without benefit. Liquid extract of ergot was tried in a large number of cases in twenty-minim doses three times a day. It generally diminished the amount of blood for a time, but it did not appear to be responsible for bringing the hæmaturia to an end. Tincture of hamamelis was also tried, but did not seem to give as good results as ergot. As already pointed out, the duration of the hæmaturia was so variable that attempts to estimate the value of a drug in its treatment are beset with fallacies.

CONCLUSIONS.

(1) These cases are true examples of acute nephritis, as shown by (a) the combination of œdema with albuminous urine containing casts; (b) the tests for renal permeability; (c) the nature of the proteins in the urine; (d) post-mortem evidence.

(2) The cases have been too prevalent to be merely accidental, and the close similarity of the symptoms suggest a common cause.

(3) Exposure, water supply, metallic poisons, and intestinal toxæmia can be excluded as the cause. The prolonged cases showed a high percentage of positive Wassermann reactions.

(4) The curve of incidence suggests an infective agent as the cause; this is supported by the degree of affection of the glomeruli, as shown by the chemical tests and the post-mortem evidence.

(6) Bacteria can apparently be excluded as the infective agent, but a filter-passing ultra-microscopic organism cannot be excluded. The point of entrance of the infection is possibly the tonsils.

(7) The outstanding clinical features of the epidemic are: (*a*) the frequency with which shortness of breath occurred at the beginning, which was not always associated with acidosis; (*b*) the great variability in the duration; (*c*) the tendency to remission and relapse; (*d*) the ultimately favourable prognosis.