

infected persons and their immediate surroundings.

Pneumonia is not one, but a group of diseases, and with the aid of public health and other laboratories, an etiological diagnosis should be made in every case. Better treatment directed toward the alleviation of important symptoms may accomplish something, but more important in effecting a reduction in mortality is proper serum treatment, especially in the Type I cases. The present methods of serum treatment are not ideal, but results may be much improved by recognition of the importance of early diagnosis and treatment, by the employment of sufficient amounts of serum of high potency, and by continuing the treatment until evidence of recovery is manifested by positive skin reactions following the injection of the soluble specific substance. It is possible that even the general and strict application of all the measures I have mentioned may produce only a moderate reduction in the enormous number of cases and large number of deaths that at present occur in this country. But when we consider the apparent hopelessness of the situation twenty-five years ago, even a moderate degree of control of this

devastating malady should be a source of satisfaction. Typhoid fever was not overcome in a day. Indeed, owing to natural inertia, it is not yet entirely eliminated. Moreover, no single measure has been responsible for the great diminution in the effects of that disease. The fact that new knowledge concerning pneumonia is rapidly accumulating is heartening and should stimulate the energetic employment of the methods which we now possess.

The study of pneumonia by modern methods has been actively pursued for only a relatively short time. We must not expect too much. It is characteristic of youth to be impatient of delays and to desire immediate fulfilment, while old age, which should be more restless, for the time for achievement grows short and "death touches on the shoulder," is more willing to proceed with greater deliberation and to count each step a gain. Possibly, it is significant of my own changing status that I refuse to be hopeless regarding the outlook for pneumonia, and that I still feel that the time may come when acute infections of the respiratory tract will be as infrequent and as harmless as now are infections involving the gastro-intestinal system.

CLINICAL STUDIES WITH THE UREA-CLEARANCE TEST*

BY LENNOX G. BELL,† M.D., M.R.C.P., C. R. GILMOUR, M.D., F.R.C.P.(C.), AND
A. T. CAMERON, D.Sc., F.R.S.C.,

Winnipeg

THE NATURE OF THE UREA-CLEARANCE TEST

AMBARD and Weill³ were the first to attempt to relate the excretion and the blood content of urea quantitatively. Their equation gave moderately accurate results for ordinarily low rates of excretion (less than 2 c.c. of urine per minute) but as the urine output increased above this limit the divergence between the calculated and actual figures of urea excretion also increased. Addis and other investigators showed that when the volume of urine excreted is fairly

large the rate of excretion of urea is directly proportional to the blood urea content.^{1, 2, 13, 17} Van Slyke *et al.*⁴ found subsequently that the direct ratio between blood urea content and the rate of urea excretion holds only when the urine volume is above the limit of 2 c.c. per minute (in adults). This limit they termed the "augmentation limit." When the urine volume falls below this level the rate of urea excretion is, on an average, proportional to the square root of the urine volume. On the basis of this and further studies Van Slyke and his collaborators have devised a test which can easily be utilized for clinical purposes.¹⁵ In using this test our procedure has been as follows.

Patients, if not bed-patients, avoided previous exercise and rested prior to and throughout the

* From the Departments of Medicine and Biochemistry, University of Manitoba, and the Winnipeg General Hospital.

The clinical details of the cases reported in this paper will be dealt with by one of us (L. G. B.) in a separate paper.

† Gordon Bell Fellow of the College of Physicians and Surgeons of Manitoba, 1930-32.

test. They were given a light breakfast (with coffee excluded). One hour later the bladder was emptied completely. (Catheterization was necessary in a few cases, to ensure complete emptying.) A glass of water was then drunk. The time of emptying the bladder (zero time) was noted accurately. Just before the expiry of one hour from this time a sample of oxalated blood was taken from an arm vein, and at the one-hour interval the bladder was again emptied, and the whole sample of urine obtained (Sample I) was kept. A second glass of water was drunk at this stage. One hour later the bladder was emptied, giving Sample II of urine.

Urea-nitrogen was determined in the sample of blood, and urea plus ammonia-nitrogen in the two samples of urine, employing the urease procedure with aspiration. Ammonia-nitrogen was separately determined in the urine samples, and deducted, the difference giving the true urea-nitrogen values for the urine. When the urine volume was below 2 c.c. per minute the *standard urea-clearance* (C_s) was determined by Van Slyke's formula:

$$C_s = \frac{U}{B} \sqrt{V}$$

where U is the number of mg. of urea-N per 100 c.c. of urine, B the number of mg. of urea-N per 100 c.c. of blood, and V the volume of urine in c.c. per minute. When the urine volume was above 2 c.c. per minute the *maximum urea-clearance* (C_m) was determined from the formula:

$$C_m = UV/B.$$

These give the volume of blood *completely cleared* of urea per minute. Van Slyke has shown that the normal standard clearance averages 54 c.c. per minute, and the normal maximum clearance 75 c.c. per minute. His charts¹⁵ were used for the actual calculations, and the results expressed in percentage of the normal values (taken as 100 per cent). Results were separately calculated for each urine sample and the mean taken. Occasionally, the two samples gave figures necessitating the use of both standard and maximum clearance, but unless there was very marked discrepancy between the two urine volumes reasonable agreement was obtained for the corresponding clearance figures.

Potential errors in the method.—Van Slyke excludes coffee from the breakfast, since it is a diuretic. Presumably tea should also come in this category, and Harding and Urquhart⁹ ex-

clude tea, coffee and milk. In one or two of our cases weak tea was not excluded, but it is doubtful if any serious error arose therefrom. The second glass of water (additional to Van Slyke's original procedure) was found to give somewhat better agreement between the two urine volumes. Where the 60-minute interval could not be exactly adhered to in collecting the urine samples, the exact time was noted and used. In a very few instances the second sample could not be voided within a reasonable time and the calculation was then based on the single sample. McIntosh, Möller and Van Slyke¹⁴ extended the method to children and undersized adults by applying a correction for body-surface:

$$[\times 1.73 / (\text{body-surface in square metres})]$$

and this correction has been applied to the few cases of children in our series.

Van Slyke's conception of urea-clearance, as already pointed out, is the volume of blood "cleared" of urea per minute, and in accordance with this view the estimation in urine is of urea, and not of urea plus ammonia. If, however, we accept the current view that the ammonia of urine is formed from urea,¹⁶ then the basis of calculation should be the ammonia plus urea of the urine contrasted with the urea of the blood. It is doubtful if the difference is often significant, judging by the figures from actual cases shown in Table I, but such a modification would certainly simplify the ordinary clinical estimation, since few clinical laboratories will ever employ the gasometric methods of the original procedure.²⁰

TABLE I

<i>Comparison of Clearance Values, Using Urea, and Urea plus Ammonia</i>			
<i>Standard Clearances Based on Urine</i>		<i>Maximum Clearances Based on Urine</i>	
<i>Urea</i>	<i>Urea + NH₃</i>	<i>Urea</i>	<i>Urea + NH₃</i>
Percentage	Percentage	Percentage	Percentage
8	8	8	8
15	16	15	16
24	25	25	25
34	36	30	33
52	53	49	56
61	65	62	64
65	67	71	73
72	79	105	118
82	88		
95	98		
118	125		

Were the enhanced values to be employed, of course Van Slyke's standards would also require modification. In determining the results re-

corded in this paper urine-urea values have been employed. As far as our experience goes, in employing the method as a routine clinical procedure the chief source of error lies in wrong timing of the urine samples. Obviously cases in which there is likely to be bladder retention require special attention.

THE CLINICAL APPLICATION OF THE UREA-CLEARANCE TEST

The urea-clearance test shows marked variations with normal persons, so that figures between 75 and 120 per cent have to be regarded as within normal limits. Yet this, alone of kidney functional tests, gives results which can be considered as giving some quantitative estimate of the remaining degree of function in pathological kidney conditions. The test calls for no unusual technical skill, and but little cooperation on the part of the patient, nor does its accuracy depend on that cooperation. From the patient's point of view it is probably the easiest test for the purpose, and even the laboratories of small hospitals should be capable of carrying out the necessary biochemical work.

Van Slyke, Alving and Rose²¹ find that posture and slight exercise do not affect the clearance values of normal persons or of nephritics whose values are above 50 per cent, but when, with resting nephritic patients, the clearance values are less than 50 per cent, if measurements are made when the patients are up and about the values are markedly depressed. On the other hand Bruger and Mosenthal⁵ state that moderate exercise definitely increases the clearance values of normal persons, while low values are not affected in cases of Bright's disease. They state further that not only does a normal person exhibit marked differences of clearance values at different times, but that *single* determinations giving values even as low as 52 per cent do not necessarily indicate diminished renal activity. They agree that values above 75 per cent usually indicate that there is no impairment of kidney function, but consider that 50 to 75 per cent is a doubtful range, and that when figures fall within it other functional tests should also be employed.

Van Slyke and his co-workers²² have compared the urea-clearance test with other kidney functional tests. They found that in patients with diminished renal function the clearance test

shows evidence of this diminution before blood changes in urea and creatinine are apparent or the phenolsulphonephthalein test gives definitely positive results. Usually the clearance test gives values below 50 per cent before other changes are found, and below 20 per cent before all of these are definitely abnormal. (On the other hand, during the recovery period from acute nephritis the dye test sometimes signals improvement much earlier than the clearance test.) Bruger and Mosenthal⁶ are in general agreement with Van Slyke, although they state that in the early stages of renal insufficiency the blood uric acid is occasionally raised before the urea clearance values are definitely low.

The test appears to be equally valuable in all types of cases where there is diminished kidney function, in the various stages of glomerulonephritis, the arteriosclerotic kidney, and in nephrosis. Cases of acute nephritis may show all stages of low values; the latent stage gives subnormal values, the second stage values above 20 per cent, but falling values, and the terminal stage values below 20 per cent (Van Slyke *et al.*²³). Poulton,¹⁸ comparing the clearance test with various others, considers it the test of choice for accurate work. Harding and Urquhart⁹ carried out a large number of tests on urological cases, with excellent results, especially in indicating the desirability of one-stage or two-stage operation in prostatic cases. They consider that the prognosis is poor when such patients exhibit clearance values below 30 per cent. (Young,²⁴ however, stresses the value of the phenolsulphonephthalein test and considers that it is clinically more useful in urological cases.)

Although Holt¹⁰ believed that the method might have marked limitations in value when extended to children, Schoenthal, Lurie and Kelly¹⁹ have found that when the surface-area correction is applied the clearance test can be safely used, even with infants. They find that in infants suffering from severe diarrhoea and vomiting (intestinal intoxication) the clearance value is often greatly reduced, and, when it can be assumed that kidney lesions are absent, they believe that the reduction is due chiefly to dehydration. Goldring⁸ finds that in the acute febrile stages of rheumatic infection clearance values are usually above high normal, while in the afebrile convalescent period they are below low normal.

Hurwitz and Ohler¹² find values above high

normal in normal pregnancy, normal values in the toxæmias of pregnancy, and decreased values in the acute stages of eclampsia. The high values are presumably due to the low concentration of urea in blood during normal pregnancy. Cantarow and Ricchiuti,⁷ in a more extensive study of 39 cases of normal pregnancy, found that 19 varied from 75 to 120 per cent, and 16 from 50 to 74 per cent. Figures as low as 28 per cent were obtained. The urea clearance tends to drop sharply in the last two or three months of pregnancy and to rise steeply during the first few days after delivery. The low results are attributed to increasing nitrogen retention. Of their abnormal cases 7 patients with chronic glomerulonephritis gave figures ranging from 20 to 51 per cent. They conclude that "the value of the urea-clearance test as an accurate index of renal functional efficiency in pregnancy diminishes as the period of gestation lengthens. Subnormal values obtained during the last two months of pregnancy must be interpreted with extreme caution, particularly in the absence of clinical and laboratory evidence of renal functional insufficiency."

RESULTS OBTAINED IN THE PRESENT STUDIES

Normal cases.—We have carried out tests on 55 patients who were normal to the extent that, clinically, they showed no evidence of damaged kidney function, or any arteriosclerotic condition, of any urological condition, or of any febrile condition. Of this total 50 were within the normal limits of 75 and 120 per cent, 2 were between 64 and 75 per cent, and 3 were above the high normal limit. Those strictly within the accepted normal limits included cases (in the afebrile stage) convalescing from transient infections such as influenza, gastrointestinal cases such as duodenal ulcer, patients with certain neurological conditions such as sciatica, disseminated sclerosis, and brain tumour, a case of hyperthyroidism, several cases of myocardial damage without heart failure, and of afebrile arthritis, and a group of 10 or 12 cases that were essentially normal.

The 3 cases giving figures above normal were one of influenzal pneumonia (175 per cent; blood urea-N 14 mg. per 100 c.c.), one of hyperthyroidism (142 per cent; blood urea-N 14 mg. per 100 c.c.), and one essentially normal and undiagnosed (138 per cent; blood urea-N 17 mg. per 100 c.c.).

The cases giving figures below 75 per cent were one of peptic ulcer, with a clearance of 64 per cent, a blood urea-N of 15 mg. per 100 c.c., and with kidney function normal as checked by other procedures, and one exhibiting a neurosis, but otherwise undiagnosed, (65 per cent clearance; blood urea-N 21 mg.).

Cases of Bright's disease.—Tests have been carried out on 15 cases. Our findings are in complete agreement with those of Van Slyke.²¹ Following the usual classification the series may be subdivided as follows.

Acute nephritis with complete recovery.—2 cases.

1. V.F., male, aged 17. He had had chronic recurrent osteomyelitis of the left tibia, right humerus, and right femur for 8 years. In July, 1932, while in hospital for excision of a sinus, he developed severe headache and malaise with a slight rise in temperature. The urine was found to contain albumin, red blood cells, and granular casts. No œdema was present, but the blood pressure rose to 160/108. On July 8th the urea-clearance value was 51 per cent, with a blood urea-N of 34 mg. per 100 c.c. The urine continued to show albumin, blood, and casts with a relatively high specific gravity (*e.g.*, 1.018). On July 25th the urea-clearance value was 45 per cent, the blood urea-N 27 mg. Subsequently the blood pressure fell gradually to 135/85, but the urine showed albumin, casts, and red blood cells until August 4th, when the albumin disappeared; the sediment gradually cleared of red cells. On August 10th the clearance value had risen to 61 per cent, with a normal blood urea, and the urine was normal. He was discharged well on August 20th. He returned to the Out-patients' Department on September 10th for check-up and at that time the urine showed no abnormality and the urea clearance test was 88 per cent, with blood urea-N of 16 mg.

2. A.H., male, aged 37. Admitted to hospital on November 20, 1932. For three weeks prior to admission he had suffered from a severe attack of tonsillitis, and this was followed in about 18 days by lumbar pain, headache, and malaise, with slight œdema about the face. At that time the urine showed marked albumin and some red blood cells and casts. On admission there was no perceptible œdema. Fundus examination was negative. The heart was not enlarged and the blood pressure was 135/80. The urine showed a definite trace of albumin, 20 red blood cells per high power field, and a few granular casts. The urea-clearance figure was 38 per cent, with blood urea-N 17 mg. A urine-concentration test gave specific gravity 1.015 to 1.017. By December 1st the urine showed only a trace of albumin and no red blood cells, the urea-clearance value had risen to 52 per cent and the patient felt perfectly well. On February 2nd the clearance value was 73 per cent; blood urea-N 17 mg. At this time the urine was entirely negative.

Acute nephritis passing to the second and terminal stages.—1 case.

R.O., a male, aged 24, was operated on for infected antra in June, 1930. Two weeks after the operation he developed progressive œdema of the face and ankles, and noticed that his urine was dark and smoky. He was admitted to the Winnipeg General Hospital on June 21, 1930, with a typical acute nephritis. The blood pressure was 159/94, the urine showed marked albumin and many red blood cells and granular casts, and the blood urea-N at this time was 25 mg. per 100 c.c. He gradually improved until by July 17th the œdema had disappeared

and no blood was present in the urine. From that time until December, 1930, he suffered from recurrent oedema, with massive albuminuria and variable hæmaturia. The blood urea-N remained between 25 and 30 mg. Early in 1931 he improved considerably, the oedema disappeared, and he felt well enough to work. He was not seen again until May, 1931, when he again developed a massive hæmaturia and oedema of the face. At this time a urea-clearance test gave a value of 20 per cent, with blood urea-N 33 mg. His condition showed little change until August, 1931, when the oedema again cleared up and he returned to work. He reappeared in June, 1932. At this time he had no oedema but was suffering from severe headaches. His blood pressure was now 165/100. A marked secondary anæmia was present, and the urine showed a specific gravity fixed at 1.010, a definite trace of albumin, and a few red blood cells. A clearance test on June 14th showed 18 per cent function, with blood urea-N 69 mg. From this time on he presented a classical picture of terminal nephritis, with a rising blood pressure, increasing anæmia, and a steady drop in renal function as measured by the clearance test. In October the value was 12 per cent (blood urea-N 74 mg.). He was not seen again until May, 1933, when he was admitted to hospital in a state of coma and died within a few hours. At autopsy the kidneys presented a typical picture of terminal glomerulonephritis.

Latent stage of nephritis.—1 case.

G., male, aged 28, was first seen in 1927. Three weeks prior to admission he had suffered from a severe tonsillitis from which he made a good recovery. About two weeks later, however, he developed pain in the lumbar region, frequency and generalized oedema, and on examination was found to have blood, albumin and casts in the urine. No record of blood pressure or of kidney function was made. The oedema lasted about two months, but finally cleared up completely; at the time of its disappearance the urine contained a trace of albumin, but no blood.

He was examined in December, 1931, at which time he was complaining of vague pains in the chest, for which no cause could be ascertained. The urine showed a definite trace of albumin at all examinations, but no red cells could be found in the concentrated specimen. There was no elevation of blood pressure or anæmia. A urea-clearance test gave a result of 51 per cent, with a blood urea-N of 20 mg. The test repeated some months later gave an almost identical result.

Chronic nephritis (second stage).—6 cases.

The urea clearances recorded in this group were as follows: Case 1, 50 per cent, falling in 5 months to 34 per cent; Case 2, 26 per cent, changing in 6 months to 34 per cent (it is doubtful if this difference can be stressed); Case 3, 65 per cent, falling in 5 months to 32 per cent (death following, and probably associated with an extreme oedema); Case 4, 66 per cent, falling in 3 months to 16 per cent, Case 5, 54 per cent; and Case 6, 27 per cent. All these cases showed the classical picture of the second stage, marked oedema, albuminuria, and hæmaturia.

Chronic nephritis (second stage passing into the terminal stage).—1 case.

S.C., female, aged 12, was admitted to hospital on July 19, 1930, with generalized oedema, weakness, and vomiting. The history dated back to December, 1929, when there was an insidious onset of oedema, scanty

urine, and weakness, with no definite evidence of an acute nephritis. She had had a varying amount of oedema since that time. On admission she was found to have a generalized oedema. The blood count showed normal values for red cells and hæmoglobin. The heart was normal in size. Blood pressure 112/88. The urine showed massive albuminuria with numerous hyaline and granular casts, but no red cells. Blood analyses gave plasma-albumin 1.83 per cent, cholesterol 362 mg., and urea-N 17 mg. per 100 c.c. She remained in hospital until July, 1930, with little improvement, when she was discharged. She returned to the Out-patient Department in October, 1931, with slight oedema. The urine showed marked albumin and a few red blood cells and casts. A urea-clearance test at this time gave a function of 23 per cent, with blood urea-N 30 mg. By January, 1932, the oedema had disappeared, and the albumin in the urine had lessened considerably, but she now exhibited a slight secondary anæmia (red blood cells 4,000,000; hæmoglobin, 55 per cent) and the blood-pressure was 154/110. She had obviously entered into the terminal stage. By May, 1933, she was markedly anæmic; her blood pressure was now 165/110; and there was considerable cardiac enlargement. The urine showed a specific gravity fixed at 1.010; it contained albumin, a few red blood cells, and granular casts. A clearance test at this date gave the figure 8.5 per cent, with blood urea-N 74 mg. The corresponding figures on November 30 were 8 per cent and 98 mg.

Chronic nephritis (terminal stage).—4 typical cases, admitted to hospital in uræmia and a few days prior to death, gave urea-clearance values of 14, 5, 3.5, and 3 per cent, respectively.

Cases of essential hypertension.—In all, 39 cases of essential hypertension have been examined by this test. These can be divided into two groups, which, for the present purpose, can conveniently be termed *benign* and *malignant*. The "benign" group numbered 20 cases; the results of their clearance tests varied between 42 and 69 per cent. For 16 of the 20 the limits were 54 and 61 per cent. In this group the average age was relatively high—55 years—the extremes being 40 and 66 years. The average history was fairly long, and the symptoms were cardiac or cerebral rather than renal in nature. In none of these patients were the eye-grounds typical of an advanced hypertensive retinitis. In those cases which were followed over some months the urea-clearance remained at the same level. Albuminuria was absent in the early stages, but was often present in slight amount later on, with concurrent slightly depressed clearance values, suggesting that the kidneys were secondarily affected. The essential feature of the group is the very slow progressive change. The case history of a typical patient is given.

Mrs. K., aged 55, was admitted to hospital on January 5, 1932, suffering from severe headache, vertigo and dyspnoea on exertion. These symptoms dated back about 4 years, and had become gradually intensified. In 1929 a systolic blood pressure of 190 had been recorded.

On admission she was found to have a pressure of 230/140. The heart showed considerable enlargement to the left, with accentuation of the aortic second sound. The rhythm was normal. The fundi showed fairly marked arteriosclerosis. The urine showed a definite trace of albumin on all examinations, but was microscopically negative, and concentrated to 1.023. The urea-clearance was 55 per cent, with blood urea-N 23 mg. per 100 c.c. Subsequent examinations over a period of one year gave findings practically identical with those just recorded.

There were 13 cases definitely in the "malignant" group. The initial values of the urea-clearance test varied from 69 to 8 per cent, although only 2 exceeded 39 per cent. The average age of the group was 41 years (extremes, 25 and 62 years). The characteristics of the group were the younger age limit, the short history, the extremely high levels for blood pressure (in most patients the diastolic pressure was over 130 mm.) and the severity of all symptoms, especially those of renal failure. Nine patients showed severe hypertensive retinitis. Practically all exhibited albuminuria; four had hæmaturia. A fairly typical case history is as follows.

K., a Ukrainian labourer, aged 41, came to the Out-patient Department and was admitted to hospital in January, 1931, complaining of pain and swelling of both ankles and of the right elbow. He had suffered from recurrent attacks of pain and swelling in these joints for four years. Aside from these complaints he felt perfectly well, although on direct questioning he admitted that he had suffered from occasional headaches during the previous two years. He had worked hard as a labourer all his life.

Examination revealed swollen joints which were reddened and very painful on movement. The pulse was noticed to be very hard and the peripheral arteries showed moderate sclerosis. The heart was considerably enlarged to the left and a soft apical systolic murmur was present, with accentuation of the aortic second sound. On this occasion the blood pressure was 280/168. The urine showed a specific gravity fixed at 1.010, with a moderate amount of albumin and a few granular casts. The urea-clearance value was 19 per cent, with blood urea-N 43 mg. per 100 c.c. The eye-grounds showed a marked degree of hypertensive retinitis with papilloedema, contracted and markedly sclerosed arteries, and areas of soft white exudate.

He was discharged on February 9, 1931, with a diagnosis of malignant hypertension. He returned to the Out-patient Department on April 6th, when his blood pressure was 230/150, and the urine as before. On this occasion he maintained that he felt perfectly well, and he again disappeared, until June 2nd, when he returned complaining of vertigo and severe headaches. The blood pressure was now 250/162, and the urine showed marked albumin and some red cells. The blood urea-N had risen to 74 mg., with a clearance value of 10 per cent. He was again admitted but after a few days in bed his symptoms cleared up and he left the hospital. During July he felt fairly well, except for occasional headaches. His blood pressure varied between 230/125 and 260/158. On July 21st the urea-clearance value was 8.5 per cent, with blood urea-N 78 mg. At this time he had again developed a severe arthritis of the right ankle, and was admitted for treatment. The joint condition cleared up under heat and rest, but the headaches and dizziness became progressively worse. By August 10th he was

becoming drowsy, and the vision in the right eye suddenly failed. He developed obstinate hiccough and relapsed into a stupor. The blood pressure fell to 140/110, the urinary output fell steeply to 100 c.c. per 24 hours, and he died in coma on August 15th. Autopsy revealed typical malignant nephrosclerosis with arteriolonecrosis, etc.

This case, while not absolutely typical of the group, demonstrates how fulminant this condition can be, while causing few symptoms until the onset of uræmia. Many of the cases showed a combination of cardiac, cerebral, and renal symptoms, but in practically all of them there were very marked evidences of renal damage.

The remaining 6 cases, owing to the indefinite history, could not be definitely classified, but the clinical findings, with usually a urea-clearance of somewhat below 50 per cent, suggested that they might represent the end-picture of the benign type of case.

OTHER CASES

Diffuse nephritis in subacute bacterial endocarditis.—1 case showing typical decreasing renal failure.

The patient was a man of 32 with a long history of repeated attacks of rheumatic fever followed by aortic incompetence. During 1932 he developed fever, weakness, progressive anæmia, and various embolic phenomena typical of subacute bacterial endocarditis. A positive blood culture for *S. viridans* was obtained. When he was first seen the urine contained microscopic blood and a trace of albumin. At this time a urea-clearance test gave the value of 42 per cent, with blood urea-N 33 mg. In the course of three months the urine became loaded with albumin and macroscopic blood appeared. There was progressive renal failure. Two weeks prior to death the urea-clearance figure was 19 per cent, with blood urea-N 42 mg.

Amyloid contracted kidney.—3 cases, showing typical decreasing kidney failure. Details of two of these cases are given.

1. A man of 35 had suffered from recurrent osteomyelitis for 12 years. In 1927 he developed diarrhœa, weakness, generalized œdema and albuminuria. The picture was one of generalized amyloidosis with nephrosis. By October, 1931, the urine showed a specific gravity fixed at 1.010, marked albumin, but no red blood cells. The urea-clearance figure was 19 per cent; blood urea-N 39 mg. The blood pressure was low, ranging from 100/50 to 85/50. During the next three months he went steadily downhill with progressive failure of renal function and died in December, 1931, in uræmia. Autopsy showed typical amyloid disease with contracted amyloid kidneys.

2. A woman of 52 entered the hospital on May 27, 1932, complaining of weakness, recurrent œdema, and diarrhœa of some six months' duration. She was found to have an enlarged, firm spleen and liver, and some œdema. The heart was normal in size; the blood pressure 135/75. A marked degree of luetic choroiditis was present in both eyes. Wassermann, ++++. The urine showed on all occasions marked albumin and a few hyaline casts. On June 1st the urea-clearance test gave the value 19 per cent, with blood urea-N 28 mg. A

Congo-red test showed 90 per cent absorption of the dye in 1 hour. The progressive failure of renal function is shown by the following figures:

October 11, 1932. Urea-clearance 15 per cent.
Blood urea-N 45 mg. per 100 c.c.
November 1, 1932. Urea-clearance 11 per cent.
Blood urea-N 43 mg. per 100 c.c.

On November 5th she sank into coma and died the same day.

Acute syphilitic nephritis with recovery.—1 case.

The patient, a man aged 32, was admitted to hospital on November 16, 1932. He had developed a primary chancre six weeks previously, and on admission had a well marked secondary rash. Some oedema of the face had been noted for a few days, and examination of the urine showed an extreme degree of albuminuria with a few casts in the sediment. A urea-clearance test at this time gave the figure 51 per cent, with blood urea-N 21 mg. Treatment was instituted, with rapid disappearance of all the albuminuria and oedema. A clearance test on December 4th gave 90 per cent, with blood urea-N 13.2 mg.

Toxæmias of pregnancy.—4 cases, summarized in Table II.

TABLE II

Urea-Clearance Test in Toxæmias of Pregnancy		
Nature of Case	Urea-Clearance	Blood Urea-N
	Percentage	mg. per 100 c.c.
Pre-eclamptic	63	18
Toxæmia (not eclamptic) ..	74	10
Toxæmia (not eclamptic) ..	75	20
Chorea of pregnancy	65	10

Some unrelated cases.—A case of adrenal cortical tumour with hypertension, which has been reported already by Hunter¹¹ gave a urea-clearance of 44 per cent, with blood urea-N 17 mg. A child with long continued obstruction due to a congenital defect in the urethra gave the figure 9 per cent, with blood urea-N 118 mg. A case of influenzal pneumonia in the febrile stage gave the figure 46 per cent, with blood urea-N 21 mg. and exhibited slight albuminuria. Two cases of congestive heart failure due to rheumatic carditis showed clearances of 66 and 62 per cent, with blood urea-N 15 and 22 mg., respectively. The urine was normal in both cases. One case of severe secondary anæmia gave a clearance figure of 52 per cent, with blood urea-N of 12 mg. When the red blood cell count had returned to normal the clearance figure had risen to 85 per cent.

CONCLUSIONS AS TO THE VALUE OF THE TEST

One of the pleasing features about the urea-clearance test is the agreement on all essential

details amongst those who have published reports concerning its clinical applications. Our results in the nephritic cases are in full agreement with those of Van Slyke; the small group of pregnancy cases gave results in agreement with the findings of Hurwitz and Ohler. Our findings in the series of cases of essential hypertension are those to be expected from present knowledge of the condition of the kidney in this disease.

The results obtained with the test are less dependent on changing conditions, such as oedema, than are those given by most of the other tests of kidney function.

As the number of published cases increases, the value of the test in prognosis in chronic conditions becomes more apparent.

Contrasted with other methods of ascertaining kidney function, the test seems to be the most preferable, because (1) the result given is definite, (2) the result is easily obtained, with relatively small laboratory facilities, and (3) the test eliminates the patient as a source of error.

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