A STUDY
of the
UREA CONCENTRATION TEST
in
62 CASES OF DISEASE.

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Introductory.

To the clinical and pathological classifications of renal disease there must now be added the biochemical classifications introduced by McLean.[1] Little attempt seems to have been made to combine the three classifications into a single comprehensive system. It has even been maintained that the clinical, pathological, and biochemical findings can never be correlated, but surely they must be related, for after all the structural changes must affect the biochemical efficiency of the kidney, and this is what gives the clinical picture. That our rather chaotic scientific knowledge goes only a short way along each road does not connote that the three ways will not eventually be connected and a complete picture be obtained at the meeting of the ways. With this in view I have tried to investigate my cases from the three points of view, when opportunity occurred.

From among the many methods of estimating renal efficiency the urea concentration test stands out as the most generally useful. It is simple to carry out, and has the great advantage of being based on one of the normal functions of the kidney, namely, the excretion and concentration of urea. This test was elaborated and popularised by McLean and De Wesselow,[1] and the term "urea concentration test" has come to be used for the concentration of urea found in the urine in each one of the first three hours after taking 15 grms. of urea by the mouth. Judging from this test alone, McLean holds that the concentration of urea in the urine in the first, second, or third hour after the exhibition of 15 grms. of urea should lie between 2% - 4%. Personally I agree with

Harrison[2] that 2% is too low, and with Combie (B.M.J. Dec.2nd, 1922), that 4% is often exceeded in healthy subjects. Urea is a diuretic, and hence it tends to produce diuresis, thus abnormally diluting the urine and lowering the concentration. This effect usually passes off after the first one or two hours, hence it is advisable to collect three separate specimens, in one of which a true result will be obtained.

When this test gives border-line or poor results McLean advises that the blood urea should be estimated. This is a slightly more complicated test, the technique of which is described in McLean's book. The urea concentration in the blood shows wide variations in the normal subject, but McLean holds that it may be taken as normal if the figure lies between 15 and 40mgms. per 100c.c. If the concentration of urea in the urine, passed in the same hour in which the blood is withdrawn, be estimated, the urea concentration factor $\left(\text{U.C.F.}, \frac{\text{milligrammes of urea per 100c.c. of urine}}{\text{milligrammes of urea per 100c.c. of blood}}\right)$ can be calculated. McLean holds that where this factor falls below 10 the condition is very grave.

Thus it is seen that the blood urea concentration with the U.C.F., and the urea concentration test, are estimated at different times respectively and under different conditions, and therefore cannot be compared or correlated. Harrison[2] suggested performing the two tests at the same time, and withdrew the blood 2½ hours after giving the 15 grms. urea by the mouth, thus obtaining an immediate and complete biochemical picture of the excretion of urea in his patient. The normal blood urea concentration 2½ hours after taking 15 grms. of urea has not been established, but it seems

to lie well below 90mgms. per 100c.c. The U.C.F. should not fall below 20.

Harrison also eliminated the confusing factor of diuresis and active digestion due to food and fluid taken immediately before the test, by making his patients fast completely for six hours before taking the 15 grms. of urea. Another difficulty which arises, especially in cases of chronic nephritis, is the variable gastro-intestinal efficiency. Patients suffering from chronic renal disease, whether of renal-vascular or obstructive origin, all tend to suffer from gastro-intestinal disorders which are likely to have an effect on the absorption of the urea. Hence it is possible that a poor result from a renal efficiency test might be due, not so much to inefficient kidneys, as to inefficiency on the part of the gastro-intestinal mucosa. This inaccuracy is eliminated if the blood urea is known and the U.C.F. can be estimated. It is necessary to discover what the kidneys can do under known conditions, and those conditions are not known unless the concentration of urea carried to the kidneys by the blood is determined. It seems unwise to judge of the renal efficiency when only the work done by the kidneys is considered, and the constitution of the material with which they have to deal is neglected.

For these reasons the routine followed throughout this research was Harrison's[2] modification of the method used by Mclean and De Wesselow[1]. Except in a few cases which were too ill or distressed, the patients fasted completely for six hours before the dose of 15 grms. of urea was given. Having completed the six-hour

fast, the patient was asked to empty the bladder, and this urine formed part of a 24 hour specimen. Immediately on emptying the bladder the patient was given 15 grms. of urea dissolved in 100c.c. of water and flavoured with a little tincture of orange. After this, hourly specimens of urine were collected and measured separately for three hours. Two and a half hours after the urea had been teken, about 8 or 9c.c. of blood were taken from a vein in the arm in the usual way, a few crystals of potassium oxalate being added to the blood to prevent clotting. As soon as convenient the urea concentration was estimated in the urine and blood, as described in McLean's book, the only difference being that a Gerard's ureometer was used. The urea in the 24 hour specimen of urine was also estimated, as giving an idea of what was the patient's usual output of urea.

The urea concentration factor (U.C.F.) was calculated from the information so obtained, and at once a complete statement of the output of urea was obtained.

Kidney disease: inflammatory group.

In studying kidney disease the main difficulty is that so little is known about the manner in which the normal kidney performs its functions. The most generally accepted theory is that of Cushny[3]. This theory states that a dilute solution of the normal urinary constituents is filtered through the glomerulus. This solution contains the soluble constituents of the blood in the same concentration as in the blood, with the exception of albumin, which being a large molecule is not passed through the filtering membrane

of the glomerular tuft. The tubules absorb water, sugar, and other useful substances back into the blood stream, thus concentrating the urine, and in this process oxygen is used and work done by the tubular epithelium against osmosis.

This theory may be accepted as representing the facts better than any other. How can it explain the clinical, biochemical, and pathological findings in renal diseases?

It is impossible to differentiate the various forms of acute nephritis clinically. They all show certain common signs, the most prominent of which are albuminuria, haematuria, casts, and oliguria. The albumin is due to an inflammatory exudate either from the glomeruli or the tubules, or to albumin passed through the membrane of damaged glomerular tufts; the haematuria is due to ruptured capillaries in the glomeruli or to inflammatory extravasations of blood. Thus neither the presence of albumin nor of blood affords a clue to the type of nephritis under consideration. The casts found in the urine of cases of acute nephritis give no help in this problem. These casts are either blood, epithelial, granular, or hyaline. The origin of blood casts is obvious. Cushny holds that the albumin passes through the glomerular tufts in solution, the reaction of the fluid being slightly alkaline; in the tubules the reaction changes to acid, and the protein is precipitated. This forms the hyaline cast, which on its way down the tubule gathers epithelial cells, and, if these are recognisable, an epithelial cast results, while if the cells are degenerated they form a granular cast. Thus the type of cast does not help to differentiate the form

of nephritis for if the protein skeleton does not come from the glomerulus it will come from the inflammatory exudate from the tubules themselves.

Loehlein[4] holds that the oliguria occurring in a case of acute nephritis is directly proportional to the ~~glomeruli~~ glomerulitis. This is of some assistance, but the exact relationship of the two conditions has not yet been established.

Acute nephritis: Group I.

There are two groups of acute nephritis fully described by Loehlein and referred to by Gaskell[5], in which the glomeruli escape almost entirely.

The first of these comprises the toxic albuminurias of diphtheria, and of the initial stages of various fevers. Closely allied to these are those due to inorganic irritants, such as corrisive sublimate and phospherus, etc. These authors include the albuminurias of pregnancy in this group. In this condition the epithelium of the convoluted tubules is primarily and chiefly affected. If the condition is not too severe and recovery takes place, Heinecke[6] has shown that complete regeneration of the tubular epithelium occurrs and the function of the kidney is restored. The only trace left is some thickening between the tubules.

Gaskell considers that in these cases it is probable that the epithelium of the convoluted tubules is damaged by the excretion of the various irritants through the normal channels, thereby implying that the normal channel of excretion is through the tubular epithelium. This explanation is adequate if the urine is concentrated by the

tubular epithelium excreting substances into it, but not if Cushny's theory be valid.

There is however another possible explanation, that the poison passes through the glomeruli in such dilution as to be harmless, and that only when the convoluted tubules have concentrated the urine does the poison begin to act. That it should act first and most severely on the highly specialised and delicate epithelium of the convoluted tubules where the convolutions cause delay, is to be expected.

In the present series only one such case of purely tubular involvement was examined (No. 12. A.12 at 5 c. Table I). This case was a definite eclampsia. The patient came under observation three days after delivery, and the coma was disappearing when the test was performed. The urine showed a urea concentration of 5% in the second hour. This is rather above normal, and denoted an excellent renal efficiency, and therefore a good prognosis. The blood urea 2½ hours after taking 15 grms. of urea was not outside normal limits, and the U.C.F. was 67. This confirmed the good prognosis, and physically the patient made a good recovery but had to be sent to the asylum, as the mental condition remained very bad. This is not surprising, as such a widespread toxaemia as that causing eclampsia does not limit its action to the kidney.

From the clinical and pathological findings in the type of case described above, a poor renal efficiency in the early stages might be expected. In the slighter cases this would quickly improve, returning to normal as the epithelium recovered; in the

severer cases the renal efficiency would decrease to the point of incompatibility with life, and the patient die in the acute condition. This however is pure speculation based on Cushny's theory, and remains to be proved or disproved by combinec clinical, biochemical, and pathological investigation.

Acute nephritis: Group II.

The second form of acute tubular nephritis is found in the early stages of scarlet fever. "It is characterised by great infiltration of round cells around the large vessels, and later around the glomeruli." (Gaskell)(5). It has been fully described by Councilman[7], Chapman[8], and Reichel[9], and mentioned by Gaskell, who insists that the glomeruli are unaffected. They only find this form in cases dying in the first fourteen days of the disease, and therefore probably it only occurs in cases which prove fatal in the early stages. It is doubtful whether these cases die owing to the severity of the scarlet fever or from the renal involvement.

Chapman holds that the true scarlatinal nephritis, which leaves a lasting scar on the kidney, is a glomerular nephritis. Aschoff[10] in his text-book suggests that this may be the origin of the "genuine schrumpfniere," but Gaskell points out that the primary change in "genuine schrumpfniere" is a vascular change, but doubt has since been cast on this.

Acute nephritis: Group III.

There is a large number of observers, headed by Müller[11] and Loehlein[4], who hold that all forms of lasting nephritis are cases of glomerulo-tubular nephritis.

McLean and De Wesselow own that the results obtained from the urea concentration test have been very conflicting in acute conditions. It might be suggested that the solution of this lies in the pathology of each individual case. If the glomerulitis be so severe that all renal function is suspended, there must be an accumulation of all the urinary toxins in the system and retention of fluid, the patient dying from the effects of these on the other vital processes. On the other hand, supposing that it is possible to re-establish the function of sufficient glomeruli, then the comparatively healthy tubules will concentrate urea and other substances well. This is seen in Case 27. Table I. Page 12., who after an almost complete anuria lasting over 24 hours, during part of which the patient was unconscious, respended to McLean's urea test by passing 205c.c. of urine of a 5% urea concentration three hours after taking 15 grms. of urea by the mouth, the blood urea being 46mgms. per 100c.c. 2½ hours after taking the urea, which is well within the normal limits. McLean holds that such cases, giving good urea concentration tests and showing slight or no retention of urea in the blood, should not be classed as cases of ureaemia. Even if the condition remain unclassified the fact remains that the patient had not passed urine for 24 hours, and on admission to the Infirmary only about an ounce of urine, which contained blood and albumin, was withdrawn by catheter. The next specimen obtained was that yielding 5% urea, as described above.

On the other hand, if the glomeruli are only slightly affected and the tubules severely so, although the oliguria may be

slight the renal efficiency would be poor, and the prognosis would depend on the speed and degree of recovery of this function. Thus in acute conditions a good renal efficiency would not necessarily mean a slight attack of nephritis, and a good prognosis could not be based on the result of the urea concentration test or U.C.F. until the advance of the inflammation had been checked and recovery had set in. If however the renal efficiency as estimated from the urea concentration test and the U.C.F. were poor, a definitely bad prognosis could not be based on these biochemical tests, as either recovery or death might follow at any time irrespective of them. Thus this test is of no actual prognostic value during the acute stage of a nephritis.

This discussion of the results obtained from the urea concentration test in acute nephritis is of course purely theoretical.

Table I., page 12½ which tabulates the results obtained in the eight cases of acute nephritis dealt with here, shows one or two interesting points not previously mentioned.

Case 1 seems to have been an infective nephritis. Her brother had a similar illness at the same time, but unfortunately was under other care and could not be tested. Neither however showed any signs of scarlet fever, and both were nursed in an open ward, with no ill results to the other patients.

Cases 9 and 29 both suffered from acute focal nephritis, the illness in Case 9 being secondary to an acute axillary abscess, and the two conditions cleared up simultaneously. Case 29 however died of the primary condition, namely, a malignant endocarditis. It

is interesting to note that the urea concentration in Case 29 was very good, death being due to the cardiac condition - not to the renal complication. Post-mortem examination confirmed the diagnosis. Histological examination of the kidney showed the condition to be that typical of these cases, namely, foci of round-celled infiltration round the convoluted tubules and glomeruli. The tubular epithelium showed cloudy swelling and destruction, with formation of blood and epithelial casts as described by Gaskell and others.

Sections of the renal and small mesenteric vessels showed no abnormality. (see slides No. 29).

Case 39 was that of a child aged ten, showing a moderate degree of oedema, whose urea concentration test was low, with a high blood urea content and a low U.C.F. Although this patient at one time seemed to improve a little, he died a few days later. No post-mortem examination was obtained. It will be noticed that this was the only case showing a low renal efficiency test, and that it is the only death from renal disease in the series.

TABLE I.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
9.	Nephritis (acute) with axillary abscess.	4.3.22.	2·6% 528;	2·8% 72;	2·9% 132.	2·9% 69.	70.	42.	normal.	24.	Epithelial cells and blood present.	Well.
		25.1.23.	2·3% 60;	2·3% 90:	3·3% 90;	3·5% 60.	109.	32.	120.	25.	Albumen free.	Well.
12.	Eclampsia.	4.3.22.	4%.	4·4% 53;	5% 39;	4·6% 53.	69.	67.			9th pregnancy. Induction of labour at term on account of convulsions. No history of renal disease. Albumen and a few casts present.	Physically well. Mentality poor.
14.	Acute Nephritis.	29.2.22.		2·1% 104;	3·4% 26;	3% 26.	61.	49.	125.	6 5/12.	Albumen present and a few epithelial cells.	Well.
		8.2.22.	1·5%.	1·6% 60;	2·1% 150;	3·2% 60.	88.	36.		7.	Albumen free.	Well.
27.	Uraemia.	12.4.22.				5% 205.	46.	108.	210.	33.	Blood and alb. present, also casts and epithelial cells. Previous history of renal disease. Almost complete anuria for 24 hours previous to test.	Improved.
		25.1.23.	·85% 240;	1·3% 150;	2% 120;	2·2% 45.	62.	35.	160.	34.	Albumen free.	Well.
29.	Malignant Endocarditis.	15.4.22.	3·7% 634;	3·8% 66;	3·9% 79;	4% 53.	22.	181.	low.	38.	Albumen abundant.	Died.

TABLE I. (Con).

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
39.	Acute Nephritis.	1.7.22.	1·3% 360;			1·7% 90.	113.	15.	95.	10.	Blood and epithelial cells abundant.	Died.
41.	Acute Nephritis.	18.5.22.	2·9% 336;			4·5% 196.	91.	46.	150.	23.	Blood cells and granular casts present.	Improved
		8.2.23.	2·5%.	1% 270;	1·2% (120).	2·1% 120.	46.	45.	125.	23.	Haze of albumen present in urine; otherwise well.	Improved
51.	Acute Nephritis.	7.7.22.	3·2% 720;	1·8% 90;	4·2% 90;	2·2% 60.	52.	41.	140.	16.	Blood and alb. present a week before test applied. Epithelial cells and granular casts present; no blood.	
		2.5.23.	1·6%;	1·7% 120;	2·5% 120;	2·5% 90.	37.	67.			Alb. free.	Well.

Chronic nephritis.

Should the patient recover from the first acute attack of nephritis, one of three things may happen. Recovery may be complete, in which case as far as renal disease is concerned the later history will be negative, or recovery may seem complete but the patient remain susceptible to recurrent, subacute attacks of nephritis, or the condition may become chronic and advance in a slow insidious manner; in either case a granular kidney will result. The onset may be chronic and insidious from the beginning, the presence of renal disease being discovered late.

GROUP I.

Asotemic nephritis.

McLean uses the term asotemic nephritis to denote those cases of chronic nephritis which show slight albuminuria, casts, no or very slight oedema, with marked polyuria, raised blood pressure, and some enlargement of the heart, which however need not be marked. Although these cases do not show marked oedema, some, as McLean points out, show varying degrees of hydraemia, This is seen if the specimen of oxalated blood be allowed to stand for a few hours, when a distinct watery layer forms on top of the blood. This phenomenon however varies so much that as yet no clinical significance can be attached to it.

The commonly accepted explanation of the high blood pressure is that the renal change is a chronic inflammatory one,

followed, as are all such lesions, by fibrosis. Many glomeruli are completely destroyed, and in others the filtering membrane is thickened and a greater filtering pressure is required. This at once throws more work on the heart, which responds by hypertrophying. The increased pressure throws more work on the arteries throughout the body, and these also hypertrophy. It is held that the presence of toxins in the circulating blood assists in the process, and the common association of this form of chronic nephritis with arterio-sclerosis is a problem which cannot be overlooked. Crofton [12] holds that both the vascular change and the nephritis are due to the same causal agent, namely, a micro-organism of some kind, probably varying in each case; he does not state whether in his opinion the organisms act directly on the kidneys and vessels, or whether the results are produced by the toxins they elaborate. Certainly the intimal changes found in these cases (Cases Nos. 15 and 20) do seem to support the view that the changes are directly due to a chronic form of microbic invasion.

The clinical picture presented by a case of chronic asotemic nephritis shows the slow advance of the condition. From the early attacks the patient makes what appears to be a complete recovery. Between the attacks there may be no or only a trace of albumin in the urine, which is normal in quantity, and the patient feels well. Some years later a second attack of acute, or, more likely, subacute nephritis follows exposure or fatigue of some kind. Again the patient makes a good recovery, but this time there is rather more albumin in the urine, and recovery may be rather slower and less

complete. This is repeated again and again, the intervals of well-being becoming ever shorter until the patient complains of polyuria and continual fatigue, ill-health and albuminuria retinitis. With remissions this continues until the patient finally dies of the chronic uraemic condition so typical in these cases.

Pathologically these cases are generally classed as chronic interstitial nephritis. The size and colour of the kidneys vary, but McLean holds that to consider these characters only confuses an already complex problem. What is really significant is the correlation between the clinical picture, the histological findings, and the biochemistry. Histologically these cases show a chronic glomerulo-tubular nephritis, accompanied by a marked degree of interstitial fibrosis. Whether the condition starts as an interstitial fibrosis, with secondary destruction of the glomeruli and tubules, or whether the changes in the three tissue elements progress simultaneously, is not yet decided. One thing plainly seen in the two cases shown here is that the chief change is a round-celled infiltration followed by fibrosis. In Case 17 hyaline degeneration had followed the fibrous change; this is a common sequence of events and denotes that the condition has been of long standing. These renal changes are accompanied by arterio-sclerosis and consists in a thickened and generated intima, the thickening being sometimes of a patchy character, increase and multiplication of the internal elastic lamina and hypertrophy, with fibrosis of the muscular layer. This change may be more marked in the renal vessels, but is also diffused throughout the body. The mesenteric vessels are particularly

liable to this change, and thus assist in the production of the gastro-intestinal inefficiency so often observed in these cases.

Now what are the results obtained from the urea concentration test during the course of an asotemic nephritis? Except perhaps during the acute or subacute stages the urea concentration test is satisfactory until the polyuria begins. With the onset of the polyuria however the urea concentration fails, and the prognosis becomes grave. What has happened to affect the renal efficiency? The disease has advanced until so many tubules have been destroyed that the concentrating function of the kidney has been seriously interfered with. That it is not the glomeruli that are really the cause of the trouble is proved by the fact that these patients seldom waterlog and die, still passing abnormally large quantities of urine.

In the light of the histological change the gradual failure of renal efficiency is easily explained. Cushny holds that the glomeruli act as mechanical filters. It is a fact of elementary physics that the pressure required to filter a solution through a membrane varies directly with the permeability of the membrane. In this form of nephritis the filtering membrane of many, if not of all the glomeruli is thickened, and this necessitates an increased pressure in the blood vessels. The arterioles contract~~contract~~ and hypertrophy. This throws more work on the heart, and it also hypertrophies, and this continues in a vicious circle until heart-failure sets in. In the blood-vascular system as elsewhere, fibrosis follows prolonged hypertrophy, and this

precipitates the heart-failure. The increased pressure affects not only the damaged but all the glomeruli, and thus more fluid is forced through the healthy glomeruli, taking the albumin with it. There will however be no polyuria until the tubules fail to concentrate the urine by resorption. This failure in function may be due to several causes. As soon as a glomerulus is completely destroyed, the corresponding tubules receive no fluid and cease to function and become fibrosed. Other tubules become directly involved in the slowly advancing inflammation and fibrosis, and thus the epithelium of the convoluted tubules, where the concentration takes place, is destroyed. When destruction of the tubules has advanced to a certain stage the function of the kidneys as a whole is interfered with, and the urine passed is nearly as dilute as that newly filtered through the glomeruli.

Table II (Page 28 a/s) gives the particulars of the urea concentration test applied to 14 cases of asotemic nephritis. Of these 14 cases two, Nos. 15 and 20, died in hospital, all the others showing marked improvement. Case 11 however died at home two months after leaving hospital. In spite of clinical improvement this patient always gave poor biochemical findings. Four of these cases were of special interest.

Case 16. Male, aged 40. Admitted 13.2.22. Gave a history of scarlet fever when four years old, measles and pleurisy when at school. He then had good health till October, 1921, when he noticed that his ankles were swelling, and that he had a swelling in front of his neck. A week later his Doctor noticed that he had

albuminuria. This cleared up after three months' treatment, but returned again about three weeks before admission to hospital.

On admission he was found to have a very much enlarged thyroid, the right lobe being more enlarged than the left. There was no exophthalmos nor tremor, and no increase in the pulse rate. There was some oedema of the feet and ankles and some enlargement of the heart, but this was very slight, the lower border being a little outside the nipple line. The cardiac sounds were normal and the blood pressure 140mms. Hg.

As is seen in Table II, p. 28 et seq. the results of the urea concentration test were never very satisfactory, but in spite of this the patient began to improve as soon as he was given daily small doses of thyroid extract. He was dismissed much improved in general health, though still passing albumin and casts in his urine. This improvement, as is seen in the Table, was maintained for twelve months. Had the urine alone been studied in this case a very poor prognosis would have been given. The interpretation of the low figure obtained from the urea concentration test is greatly modified by the normal blood urea content and the high U.C.F.

Case 11, a female, aged 44, was admitted to the Victoria Infirmary suffering from a slight chronic uraemic condition due to long standing chronic renal disease. As is seen from Table II, p. 28 et seq. the first urea concentration test gave fairly good results. The blood urea was not estimated. The patient, however, was very ill. She gradually improved, and the second test, contrary to

expectation, showed a lowered renal efficiency, the blood urea being 208, an extremely high figure. The U.C.F. was very low, and the prognosis now appeared to be very bad in spite of clinical improvement.

This patient was sent home feeling very much better, free from headache or other distressing symptoms. The urea concentration was still very low, but the blood urea was reduced to 188. The U.C.F. was slightly raised, but still very poor. The blood pressure remained practically constant. Two months after leaving hospital the patient died at home.

The good renal efficiency shown in the first test is apt to be obtained in cases showing acute exacerbations of a chronic renal disease, and is most misleading. The same type of result is seen in the first test performed on Case 30. Table IV. (Page).

Case 15, Male, aged 41. Carter. Admitted to Hospital 7.11.21. suffering from nephritis. Patient gave no history of scarlet fever, but had had measles and chorea in childhood, and while in the Army in Salonica in 1917 he had malaria and rheumatic fever. Since 1917 he had had slight shiverings, accompanied by vomiting at night, but these did not interfere with his work. Patient had slight polyuria for a number of years, and a cough which was worse at night. For three weeks previous to admission patient suffered from severe headache.

Examination. There was marked oedema below the eyes, and the conjunctivae were oedamatous. There was no swelling of the legs.

Heart. The apex beat was in the 5th interspace outside the nipple line. A systolic murmur was audible in the mitral area, which was conducted into the axilla. In the pulmonary area a systolic murmur was heard and reduplication of the second sound. A systolic murmur was conducted into the carotids.

The urine contained albumin, granular casts, and red blood corpuscles. The amount of the albumin was never above ·175%.

9. 11. 21. Patient had a rigor, and his temperature rose to 103°F., but dropped quickly and the patient seemed in his former condition. The albumin rapidly cleared up, and he improved generally. On 7.12.21. he was dismissed to the Convalescent Home. While there his feet began to swell. Once while sitting in a chair he lost the feeling in his left leg, and could not move for 15 minutes. A few days later, while playing billiards, he turned from the table to speak to a companion, but could not say what he desired, and the cue fell from his hand. It was 2o minutes before he could speak at all, and two days before he regained the power of his arm. During this time he had severe headaches.

On readmission to the Infirmary 20.12.21. it was found that the patient hesitated in his speech and was easily confused in his argument. There was also paresis of the arm and leg muscles on the right side. His coordination was good, but there was loss of tactile sense limited to the palm of the right hand. Knee and ankle reflexes were normal and equal, but arm reflexes were not elicited. The cardiac condition showed no change, but

the urine contained 1·23% albumin. This rapidly diminished, and the patient was discharged well on 31.1.23.

He was readmitted 20.3.22. He stated that since his discharge he had been at work in spite of the fact that he had been suffering from dyspnoea, vomiting, and swelling of the feet. On admission his face and conjunctivae were oedematous and his lips cyanosed. The pulse was regular, the tension being above normal. The cardiac sounds were much the same as on his first admission, but somewhat obscured by rhonchi and crepitations in both lungs. The arm reflexes were somewhat exaggerated. Knee jerks not elicited.

Babinski's sign was negative.

Liver was enlarged and tender.

Blood pressure 145mm. Hg.

The urea concentration was poor. The highest reached was 1·1% in the third hour. The blood urea was 66mgms. per 100c.c., and the U.C.F. - 16. The prognosis was bad, although the blood urea was not abnormally high, but the U.C.F. was abnormally low. The patient did not improve in spite of treatment, and died on 29.3.22.

Post-mortem examination showed a somewhat enlarged heart, with fibrous adhesions to the pericardium. Both auricles and ventricles showed hypertrophy and some dilation. The aortic valves were incompetent, and showed acute vegetations superimposed upon a chronic induration, especially at the bases of the curtains, where there was also some calcareous change. The mitral valve was stenosed, admitting two fingers with difficulty. There was

also thickening of the free margins and adhesions between the septal margins of the valve curtains. There was also evidence of an acute condition here. There was a decrease of external fat and pressure patches on the external surface of the left ventricle. The coronary artery and aorta were healthy. The lungs were both free. They were congested, and there was some bronchitis in the smaller tubes, also oedema, which was more marked in the right lung.

The spleen was enlarged with diffluent pulp, as is found in septic conditions. Considerable perisplenitis and perihepatitis of long standing, with adhesion to the colon, stomach, and kidneys. The liver was very much enlarged, and nutmeg in type. The gall-bladder was healthy. The stomach was congested and dilated, and showed a chronic catarrh. The pancreas was oedematous. The kidneys were enlarged, the capsules were adherent; there was chronic venous congestion. The cortex was atrophied in parts, in others enlarged, with dipping between the medullary pyramids. There was no marked fatty change. The type of kidney is that got in chronic subacute parenchymatous nephritis. The glomeruli were irregular and prominent.

The brain was oedematous. No haemorrhage or softening seen.

The cardiac condition may have accounted for the seizure observed at the Convalescent Home, though no gross lesion was found in the brain.

Histological examination of the kidneys showed that there

was marked interstitial fibrosis. This process also involved the glomeruli, many of which were completely destroyed. Bowman's capsules were similarly involved, showing all stages of obliteration. There was also marked round-celled infiltration round the glomeruli. (Plate I).

The tubules leading from the destroyed glomeruli were obliterated; others were more or less healthy, there being considerable cloudy swelling and destruction of epithelium, with formation of casts.

The blood vessels were more difficult to find when the ordinary stains were used, but with Weigert's elastic tissue stain they showed up clearly, with thickened walls and increased elastic tissue.

The renal and mesenteric arteries large and small were sectioned. The walls of these vessels all showed marked thickening and fibrosis of the muscular coat, with increase and multiplication of the internal elastic lamina, with patchy thickening and degeneration of the intima.

These conditions were found to be more marked in Cases 17 and 31. (See Table IV p.54, Plates IV., V., VI., and VII p. 56 et seq.

Case No. 20 also belonged to this series. He was admitted to hospital 17.3.22. complaining of headache and dimness of vision of 18 days' duration. The condition began with headache and great thirst. Patient had a severe cold in the head at the time, and there was a tendency to epistaxis. The headache was sometimes frontal and sometimes occipital, and always dull in character.

The dimness of vision set in about the same time. Also he complained of constipation and vomiting for the last week. There was also some polyuria of a week's duration. His mother died of kidney disease. The patient was a heavy drinker and smoker.

Past health. There was no history of acute or subacute nephritis, nor of scarlet fever. The patient had sustained slight flesh wounds of the chest and left forearm during the war, but these had healed rapidly.

Examination. Patient's complexion was pale and pasty. There was marked oedema below the eyes and under the conjunctivae. There was a fan-shaped sclerotic haemorrhage on the outer side of the left eye, with its base towards the cornea. This is said to have been present for about two days.

Circulatory system. The pulse was irregular in rhythm and force, with occasional missed beats. The vessel walls were greatly thickened, and the tension very high. There were dilated veins on the chest, and the apex beat was visible in the 5th and 6th interspaces in the anterior axillary line. There was epigastric pulsation and pulsation in the veins of the neck.

The left border of the heart was found by percussion to be 4" from mid line just outside the nipple line. The second sound was accentuated in the aortic area, and the other sounds were forcible; otherwise there was nothing abnormal made out.

There was no evidence of free fluid in the abdomen or pleurae. The urine contained blood and albumin. The blood pressure was 220mms. Hg. There was intense neuro-retinitis with haemorrhage

in both eyes.

Two days later there was distinct friction sounds heard at the base of the heart, and bright blood was passed per rectum.

21.3.22. The urea concentration test was carried out, and the highest concentration reached was 1·7% in the second hour. The blood urea in the third hour was 266·4mgms. per 100c.c., and the U.C.F. = ·6. These were quite the worst results obtained during the whole investigation.

The patient made no progress, and suffered from considerable vomiting. The vomitus contained blood, and blood was passed per rectum. The patient was restless and semi-delirious, and died 30.3.22.

Post-mortem examination showed that the heart was hypertrophied. The left ventricle showed some cupping. The aortic and pulmonary valves were competent. The mitral valve also was healthy. The coronary arteries showed adhesion.

The lungs were oedematous and congested.

The liver was enlarged, congested, and dark in colour.

The spleen was enlarged, congested, and indurated.

The pancreas was normal.

The kidneys were slightly smaller than normal, with narrowed cortices and irregularity of the cortical markings. There were areas of fatty change in the remaining parenchyma of the cortex, and there was a cyst in the left kidney. The blood vessels showed some arterio-sclerosis, but this change was not marked.

The stomach was congested, with considerable chronic mucous catarrh.

The intestines were congested at the upper and lower ends.

Histological examination of the kidneys showed the presence of marked general small-celled infiltration, with fibrosis of the interstitial tissue, which had caused widening and destruction of numerous tubules, many of which were filled with hyaline and granular casts. The glomeruli were fibrosed, many being completely destroyed. Bowman's capsules showed generalised thickening, the capsular space being obliterated in many instances. Fatty degeneration was very marked in this case. This is specially seen in the tubular epithelium, which shows marked cloudy swelling. (Plate II, p. 34).

The renal and mesenteric arteries sectioned showed thickening and fibrosis of the muscular coat, with increase and multiplication of the internal elastic lamina, and also patchy thickening of the intima. These changes were more marked in the renal than in the mesenteric arteries. (See Slides).

Although the clinical history did not suggest foci of infection outside the kidney in Case 15, the post-mortem examination showed indubitable evidence of the presence at one time of an active infecting agency in the upper abdomen and pericardium. Case 20, on the other hand, suggested an acute exacerbation of a chronic infection clinically, but did not give such striking evidence of it at the post-mortem examination, where after all only gross lesions can be detected.

T A B L E II.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
1.	Chronic Nephritis.	27.1.22.	2·4% 686.	2·2%						53.	Albumen haze, granular casts, and degenerated epithelial cells.	V. Improved.
		30.1.23.	1·7%.	2·1%;	2·7%.	2·5%.	77	32	105	54.		
5.	Chronic Nephritis.	12.3.22.	1·6%.	2% 264;	1·9% 26;					46.	Haze alb. Blood trace.	maintained.
		18.1.23.	·6%;	1·5% 180;	3·2% 90;	3·5% 60.	84.	41.	135.		Alb. free.	Improved.
6.	Chronic Nephritis. and V.D.H.	22.2.22.	1·1% 190;	1·5% 53;	2·5% 39:				160.	51.	Alb. abundant. No oedema. Cleared up rapidly.	V. Improved.
7.	Chronic Nephritis.	20.1.22.	1%.	1·1%.	2·7%.				120.	42.	Alb. and blood in urine. Cleared up rapidly.	V. Improved.
11.	Chronic Nephritis.	22.2.22.	1·4% 1188;	1·5% 132;	2·2% 53;				205.	44.	Ureomic symptoms slight. Alb. cloud casts and epithelial.	Improved, but died at home 2 months later.
		3.3.22.	1·4% 9768;	1.4%;	1·4% 79;	1·3% 79.	208.	6.	200.		Cells present.	
		23.3.22.	1·1%;	1·0% 106;	1·4% 105;	1·4% 73.	158.	9.	210.			

T A B L E II. (Con).

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
15.	Chronic Nephritis.	23.3.22.	0·5%;	1·1% 158;	1% 106;	1·1% 53.	66.	17.	145.	41.	Blood and epithelial cells. Blood and granular casts. Alb. cloud.	Died. P.M.
16.	Chronic Nephritis with enlarged Thyroid.	24.2.22.			1·5% 30;	2% 150.	50.	40.	140.	40.	A few degenerated epithelial cells. Alb. very abundant.	Improved.
		28.3.22.	1·4% 2184;	1·3%104;	1·9%78;	1·9% 52.	29.	66.	150.			
		5.5.22.	0·4% 3168;	1·5% 132;	1·5%66;	1·8% 36.	46.	39.	146.			
		20.7.22.		0·65%120;	1·3%105;	1·5%90.	43.	34.				
		20.4.23.	1%.	1·2% 90;	1·2% 75;	1·5%120.	49.	30.			Alb. epithelial, granular, hyaline casts abundant, also epithelial cells.	Improved.
18.	Nephritis (Chronic). with oedema of lungs.	12.3.22.		2% 75;	1·9% 105;	2%158.	62.	32.	105.	33.	Alb. abundant, some epithelial cells, and granular casts.	Improved.
		30.3:22.	1·1%.	2·2% 53;	2·5%53;	3·8%53.	37.	102.	105.		Alb.very much less; still some degenerated epithelial cells.	
		25.1.23.	·9%;	3% 90;	3% 120;	3·6%45.	48.	69.	100.		Alb. free.	Well.
20.	Chronic Nephritis.	21.3.22.	1·7%;	1·5% 79;	1·7%;	1·5%.	266.	6.	220.	27.	Blood and granular casts. Oedema not marked. Severe nephritis. alcoholic.	Died. P.M.

T A B L E II. (Con).

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
30.	Chronic Nephritis.	21.4.22.	1·7% 1373;	2% 132;	2·2% 105;	2·2% 79.	41.	53.	low.	42.	Pus and degenerated epithelial cells present. Alb. slight.	Well.
		30.1.23.	1·7%;	1·9% 120;	2·1%120;	2·2% 120.	47.	46.	140.	44.	Abundant deposit of pus.	
38.	Chronic Nephritis.	11.5.22.	2·5%;	2·4% 26;	3·1% 132;	2·6% 53.	41.	63.	165.	46.	Epithelial cells; abundant alb.	Improved.
46.	Chronic Nephritis.	30.6.22.	1·5% 1260;	2% 90;	1·9% 60;	2·4% 67.	45.	53.	140.	53.	Alb., epithelial cells, granular and epithelial casts. Several attacks.	Well.
59.	Chronic Nephritis.	3.8.22.	1·5% 240;	1·5% 120;	1·0% 120;	1·9% 180.	35.	54.	170.	25.	Alb., a few epithelial cells and granular casts.	
		16.8.22.	1·2% 660:	1·6% 60;	2·3% 60:	2% 30.	36.	55.	150.		Alb., a few epithelial cells and granular casts.	
64.	Chronic Nephritis.	28.8.22.	·7%;	1·0% 90;	0·7% 120.		77.	9.	210.	37.	Epithelial cells and granular casts. Scanty alb. slight.	

PLATE I.

Case 15. Thickening and fibrosis of the glomeruli and of Bowman's capsule. Round-celled infiltration around the glomeruli.

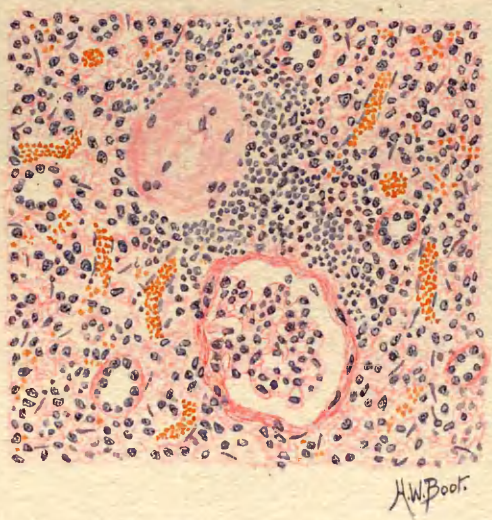

Plate I

PLATE II.

Case 20. Fatty degeneration of the kidney substance.

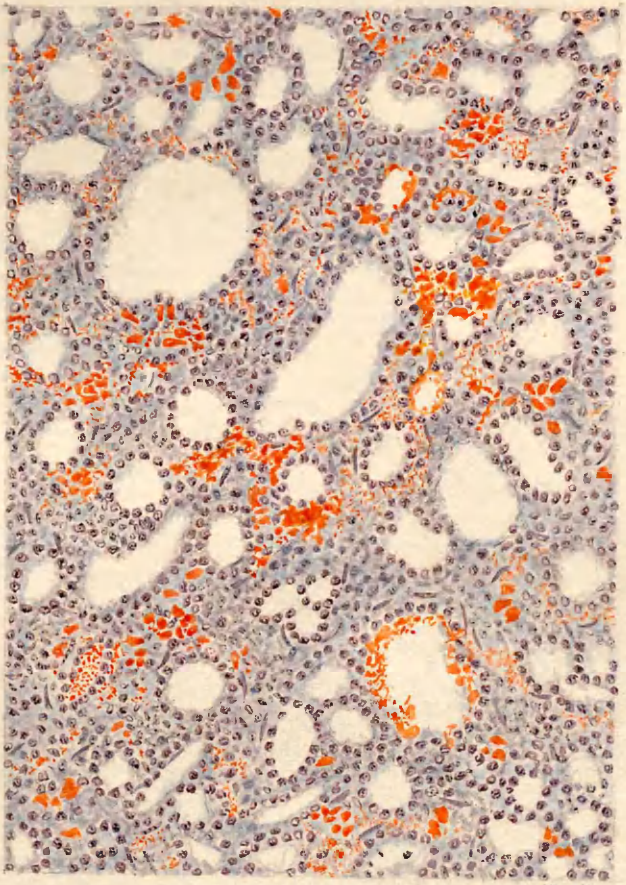

Plate II

Chronic nephritis: Group II., hydraemic types.

Hydraemic nephritis is a distinct clinical form of subacute nephritis. The patients present a very typical appearance, and great oedema and anaemia are the most obvious signs. There is also obstinate oliguria and prostration. The illness is a long one, but if oedema of the lungs is not severe recovery generally takes place slowly; relapses however are frequent during convalescence, and repeated attacks are common. The condition may pass into the asotemic type of nephritis after several attacks.

Pathologically this condition is associated with what is commonly termed a large white kidney, but the size and colour of the kidney is not constant, and McLean holds that no importance should be attributed to the microscopical appearance.

Histologically the condition is a glomerulo-tubular nephritis, with little interstitial change and practically no fibrosis or contraction. In the later stages however this may be a prominent feature, and the condition resemble that found in chronic interstitial nephritis. This histological change is accompanied by a corresponding change in the clinical picture, the case becoming one of asotemic nephritis.

The chief biochemical difficulty in these cases seems to be the elimination of salts. McLean has shown that these cases concentrate urea well. From the following Table it is seen that the present work confirms this result. The only low concentration test was given by Case 56, who however had good health in spite of this.

Among the five cases examined two were brothers, who deserve special mention. Three members of the family suffered from albuminuria - the two brothers mentioned here and one sister, who however died shortly after the albuminuria was discovered. The two brothers took ill in 1912. The elder, Case 55, was eight years, and the younger, Case 56, was six years old. They were both admitted to the Victoria Infirmary under Dr. MacKenzie's care.

Case 55 was admitted (1912) with a very marked degree of oedema, oliguria, and albuminuria. The condition yielded to treatment, and the patient passed large quantities of urine, the oedema being quickly reduced, but in a few days it recurred as severely as before. He relapsed and the oedema, oliguria, and albumin returned several times, and the patient was taken home by his mother and continued to suffer from attacks of oedema and oliguria for a few weeks, each attack being less severe than the previous one. The patient remained well till 7/11/19, when he was readmitted to hospital suffering from marked oedema and oliguria, and his urine contained albumin in large quantities, with casts and epithelial cells. The oedema increased, and the patient's temperature rose to 102·5F., and patient complained of pain and some tenderness in the right side. The advisability of tapping the abdomen and inserting Southey's tubes was being considered, but before this was done the patient began to pass large quantities of urine, and within 24 hours the oedema had completely drained, and the patient, from being very swollen,

had become very thin - so much so that he was not recognised by a friend. When the quantity of urine became large the albumin disappeared, but on a return to normal a slight amount of albumin returned. Most probably the albumin was so diluted as not to be detected. The patient was dismissed physically well, but passing a small amount of albumin.

The patient was not seen again till 25/7/22, when he stated that he had been well since 1920. The urea concentration test was carried out, and as is seen in the Table the result was good all through.

Case 56 was treated differently. In 1912 he proved to be a similar but more obstinate case than his brother, and it was attempted to decapsulate his kidneys. This was found impossible, and they were incised. The wounds gave considerable trouble during healing, but finally the child was well enough to be sent home, having been eleven months in hospital. Patient was first seen by me in 1919, when he was physically well and attending school regularly, though passing some albumin. In 15/7/22 he was well and at work in spite of a urea concentration of 1·8% in the third hour. The blood urea however was not above normal, and the U.C.F. was high, as is seen in Table III. p. 38

Cases 53 and 54 both gave good urea concentration tests in spite of hydraemic nephritis - in Case 53 in childhood and in Case 54 in 1919, when 44 years of age, at which time the latter was very ill, the oedema being very obstinate and the albumin excessive, 2·6%. In both cases the condition yielded slowly to blood-letting

and diuretics.

Case 25 was a similar condition, but as the oedema did not yield rapidly Southey's tubes were inserted into the legs. At first these drained well and gave great relief, but sepsis set in and the patient died. No post-mortem examination was obtained.

The question now arises as to what constitutes the real difference between these two types of chronic nephritis.

Asotemic nephritis.	Hydraemic nephritis.
Oedema absent or slight.	Oedema extreme.
Anaemia slight and late.	Anaemia marked and early.
Polyuria.	Oliguria.
Blood pressure high.	Blood pressure low.
Albuminuria slight.	Albuminuria very marked.
Granular kidney.	Large white kidney, which may become granular.

The above columns contrast these two types of chronic nephritis. McLean does not allow that the pathology is essentially different in the two types, and holds that the difference is wholly biochemical and clinical. Essentially, the pathology is a glomerulo-tubular nephritis in both types; the size and colour of the kidney is held to be different by many pathologists; others however hold that this varies so much that no importance can be laid on this point. The old idea that the hydraemic type of nephritis, with a large white kidney passed into the smaller white granular kidney, is now no longer held. A large white kidney may pass into a small white kidney and the clinical type

of nephritis tend toward the asotemic type, but often the clinical, pathological, and biochemical conditions remain the same to the end. A small white kidney may be found in the asotemic type of nephritis, although a small red kidney is more usual. In many cases dying of asotemic nephritis the contraction of the kidney is only slight. This variety in the gross pathological findings has made the classification of renal disease extremely difficult. Microscopically it is seen that the degree of contraction depends solely on the amount of fibrous tissue in the kidney and the degree of shrinkage which has taken place; the colour being partly due to this cause and partly to the degree of fatty change.

Thus the essential difference between these two types of chronic nephritis is apparently not directly referable to the pathology of the kidney itself, but, as McLean points out, more probably depends upon some disturbance of biochemical balance in the tissues of the body generally. This would seem to support Crofton's theory that nephritis is not primarily an affection of the kidneys but the manifestation of a bodily condition, the chief signs and symptoms of which are renal.

T A B L E III.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
25.	Chronic Nephritis.	10.4.22.	2·2%;	2·1% 105;	2·4% 39;	1·8% 39.	86.	21.	150.	37.	Oedema great cyanosis marked. Southey's Tubes inserted, followed by sepsis. Alb. abundant, also casts. No P.M.	Died.
53.	Chronic Nephritis.	17.7.22.	3%;	2·8%;	3% 90;	2·9% 120.	35.	86.		18.	Albumen trace; epithelial cells abundant.	Well.
54.	Chronic Nephritis.	17.7.22.	1·2%;	1·6% 120:	2·9% 90;	2·8% 90.				47.	Albumen trace; epithelial cells abundant.	Well.
54.	Chronic Nephritis.	25.7.22.	1·9%;	1·5% 420:	1·8% 120:	2·7% 120.	40.	67.		19.	Albumen trace. No cells nor casts.	Well.
56.	Chronic Nephritis.	25.7.22.	1·2%;	1·4% 120:	1·4% 150;	1·8% 90.	37.	43.		16.	Albumen cloud. No cells nor casts.	Well.

Chronic nephritis of vascular origin.

What is usually designated as cardio-renal disease is the clinical condition caused by interstitial nephritis of vascular origin. The early manifestations of this disease are obscure and vary greatly. As is seen from the case histories dealt with here, the early signs and symptoms are not referred either to the heart or kidneys. These patients complain of indigestion, constipation alternating sometimes with diarrhoea, asthma, a feeling of fullness in the head, nervousness, and rather vague sensations of malaise. The urine may remain free from albumin for a long time, or this may be present in so slight an amount as to be overlooked or considered of little importance. The heart may be markedly enlarged, but this may not be very obvious. The blood pressure is raised. The superficial arteries are somewhat thickened, but as this is a fibrous and muscular hypertrophy the hardening is not so easily determined as in typical senile arterio-sclerosis with pipe-stem arteries. This condition is found in all walks of life, but there are two prominent factors in its causation, namely, an excitable nervous system and over-work. The over-work may be physical, but is more commonly mental. These patients are mostly obtained from the professional and business classes. Over-strain, lack of exercise, which is attended by a tendency to constipation, and a general neglect of teeth, and the minor ailments are all at least predisposing if not causal agents. Over-indulgence in a too stimulating diet is also a contributory cause, but the condition has been noted in an Irish peasant whose diet consisted largely of potatoes and tea, but whose history

showed all the other predisposing conditions.

The earliest definite sign is hypertension. In the later stages the symptoms are as various as in the earlier ones, but tend to remain fairly constant in each case, there being an increasing severity of existing symptoms and addition of new ones. A common history is that given by Case 31, where the first symptom was gastro-intestinal disturbance and some nasal congestion. These in turn were followed by polyuria, fainting fits, and finally by palpitations and general symptoms of cardiac and renal failure. As a general rule the diagnosis of cardio-renal disease is not made until there are cardiac or renal symptoms or signs, though treatment at this stage is seldom of any lasting benefit. If diagnosed early, however, the hypertension can often be controlled.

Pathologically the condition is a diffuse arterio-sclerosis with enlargement of the heart and chronic interstitial nephritis showing a vascular distribution, if the case is an early one. Diffuse arterio-sclerosis is also found in cases of chronic nephritis, and this would suggest the possibility of a common causal agent for both these vascular and renal lesions.

Histologically diffuse arterio-sclerosis consists in a more or less even thickening of the intima, with some fatty degeneration (supposedly due to the poor blood supply received by the deeper layers; increase and multiplication of the internal elastic lamina and hypertrophy with fibrous and fatty degeneration of the media. These changes are all clearly seen in the sections

cut from material from Cases 15, 17, 20, and 31, where the similarity in the arterial lesions is very striking. Case 20 however shows a rather more nodular intimal thickening than the other three.

The distribution of the lesions in the vascular system is an important point, for it is this that gives rise to the clinical picture. In different cases the distribution varies and the symptoms vary with the distribution, becoming more general as the condition spreads from one system of vessels to another. In many cases the gastro-intestinal vessels are first attacked, and in these the renal symptoms are later in appearing. In others the renal vessels are first attacked, and this gives rise to early diagnosis of renal disease.

In the kidney the condition is a chronic interstitial nephritis, beginning round narrowed or completely occluded vessels and gradually spreading to the whole organ. This suggests that one factor in the form of nephritis is a poor blood supply. The history of the syndrom in a series of cases would suggest that the kidney is only secondarily involved, and in some instances at a late stage.

Biochemically these patients show very similar results to those got in chronic interstitial nephritis. The renal efficiency estimated by the urea concentration test and the blood urea content remains high until the onset of polyuria, after which it gradually fails. When the blood urea has reached very high figures, there may be a misleading improvement in the urea

concentration test. This is seen in Case 31, the first test showing a urea concentration of 2% in the third hour. This seemed a good test, and far better than was to be expected from the severity of the clinical symptoms. When, however, the blood urea was estimated and the U.C.F. was calculated and found to be 112mgms. per 100c.c. and 18 respectively, the fallacy was clear.

Case 37 on the other hand showed no severe clinical symptoms, but had a blood pressure of 240mm.Hg., and gave a very poor urea test, and, although she left Hospital somewhat improved, died two months later. These points demonstrate the similarity between diffuse arterio-sclerosis and chronic interstitial nephritis. The question however remains whether they are different manifestations of the same disease, or different diseases with certain signs and symptoms and pathological changes in common.

Table IV. (Page 62) Case 31. Female, aged 47. Admitted to the Victoria, 14/4/22., complaining of troublesome headaches.

When questioned patient stated that she had had attacks for a number of years. Then indigestion set in. This, however, did not seem to have worried her very much. Two years previously she fell unconscious on the street, but after a week in bed she was able to resume her usual work, though from this time she was always breathless. A year later she had a similar seizure, followed by such severe asthma that she applied to the Western Infirmary for relief. There she was treated for asthma, an operation being performed on her nose for relief of this symptom. After five weeks the patient returned home somewhat better, but not free from suffering. She had frequent attacks of giddiness and occasional attacks of palpitation, but never noticed any swelling of the feet or legs. Headaches had, however, been severe. Patient also gave a history of rheumatism some twelve years ago, and of frequency and polyuria of two years' duration.

On examination a presystolic murmur was made out at the apex. The apex beat which was in the seventh interspace in mid-axillary line was thudding in character, but no thrills were noted. The blood pressure was 245mm. Hg.

There was tenderness in the right hypochondrium, probably due to an enlarged liver. The abdomen was otherwise normal.

The patient was under observation for about a month, during which time she gradually became worse, the polyuria diminishing and her legs and hands gradually becoming more and more odematous, the oedema being tense and painful. Petechial

haemorrhages appeared all over her body, but were most marked on her hands and feet. She was troubled with frequent vomiting and suffered from flatulence and constipation. During the first few days she vomited blood. Nothing except amyl-nitrite gave her any relief from the severe headaches, but this increased the oedema and other conditions. On admission there were albumin and casts in the urine.

On 20/4/22 a urea concentration test was carried out, and in the third hour the urea output reached 2·1%. This low figure was not due to diuresis, as it is seen that only 55c.c. of urine were passed in this hour. The blood urea was very high, being 112mgms. per 100c.c. This gave a U.C.F. of only 18.

From the urine alone the test might be considered as giving a pretty good result, but when the blood urea content was estimated and the U.C.F. calculated, then it was seen that the prognosis was not good.

The test was repeated on 28/4/22., when the highest concentration in the urine was 1·5% in the first hour. The blood urea was 103mgms. per 100c.c. The urea concentration factor worked out at 12, a very poor result. The low concentration in the urine may have been due to the defective absorption, as the patient vomited about 30 minutes after taking the dose of urea, but a blood urea of 103 should have stimulated the kidney to concentrate to its utmost capacity. No further tests were made on this patient, as she was too ill, and any attempt to give urea caused vomiting. Patient died 15/5/22.

Post-mortem examination. Half a pint of serous fluid was found in the peritoneum and about the same quantity in each pleural cavity, also a little in the pericardium.

Thorax. A pericarditis was found with sero-fibrinous exudate chiefly at the base. A large area of fibrous thickening was found on the surface of the right ventricle. The heart was enlarged, all the chambers taking part in the process. In the left ventricle the hypertrophy was excessive, but was also well marked in the other chambers. Dilatation was marked in the right ventricle and the auricles, but was only slight in the left ventricle. There was an ante-mortem clot in the right ventricle, and a large clot in the right auricle, the auricular appendix being distended with clot. The muscle was hypertrophied, and showed pale patchy degeneration. Aortic and pulmonary valves showed slight thickening at the corpora aurantii. There was slight atheromatous change in the aorta and coronary arteries. Mitral and tricuspid valves admitted fully two or three fingers, but the curtains were healthy. The aorta from the arch downwards showed advanced change, but no ulceration. The blood vessels of the stomach, spleen, and kidneys all showed marked thickening of their coats, and were tortuous.

Lungs. Non-adherent. The left lung showed a large recent infarction, which occupied the greater part of the lower half of the upper lobe. The lung was congested. The bronchi showed acute congestion and chronic bronchitis. The right lung was oedematous. There were 6 or 7 infarctions in all, and these

were about the size of a hazel nut, and were scattered throughout the three lobes. The bronchi were as in the left lung.

The liver was enlarged, markedly congested, and there were pale areas suggestive of fatty increase.

The gall bladder was healthy.

The spleen was slightly enlarged.

The stomach was slightly dilated; the mucosa congested. There were four or five mucosal ulcers in the pyloric region, and two about the middle of the organ on the greater curvature. The vessels were tortuous and distended.

The pancreas was oedematous and congested.

Both kidneys were of normal size, but dense in consistence, with a slight degree of thinning of the cortex. The surface was granular, with areas of congestion and pallor. The capsule stripped freely. There was marked change in the renal vessels. The bladder was healthy.

Intestines. The small intestines and rectum were congested, and showed mucosal ulcers similar to those found in the stomach, but larger in size.

Brain. There was excess of fluid in the subdural space. On section the amount of fluid was slightly increased. On section through the basal ganglion an area of softening was found in the right optic thalamus, and the corpus striatum of both sides showed prominence of the vessels. There was a small recent haemorrhage about the size of a split pea in the right occipital lobe. The vessels of the base showed atheromatous

changes of a patchy character.

Sections of the kidneys and various arteries were cut and stained, but showed nothing new or unexpected. The kidneys showed marked fibrosis distributed in areas corresponding with sclerosed vessels. The glomeruli were sclerosed; some were completely destroyed and replaced by fibrous tissue, some only showed infiltration and thickened capsules, and others showed this condition in a more advanced stage. (Plate IV. p. 56)

The kidney vessels showed increase in fibrous tissue. This was shown up by van Giessen's stain, but there was also marked increase in the elastic tissue and multiplication of the elastic lamina and thickening of the intima. (Plate V).

The tubules showed widened lamina and destruction of the epithelium, while many contained blood casts. There were also extravasations of blood into the interstitial tissue, which showed marked increase in fibrous tissue.

The renal artery showed increase in elastic tissue, with multiplication of the internal elastic lamina, fibrosis of the muscular layer, and patchy increase, with degeneration of the intima resembling patchy endarteritis obliterans. (Plate VI. p. 58

The main mesenteric artery was sectioned, and the portion cut showed a vasa vasorum with similar changes to those in the main artery, namely, increased fibrous tissue in the muscular coat and multiplication of the elastic lamina, and increased thickness of the intima.

Sections were cut from one of the branches of the mesenteric

artery, and similar changes were found. (Plate VII. fig 59.)

The still smaller arteries cut showed similar changes, but in these the intimal change was not so marked.

The splenic artery showed less multiplication of the internal elastic lamina, and more of the patchy increase of the intima than was seen anywhere except in the renal artery.

The radial, internal carotid and the basilar arteries all showed similar changes, the intima being very evenly and markedly thickened in the internal carotid artery.

Case 17. Male, aged 57. Iron Sawyer.

Admitted to the Victoria Infirmary 1/9/11. Under Dr. Love's care. At that time he was complaining of bleeding from the bowel and diarrhoea of six weeks' duration. The liver was slightly enlarged and the heart hypertrophied. There was no albumin in the urine. The patient admitted taking six glasses of whiskey daily, and more on Saturdays. A diagnosis of alcoholic cirrhosis of the liver was made. The patient improved under treatment, and went home well 1/9/11. Past health good, except for measles and whooping cough as a child.

The patient was re-admitted to the Infirmary 4/3/22 under Dr. MacKenzie's care. Since the previous admission the patient had been at work regularly, and had felt pretty well. Two months previous to re-admission he began to feel breathless; slight exertion produced such fatigue that he had to rest constantly. At this time, too, he was sleeping very badly. On examination it was found that the pulse was irregular in rythm and force.

The vessel wall was thickened and the tension was very high, the blood pressure being 222mms. Hg.

Heart. The apex beat was in the 6th intercostal space 5" from mid-sternal line. Marked epigastric pulsation was present. The sounds in the mitral area were very thudding, and were accompanied by a high-pitched murmur. In the aortic area the second sound was slapping in character.

Alimentary system. The tongue was covered with yellow fur. The abdomen showed dilated veins. The lower edge of the liver was 1" below the costal margin.

Nervous system. The left pupil was slightly larger than the right one. The right knee jerk was not elicited.

The patient became rapidly worse and Cheyne-Stokes breathing set in, death occurring 14/3/22.

On admission the patient was mentally slow, and could not concentrate his attention for more than a few minutes. He was very restless and often delirious, showing in short the chronic slight uraemia so common in these cases. On the 8/3/22 the urea concentration test gave a very poor result, both with regard to urine and blood, the U.C.F. = 13, as seen in Table IV. The albumin in the urine was slight, never above ·25%. Granular casts and epithelial cells were present.

Post-mortem examination.

Thorax. The heart was greatly enlarged, especially on the left side. The pericardium was healthy and the veins tortuous. There was hypertrophy of the muscular walls of both ventricles, especially of the left, where thickening had occurred

to such an extent that the wall measured about 1½". There was some fibrosis of the papillary muscles, one patch of which showed hyaline degeneration, but elsewhere the myocardium appeared healthy on macroscopical examination. The cardiac cavities were normal in size. The endocardium showed some fibrous thickening over the muscular septum on the side of the left ventricle. Atheroma of the cusps of the aortic valves had caused slight deformity, resulting in slight incompetence. The pulmonary valves were normal. The tricuspid orifice was dilated, admitting four fingers, but the curtains appeared healthy. The mitral valve admitted an extra finger, and the anterior cusp showed a well marked patch of atheroma. The beginning of the aorta showed several atheromatous patches, especially marked round the orifices of the coronary arteries, which were in a state of advanced atheroma.

Lungs. Old pleural adhesions were present on the right side; both lungs were slightly oedematous.

The liver was normal.

The spleen showed venous congestion.

The kidneys both showed advanced arterio-sclerotic changes, the capsules being adherent, and on being stripped left a granular surface. The renal arteries were pipe-stem. Smaller branches showed wide orifices on section. The cortex was narrowed, with marked irregularity of the radial markings. The supra-renals were slightly enlarged. The abdominal aorta showed advanced arterio-sclerosis, the lower part however being healthier than the upper.

Brain. Oedema of the meninges was not marked. A cortical haemorrhage ¾" in diameter was present in the right cerebellum.

Kidneys, histological examination. The interstitial tissue was thickened and fibrosed. The glomeruli showed increased fibrous tissue, with thickened fibrous capsules. Many were completely destroyed, and had undergone complete hyaline degeneration. (Plate VIII, p. 60)

The tubules showed wide lumina and destruction of epithelium, with numerous blood casts. The vessels showed marked sclerosis, the smaller ones being very difficult to find except in the slide stained for elastic tissue. In this slide the multiplication of the internal elastic lamina is well shown up, also the somewhat patchy increase in the intima.

The vessels examined were the renal artery, the medium-sized enteric arteries, the splenic artery, and branches. All these vessels showed fibrosis of the media, and multiplication of the internal elastic lamina, and patchy thickening and degeneration of the intima. The changes however were not as marked as in Case 31.

Case 13. Female, aged 52. Admitted to the Victoria 22/2/22. Except for some polyuria for some years, the patient had had good health till about five weeks previous to admission, when she noticed her legs swelling, and suffered from breathlessness on the least exertion.

The pulse was irregular in force and rythm. Sometimes however there were short intervals when the pulse was perfectly regular. The vessel wall was thickened, the blood pressure being

165mm.Hg. in spite of the heart failure.

The apex beat was in the 7th interspace nearly 6" from the mid-sternal line. Pulsation was seen in the 3rd., 4th., 5th., and 6th. interspaces extending to the anterior axillary line. The left border of the heart was in the anterior axillary line. The right border however corresponded with the right border of the sternum, thus showing no abnormality. A systolic murmur was heard in the mitral area. The second aortic sound was not accentuated over the pulmonary area. A short sharp murmur was heard with the first sound.

Lungs. A dull area was found at the right base, where the breath sounds were difficult to hear. Coarse crepitations were heard all over both lungs.

As is seen in Table IV. p.54, the urea concentration test gave poor results, and although the patient improved sufficiently to go home, she died a few months later. In this case there were practically no symptoms till cardiac failure set in. It is of course possible that this patient was really a case of chronic nephritis, with insidious onset and progress, and as she was only under observation for a short time and no post-mortem examination could be made, the doubt cannot be cleared up. However, from the history and general appearance of the patient I think that she belonged to this vascular group.

Case 37. Fenale, aged 55. Admitted to the Victoria 24/4/22. Complaint, indigestion, constipation, periods of excitement, with polyuria, menorrhagia, and palpitations. There had been

amenorrhea for the last two months.

The heart sounds were normal, but the heart was much enlarged to the left, and the blood pressure was 245.

The urine contained a trace of albumin. The urea concentration test gave poor results, Table IV. The patient improved a little, but died a month later.

Case 45. Female. Admitted to the Victoria Infirmary 26/6/22.

Complaint, polyuria and cough traced to cardio-renal condition.

There had been a trace of albumin in the urine a year previously. The patient however complained of not being well for the last few years, though nothing definite could be described. On admission patient was found to have an enlarged heart, with thickened vessel walls. Blood and epithelial cells as well as albumin were found in the urine. The patient improved under treatment, then relapsed and died.

Thus it is seen, as Evans [13] points out, cardio-renal disease is not a clinical entity but the terminal stage of diffuse arterio-sclerosis. Cardio-renal disease is a fatal condition; diffuse arterio-sclerosis, according to the same worker, is not necessarily fatal, but on the contrary has a tendency towards cure.

T A B L E IV.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
13.	Cardio Renal.	28.2.22.	0·5% 800;	0·7% 292;	0·8% 234;	0·7% 155.	63.	16.	165.	52.	Blood and alb. abundant. Epithelial and blood casts present. Cardiac failure.	Died one month after discharge.
	" "	23.3.22.	0·8%;	0·9% 185;		0·8% 185.	72.	11.			No blood or epithelial casts. Alb. not so marked.	
17.	Cardio Renal.	8.3.22.	1·4%;	1·5%;	1·1% 247;	1·5% 210.	119.	13.	190.		Heart enlarged. Arteries sclerosed. No oedema. Alb. slight. Heart failure.	Died.
31.	Cardio Renal.	20.4.22.	2·2% 265;	2% 53;	1·7% 53;	2·1% 53.	112.	18.	260.	44.	Alb. slight. Epithelial cells.	Died.
	" "	28.4.22.	2% 26;	1·5% 53;		1·3% 79.	103.	12.	245.		Vomited about ½ hour after urea given.	
37.	Cardio Renal.	28.4.22.	0·5% 1638;	1·4% 53;	1·3% 132;	1·2% 105.	46.	29.	240.	55.	Only slight trace of albumen.	Improved, but died a few months later.
45.	Cardio Renal.	29.6.22.	1·9% 1350;	1·6% 90;	1·6% 150;	1·6% 90.	40.	40.	240.		Blood and epithelial cells abundant. Granular, epithelial, and hyaline casts.	Improved. Since lost sight of.
64.	Cardio Renal.	22.8.22.	0·7%;	1% 90;		0.7% 120.	77.	9.			Epithelial cells and granular casts.	Died.

PLATE III.

Case 20. Patchy thickening of the intima in the renal artery.

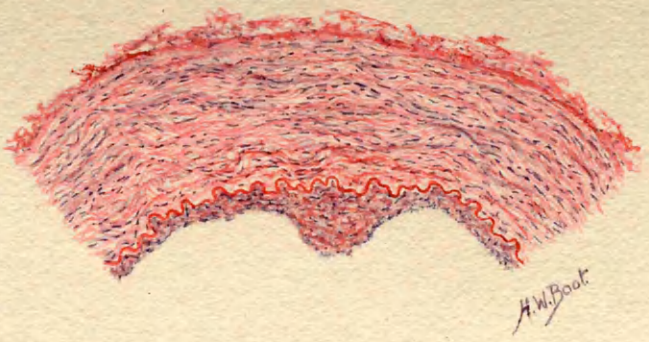

Plate. III

Plate III

PLATE IV.

Case 31. Kidney tissue stained with van Giessen's stain to show the increase of fibrous tissue.

Plate IV

PLATE V.

31. Blood vessels in the kidney stained to show the elastic tissue. Note the multiplication of the internal elastic lamina.

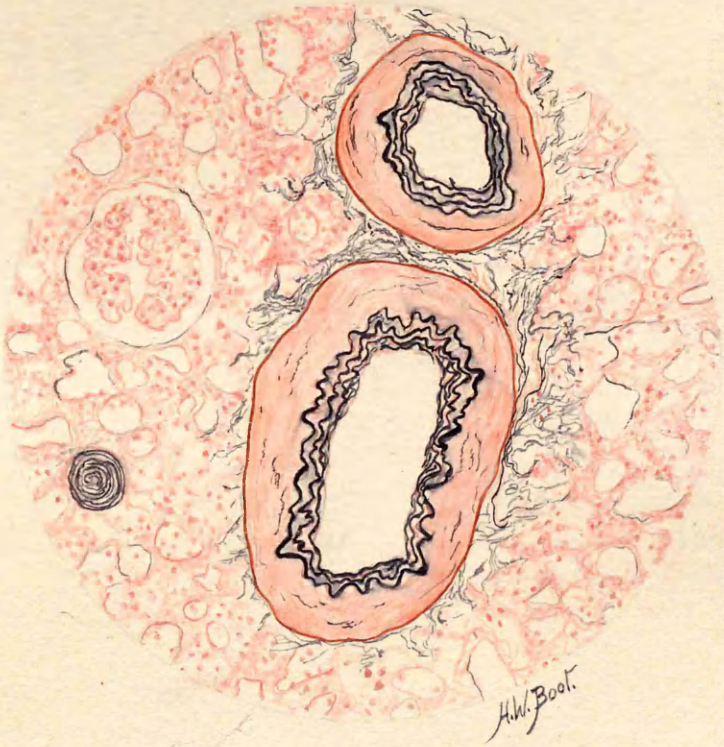

Plate V

PLATE VI.

Case 31. The renal artery (low-power drawing) to show the patchy character of the intimal degeneration.

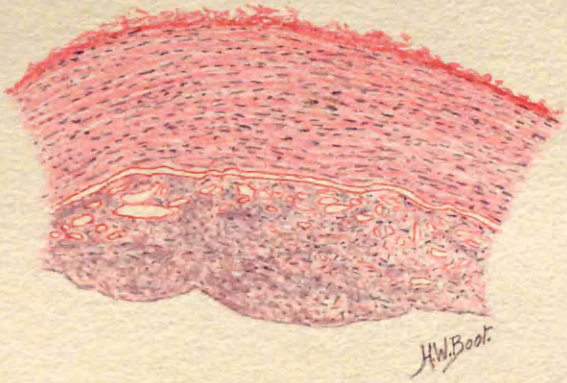

Plate VI

PLATE VII.

Case 31. Section of one of the mesenteric arteries (low-power) to show the fibrosis and the intimal thickening.

Plate VII

PLATE VIII.

Case 17. A glomerulus showing hyaline degeneration.

Plate VIII

Table V. p 62 The urea concentration test in cases of obstructed urinary discharge.

That obstruction in any of the urinary passages sooner or later sets up a nephritis has been common knowledge for a long time. Much time and thought have been spent in evolving operative measures for dealing with the various obstructions, the commonest of which are enlarged prostate and stricture of the urethra. The operative measures for the relief of both these conditions are attended with varying success, a number of the patients surviving the operation but dying of uraemia a few days later. It is on these deaths that McLean's work throws light. He showed that no albuminuric patient should be subjected to a general anaesthetic unless it could be proved that the kidneys were functioning well. McLean estimated kidney function by the urea concentration test and the blood urea content. If these gave good results, then operative measures could be undertaken; if not, then he recommends that the bladder be drained under local anaesthesia, and ,when the renal efficiency has improved under treatment,the main operation may besafely undertaken. These precautions have greatly reduced the mortality of such operations.

The following Table gives the details of seven cases of enlarged prostate, five of whom were operated on and did well. Two however were not operated on; one refused operation, and the other was not considered operable on account of advanced malignant disease.

Of the 5 operative cases 3 had the two-stage and 2 the single-stage operation. The results obtained in these cases confirm those of McLean and other workers.

T A B L E V.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
2.	Enlarged Prostate.	27.1.22.	2·3%;	2%;	2·5%;	2·5%.				79.	Acute obstruction set in. Two stage operations performed.	Well.
26.	Enlarged Prostate.	13.4.22.	1·5% 2312;	2·2% 25;	1·7% 53;	2·1% 231.	96.	23.	190.	64.	Fatty debris in urine, also degenerated epithelial cells. Operation 26.4.22.	Well.
		19.4.22.	1·5% 2586;	1·8% 40;	1·7% 53;	1·8% 72.	93.	19.	185.			
28.	Enlarged Prostate.	14.4.22.	1·3% 1294;	2% 47;	1·9% 55;	2·1% 61.	31.	68.	150.	63.	Blood and pus present. No casts (Malignant tumour. No operation).	I.S.Q.
47.	Enlarged Prostate.	30.6.22.	1·6%;	1·7% 120:	1·7% 60;	2·7% 60.	44.	61.	130.	68.	A few epithelial cells present. Operation.	Well.
58.	Stricture of Urethra.	2.8.22.		0·7% 75;	1·9% 90;	1·9% 60.	46.	41.	195.	74.	Albumen trace; no casts. (Bladder drained).	Well.
60.	Enlarged Prostate.	4.8.22.	0·9%;	1·1%;	1·1%;	1·8%.	35.	40.	115.	58.	Albumen and blood present. (Operation - 2 stage).	Well.
61.	Enlarged Prostate.	13.8.22.	·5%;	1·6%;	1·1%;	1·5%.	48.	31.	130.	47.	Blood abundant. No casts. (Operation - 2 stage).	Well.
63.	Enlarged Prostate.	16.8.22.	1%;	2·1% 90;	2% 90;	2·2%.					Blood and pus present in urine. Refused operation.	I.S.Q.

11 cases of various urino-genital conditions.

Table VI. (Page 64-65) gives the results obtained from applying the urea concentration test to 11 patients, all of whom showed some signs of urinary trouble. The results of the test in this series were nearly all good except in Case 24, where the poor renal efficiency was considered a bar to a general anaesthetic. This patient improved clinically at the time, but has since been lost sight of.

These results are in accordance with McLean's work, which proves that unless 2/3rds of the kidney tissue is destroyed the renal function suffices for health, and allows a general anaesthetic to be given with safety.

T A B L E VI.

No.	Disease.	Date.	Ureaper cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.	C.	F.	B.	P.	Age.	Remarks.	Result.
3.	? Stone in Kidney.	31.1.22.		1·8% 65;	2·0½ 290;									Epithelial cells abundant. Granular casts. Scanty pus cells. Treated and improved. Diagnosis of stone not established.	I.S.Q.
4.	Dermoid cyst with T.B. ovary, with urinary fistula.	31.1.22.		2% 65;	2·6% 65;									Blood and pus. (Operation).	Well.
8.	Malignant Tumour of Left Kidney.	11.2.22.	1·7% 1848;	1·9% 159;	2·4% 106;									Albumen free. Operation.	Well.
21.	Haematuria.	30.3.22.	1·8%;	2% 105;	2·5% 105;	2·4% 79.	86.	28.	110.				45.	Epithelial cells of deep and superficial layers, abundant. R.B.C's abundant albumen marked. Treated medically. Urine found sterile.	Well.
		25.1.23.	·8%;	1·7% 120;	3·2% 90;	3·2% 45.	54.	59.	100.					Haze alb. No blood.	
22.	Pyelitis.	3.4.22.	3% 317;	2·4% 13;	4·5% 106;	5% 53.	60.	833.	-				9.	Epithelial cells abundant. Alb. slight.	Well.
		25.4.23.	1·6% 60;	2·1% 60;	2·4% 90;	4·4% 60.			120.					Alb. free.	
24.	Cystitis ? Pyelitis.	10.4.22.	1·0% 1248;	1·1% 132;	1·7% 158;	1·3% 19.	22.	58.					43.	Alb. and epithelial cells abundant. Cystoscopic exam. Anaesthetic. No operative interference.	Improved.
		20.4.22.	9%;	1·6% 132;	1·6% 53;	1·6% 105.	41.	39.							

T A B L E VI. (Con).

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
35.	Hydropyone-phrosis.	25.4.22.	2·2%;	2·4% 92;	2·7% 97;	3% 66.	46.	61.	120.	28.	Blood pus and epithelial cells in urine. Operation.	Well.
40.	Kidney Abscess.	5.6.22.	1·2% 105;	1·7% 90;	1·2% 120;	1·8% 90.			120.	34.	Cloud alb. Epithelial cells of all layers abundant. Kidney removed.	Well.
		25.4.23.	2·5%;	1·4% 60;	2·9% 60;	1·8% 60.	55.	41.	110.	37.	Alb. free.	Well.
42.	Cystitis.	7.4.22.	1·6%;	1·9%;	1·9% 106;	2·3% 53.	54.	42.	110.	58.	Alb. cloud. Degenerated epithelial cells.	Well.
49.	Haematuria.	22.4.22.	2·5%;	3·9% 56;	3·5% 112;	2·6% 56.	51.	50.	170.	55.	Urine contains blood and alb. Cardiac murmur present. No operation.	Improved.
62.	Pyelitis.	14.8.22.	0·4% 900;	2% 90;	2·5% 60;	2·5% 90.	36.	83.		20.	Pus cells present. Alb. slight. B. coli on films and culture.	Well.
		2.5.23.	2·3%;	2·5% 60;	2·3% 90;	2·6% 90.	19.	136.			Alb. free.	Well.

9 cases of cardiac disease.

Table VII. (Page 67.). It is a well known experimental fact that ligature of the renal artery or vein even for a few minutes causes damage to the kidneys, producing albuminuria. The albuminuria found in cases of venous congestion due to heart failure was thought to be of this nature, and the urea concentration test was applied in 9 cases of cardiac disease in an attempt to establish a relationship between cardiac and renal efficiency. None however was ascertained. As is seen from the Table all the cases gave good renal efficiency tests, excepting Case 44, who on the 5/6/22 gave a poor result, but although he was jaundiced and suffering from severe venous congestion he was not as ill at this date as on the occasions of subsequent tests.

Post-mortem examination showed all the conditions usual in such cases.

Histological examination showed cloudy swelling and congestion with haemorrhages into the tubules and interstitial tissues of the kidneys. The vessels examined were branches of the renal artery and small mesenteric arteries, and these were all found to be normal. (See slides, Case 44).

T A B L E VII.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
23.	Cardiac Disease.	5.4.22.	1·5% 211;	2·5% 13;	2·7% 26;	0·8%.	75.	11.	150.	44.	Albumen abundant. Epithelial cells and granular casts found on both examinations. History of recurrent attacks of cardiac failure. No murmurs heard.	Much improved when discharged.
		12.4.22.	1·3%;		1·7% 106;	2·4% 39.	10.	240.				
		25.4.23.	2·3%;	1·2% 120;	2·4% 90;	1·7% 60.	11.	181.	150.		Some cells present. Improved, but not well.	Improved.
33.	Cardiac valvular Disease. Failure of Compensation.	21.4.22.		2·9% 105;	3% 79;	3·7% 53.	61.	61.	110.	36.	Cells, but no casts seen in urine. Alb. present.	Well.
34.	Cardiac Haemoptysis.	24.4.22.	3·5% 571;	3·3% 184;		3·2%92.	31.	91.	110.	54.	No alb. present.	Well.
36.	Cardiac valvular Disease. Failure of Compensation.	26.4.22.	3%713;	2·5% 93;		4·2% 93.	45.	93.	130.	64.	Alb. free.	Died.
44.	Aortic Disease.	5.6.22.	1·7% 900;	1·2% 210;	1·8% 150;	1·8% 90.	62.	29.			Alb. abundant. Jaundice present.	
		6.7.22.	3·3% 720;	4% 90;	4·4% 45;	4·8% 90.	28.	28.			Patient rather better than on 5.6.22. Alb. more marked.	
		1.8.22.	2·4% 1740;	2·9% 120;	3·7% 120;	3·5%90.						
		11.8.22.	4% 480;	2·8% 60;	3·8% 30;	2·5%.30.					Patient very much worse. Oedema great. Right arm veins thrombosed.	Died.

T A B L E VII. (Con).

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
48.	Cardiac Valvular Disease.	12.4.22.	1·3%;	1·7% 106;		2·4% 39.	10.	240.			Epithelial cells and granular casts.	Improved; but relapsed again.
50.	Cardiac Valvular Disease.	11.5.22.	4% 575;	3% 53;	2·5% 79;	4·2% 53.	33.	127.	130.	42.	Epithelial cells of deep and superficial layers; granular casts.	Improved.
52.	Cardiac Valvular Disease.	11.7.22.	1·8% 720;	2·1% 180;	2·7% 120;	3% 150.	36.	83.	140.	37.	Alb. free.	Well.
	Mitral Stenosis.	2.5.23.	1·9%;	1·9% 60;	2% 90;	2·4% 60.	23.	100.		38.	Alb. present.	Having frequent relapses.
65.	Cardiac Valvular Disease.	22.8.22.	3·3%;	1·2% 30;		3·2% 120.	43.	76.	110.	47.	Alb., granular debris, and epithelial cells.	Improved.

5 cases of varying medical conditions.

Table VIII. p. 71 includes 2 cases of cerebral haemorrhage (these gave good concentration results); 2 cases of excitement, on whose condition the application of this test threw no light. One of the latter cases, No. 43, was of special interest, as the excitement was accompanied by albuminuria and glycosuria, the three conditions being cyclic and recurring at intervals of a few years. The three symptoms have always cleared up simultaneously in a few weeks. Case 10, a severe case of pernicious anaemia, died, and the post-mortem examination showed the usual conditions to be present.

The pericardial sac contained about 12oz. of fluid, and there were white pressure patches on the anterior surface of the right ventricle. The myocardium showed fatty degeneration, being of the thrush-breast type. There was slight dilation of both ventricles. All the cardiac cavities contained post-mortem clot. The valves and coronary arteries were healthy.

The pleural cavities contained about a pint of fluid. The lungs were oedematous, with evidence of chronic bronchitis. There was some congestion of the bronchial mucous membrane.

The liver was slate grey in colour.

The spleen was small.

The kidney capsules were adherent; the cortices were slightly narrowed, with general fibrous and fatty changes.

The blood vessels appeared to be healthy, the bone marrow being red.

Histological examination of the kidneys showed marked cloudy swelling of the tubular epithelium, and also to a slighter extent in the glomeruli. Some of the collecting tubules were filled with blood and epithelial casts. There was marked fatty change in the tubular epithelium, the interstitial tissue, and in the glomeruli.

The blood vessels examined showed no marked changes.

T A B L E VIII.

No.	Disease.	Date.	Urea per cent. and c.c. of urine. 24 hrs.	1st hr.	2nd hr.	3rd hr.	Blood urea in mgns. per 100 c.c.	U.C.F.	B.P.	Age.	Remarks.	Result.
10.	Excitement.	1.3.22.	1·3% 1320;	2% 106;	2·7% 79;	1·9% 79.	52.	37.			Urine normal. Treated for mental condition.	Well.
19.	Pernicious Anaemia.	29.3.22.		1·7% 105;	1·8% 79;	1·9% 26.	37.	51.	low.	54.	Alb. slight cloud. Some epithelial cells and granular casts.	Died.
32.	Cerebral Haemorrhage, slight.	19.4.22.	5% 260;	4·8% 79;		5·5% 132.	73.	75.	110.	74.	Crystals of uric acid abundant, otherwise N.A.D.	Well.
43.	Recurring Excitement.	26.5.22.	2·2% 672;	2·7% 28;	2·1% 36;	2·8% 43.	75.	37.	145.	72.	Alb. present; sugar slight. Both conditions cleared up simultaneously.	Well.
57.	Hœmiplegia.	1.8.22.	2·8% 960;	1·7% 120;	1·1% 90;	1·0% 10.	48.	20.	120.	53.	Alb. trace; pus cell abundant (Vaginal discharge).	Improved.

Conclusions.

It was hoped that the information afforded by the employment of the urea concentration test would clear away many of the difficulties in the prognosis and treatment of renal disease, and generally lead to a clearer comprehension of these obscure conditions. This hope has not been altogether realised, and all that can be claimed for the urea concentration test, even when it is controlled and amplified by the estimation of the blood urea, is that it forms a valuable danger signal. In cases of chronic nephritis it indicates when two thirds of the kidney tissue have been destroyed, denoting that efforts in treatment will prove of little avail, though they may bring about a temporary improvement.

As has been shown by McLean and others, the test is of no prognostic value in acute conditions; whether it will be found to be of assistance in distinguishing between nephritis of tubular and of glomerular origin, remains to be seen. It is of undoubted value in aiding the surgeon to make a prognosis in cases of enlarged prostate and urethral stricture. These cases so frequently give unexpectedly bad results, dying of uraemia a few days after operation. Now the degree of damage done to the kidneys can be approximately and quickly estimated by the urea concentration test, and if the two-thirds line has not been reached, good results will follow operative procedures. If however the two-thirds line of morbid renal change has been reached or passed, it is advisable to drain the bladder for a

period during which, under proper care, the kidney condition will improve, and when the renal efficiency has also improved then operation under general anaesthesia can be safely undertaken.

The urea concentration test is not delicate enough to show the effect of slight changes in the renal efficiency, and is therefore of little or no help in elucidating obscure conditions in general medicine. Clinically the albuminuria and oliguria of cardiac origin indicate damage to the renal tissue, and this is confirmed histologically, but ,as far as could be made out, the damage done to the kidneys in these cases has never been extensive enough to affect the concentration of urea.

The urea concentration test is however of great value as an aid to prognosis in chronic nephritis, and is of equal value to the surgeon confronted with a case of albuminuria requiring operation under a general anaesthetic.

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