TESTS FOR RENAL FUNCTION

BY

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Three tests commonly employed for estimating renal function are the blood urea and urea clearance, the phenolphthalein test of Rountree and Geraghty (1910), and the maximum specific gravity of the urine. These tests have been carried out in sixty-four cases under my care in which it was thought that impairment of renal function might be present, and I have attempted to compare the results. The tests were made in three general hospitals by the laboratory staffs, in the course of their routine work. The patients investigated were suffering from acute glomerulonephritis (eight cases), chronic glomerulonephritis, benign hypertension, and hypertension with nephritis (malignant hypertension). This classification is at any rate descriptive of the types of cases. Oedema was present to a greater or lesser degree in all the cases of acute nephritis, but, apart from this, nephritic oedema was uncommon. Three patients had slight oedema, which was thought to be cardiac in origin.

Similar investigations have been reported by several other writers. The urea clearance test is usually regarded as the most accurate measure of renal function with the exception perhaps of the creatinine clearance test, with which it has been found to agree (Cope, 1931) if the original conditions mentioned by Addis—namely, diuresis and a raised blood urea—are adhered to; and Cope attributes the failure of Hok Lan Ong (1932) to demonstrate this parallelism to the fact that he did not observe these conditions. The normal value for the Van Slyke urea clearance (McIntosh, Möller, and Van Slyke, 1928) is 75 per cent. normal or over, and this was the clearance test used in this investigation. The phenolphthalein was given intravenously and the urine collected for two hours. The normal is 60 to 80 per cent. The fractional phenolphthalein test (Shaw, 1925; Chapman and Halsted, 1933) is said to be a better method. The maximum specific gravity test used was as described by Fishberg (1934), and is a modification of Volhard's (1918) test. The normal is 1020 and over. The modification introduced by Lashmet and Newburgh (1932) is claimed to be more sensitive, but it is more troublesome to carry out. One per cent. of dissolved protein in urine increases the specific gravity by 0.003, and an allowance must be made for this. It is recognized that in the presence of oedema the value of the maximum specific gravity test is diminished, and this must be borne in mind whenever it is being compared with other tests.

Analysis of the Cases

I have divided the sixty-four cases into two groups for the purpose of making a few comparisons between the renal function tests and the clinical signs presented by the patients. Group A (thirty-three cases) contains those cases in which one or more of the renal tests showed distinct impairment of function, and Group B (thirty-one cases) those in which no such impairment was demonstrated. Those in Group A were for the most part more seriously ill than those in Group B, but there was clinically no difference apart from the renal tests between some of the cases included in Group A and some in Group B.

Twenty-nine of the thirty-three cases in Group A had, resting in bed, a systolic blood pressure of 180 mm. or over, as compared with seventeen of the thirty-one cases in Group B. Retinal changes, usually small haemorrhages, swelling of the disks, and white spots were observed in fourteen of the Group A cases and in only three of the Group B. Red blood cells were present in the urine of fifteen of the Group A cases, as compared with seven of the Group B. Blood counts were unfortunately only carried out when anaemia was thought to be present. There were twelve of the Group A patients in whom a haemoglobin value of under 80 per cent. was found and of the Group B patients only two, but these results are not strictly comparable. From the comparisons I have made and from a consideration of the symptoms of which the patients complained I concluded that renal function tests did, in many cases, give a good estimate of the patient's condition, but, on the other hand, often there was little correlation between the tests and the clinical examination.

Group A

Montgomery (1936) as a result of his investigations states that "sufficient emphasis has not been laid upon the necessity of interpreting [the urea clearance] results in relation to their blood urea concentration." In grouping the results of the renal function tests I have made use of the blood urea where possible. The sixty-four patients investigated were all conscious and able to give sufficient co-operation. Six had a blood urea of over 100 mg. per 100 c.cm. of blood, and in each case the urea clearance was under 16 per cent. and the phenolphthalein under 11 per cent.; five were chronic cases. In four of the six cases the maximum specific gravity was between 1010 and 1012; in the fifth case, a patient who was admitted with a blood urea of 135 mg. and who later died of uraemia with a blood urea of 216 mg., the maximum specific gravity was 1018. This last case was probably an acute nephritis, as the illness was said to be of short duration, marked oedema was present, and the urine was much diminished; but, on the other hand, the patient was 60 years of age and her systolic blood pressure was 205 mm. I did not detect any retinal changes. The sixth case was one of chronic nephritis passing very little urine, with a blood urea of 256 mg. and a maximum specific gravity of 1028. There was oedema of the lower limbs and in the back. This patient was able to concentrate the urine but was unable to secrete an adequate amount. In all six cases the blood pressure was over 200 mm., and the guaiac test or the microscopical examination of the urine showed the presence of blood.

There were twelve cases, two of acute nephritis, with a blood urea between 50 mg. and 100 mg. In ten of these, including the two cases of acute nephritis, the urea clearance was 35 per cent. or less. The urea clearances in the other two were 65 per cent. and 51 per cent., the blood ureas 50 mg. and 56 mg. Both were cases of chronic nephritis in which there was a little oedema thought to be cardiac in origin; the blood pressures were high and albuminuria was present. In one retinitis was found, and she has since died of cardiac failure. The maximum specific gravity was respectively 1014 and 1020, and the phenolphthalein 36 per cent. and 26 per cent. Clinically these two patients were as likely to have a clearance under 35 per cent. as many in whom this was found to be the case. The maximum specific gravity in this group of twelve cases was under 1015 in nine cases,

and in three it was 1020 or over: one of the latter was an acute nephritis with oedema, in another there was a slight degree of cardiac failure, and one patient died later of a stroke, but all three were cases in which probably there was some failure of renal function. The phenolphthalein results were below 60 per cent. in every case. It was evident that in most patients with a blood urea of 50 mg. or over the three tests gave readings below normal, but I was unable to make out any true parallelism between the extent to which the tests were depressed.

Of the remaining forty-six cases there were fifteen—two of acute nephritis—in which one or all of the tests showed some definite abnormality, in spite of the fact that the blood urea was in many cases normal and never as high as 50 mg. It is said that half the functioning kidney tissue can be removed before the blood urea shows any rise (MacKay and MacKay, 1927), and it was expected that there would be many patients with a normal blood urea in which other tests would demonstrate a loss of function. In ten of these the urea clearance was below normal, the exact figures varying between 32 per cent. and 65 per cent. In the other five the urea clearances were normal, the blood pressures were high, there was slight albuminuria but retinitis was absent, and there were no red blood cells in any of the urines when examined. In four of these five cases the maximum specific gravity was under 1020, and in two the phenolphthalein was below normal. There was slight oedema in two of these patients, which somewhat spoils the specific gravity test; but the other two had no oedema, the blood pressures were high, there was albuminuria, and it may well be that some degree of kidney damage was present. Of the fifteen cases, in four the maximum specific gravity was normal, and yet in these the urea clearance was decidedly low. In two of these red blood cells were present in the urine, another had retinitis, but the fourth had no retinitis and no red blood cells in the urine. In five of the fifteen cases the phenolphthalein was normal when the urea clearance showed a lowering of renal function. It will again be seen that the tests do not agree closely. It is clear that in many cases of renal disease any one test may fail to demonstrate loss of renal function and another show it to be present. Freyburg (1935) found among his cases of arteriosclerotic Bright's disease thirty-eight with impaired maximum specific gravity (Lashmet and Newburgh method, 1932) and only four with a lowered urea clearance. Perhaps his patients were not so ill as many in this investigation.

Group B

In the remaining thirty-one cases (Group B) the urea clearance, the maximum specific gravity, and the phenolphthalein were all normal or very nearly so. There were eight cases of acute nephritis, and in five of these the urea clearance and the phenolphthalein were reduced, in three to a marked degree as they were severe cases. In four of the eight cases the maximum specific gravity was 1020 or above that figure whenever taken throughout the illness. In two cases it was low, even on admission, and in two it was over 1020 on admission and dropped below this figure during the course of the illness. It was interesting to follow the improvement in renal function as the acute cases recovered. Cullen, Nelson, and Holmes (1935) found that in most cases of acute nephritis renal tests showed normal results one month after the cessation of acute symptoms. Alving and Van Slyke (1934) stated that in some cases of acute nephritis the maximum specific gravity failed to return to normal in spite of the fact

that the clearances had reached normal figures; this was also observed by Freyburg (1935). Freyburg and Lashmet (1935) reported a case of mercuric chloride poisoning which recovered and in which the renal function tests were estimated frequently. The urea clearance was easily the most affected and dropped to 5 per cent., yet the non-protein nitrogen did not rise above 57 mg., and at the point when the clearance was 46 per cent. the maximum specific gravity was 1025 (Lashmet and Newburgh method, 1932) and the phenolphthalein 60 per cent.

Comparative Mortality in Groups A and B

Many cases have been followed up after leaving hospital. In Group A there have been during the past two years fourteen deaths, compared with three in Group B. Seven patients died of uraemia, two of apoplexy, three of cardiac failure, and two of pneumonia. In Group B two appeared to have died of cardiac failure and one of apoplexy. It was not possible to give an accurate prognosis from renal tests, as some cases went downhill faster than others and some severe ones maintained their position for a surprisingly long time. One chronic case when first seen had a blood urea of 46 mg., a clearance of 71 per cent., and a phenolphthalein reading of 35 per cent.; eleven months later the blood urea had risen to 120 mg. and the clearance had fallen to 14 per cent. In another case the clearance dropped in three months from 54 per cent. to 26 per cent. and the blood urea rose from 40 mg. to 75 mg. On the other hand many cases which had similar or worse renal readings when first seen are still alive and well. One case which I saw a year ago gave a phenolphthalein reading of 20 per cent., yet she is still alive, and the most recent test gave 36 per cent. The respective urea clearance results were 45 per cent. and 35 per cent.

Comparison of the Tests

In making a comparison one was struck by the fact that while on one occasion one test would seem to be the most sensitive, in another case it would seem to be the least sensitive. In many patients the maximum specific gravity appeared to be a very delicate test; in one case of uraemia, however, it gave a reading that was normal and in another nearly normal. The phenolphthalein often agreed with the urea clearance, but there were many occasions on which the one result was at variance with the other. In severe cases the agreement was good, both invariably showing marked reduction. The phenolphthalein is not regarded as a very sensitive test, yet in many cases, chiefly those with a high blood pressure, I found it to be apparently a delicate test, and low results were obtained more often than I expected. It was still more surprising to find that it sometimes showed an apparent loss of renal function before the urea clearance test. Lundsgaard and Möller (1925) believe that the dye output may be decreased in the presence of a high blood pressure, and this may account, in part at least, for the frequency of low readings in some of my cases. Chapman and Halsted (1933) state that they have observed cases of hypertension which showed depressed fractional phenolphthalein curves with few or no other signs of kidney disease, but have also seen normal curves in as many cases of hypertension in which there was no evidence of Bright's disease. Christian and O'Hare (1925) found that the two-hour phenolphthalein test did not demonstrate the earlier stages of kidney disease. MacKay and Rytand (1935) regard the phenolphthalein test as being of more value than the blood urea and the maximum specific gravity tests.

Chapman and Halsted (1933) believe the fifteen-minute phenolphthalein test to be more valuable than the two-hour test.

Elliot and Nuzum (1936) observed little correlation between the maximum specific gravity test, the phenolphthalein test, and the urea clearance test, and thought that what agreement there was between them was little better than could be expected as a chance occurrence. Riches and Robertson (1935) found the urea clearance to be a good index of renal function. Hutchison (1936) agrees with this view. Fowweather (1934) found it hard to establish even the normal clearance until he gave urea before the test. Van Slyke (1930) regards the urea clearance test as more accurate than the phenolphthalein.

None of these tests help us to give an accurate prognosis. Indeed, Elliot and Nuzum (1936) agree with Addis (1931) that none of the accepted methods of clinical examination can differentiate between patients likely to die in a year or two and those likely to live many years. Cope (1934) appears to hold a somewhat similar view. The rate at which renal function will depreciate varies from case to case, and Cope (1934) further states that even repeating the tests at intervals does not furnish information reliable enough to predict the course of the disease. This seems the more promising method. An increasing blood urea due to chronic nephritis means a bad prognosis, and, generally speaking, the higher the blood urea and the lower the results of renal function tests the sooner death will take place. The fact that tests of renal function are not all that one could wish for makes the ordinary clinical examination of the patient as important as ever it was.

Summary and Conclusions

Renal function tests have been carried out in sixty-four cases in which it was thought that kidney disease might be present. The tests used were the blood urea and urea clearance test, the maximum specific gravity test, and the phenolphthalein test. In the first group of thirty-three cases some loss of renal function was demonstrated, and the patients comprising this group were on the whole more incapacitated and death was commoner than among the second group of thirty-one cases, in which no loss of renal function was observed. Many of the cases were followed up after their discharge from hospital. On clinical grounds alone some of those included in the first group because of loss of renal function might have been included in the second group without causing the least surprise. The reverse is equally true.

With pronounced renal failure, as indicated by a high blood urea, the urea clearance and phenolphthalein tests showed marked depression of renal function, but this was not true of the maximum specific gravity. On two occasions it was normal, or nearly so, when the blood urea was over 100 mg. In both cases there was oedema and the patient was passing very little urine. The ability to secrete urine was at fault, but the ability to concentrate was normal. In some cases where renal function was apparently not nearly as severely impaired this test seemed to be very delicate, and the same may be said of the urea clearance test and the phenolphthalein test, each in some cases appearing to be the most sensitive. A surprising number of patients showed a lowered phenolphthalein excretion, but this may possibly be due to the fact that many had a high blood pressure. The lack of parallelism between the tests, especially in the lesser grades of renal damage, was most disappointing. None of them appear to be capable of enabling the clinician

to give a very much more accurate prognosis than is possible from a knowledge of the blood urea alone. However, if any of the tests show marked loss of renal function in the absence of a raised blood urea it would probably be best to give a guarded prognosis. A re-examination of the patient in three months might help. Clinical examination will often furnish very valuable information, and must still be regarded as of the foremost importance.

To conclude, the failure of the tests to agree closely with one another suggests either that they are not completely reliable or that different renal functions are being measured.

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E. W. Twining (*Brit. J. Radiol.*, April, 1937, p. 332) describes an ingenious way of converting the ordinary Bucky couch into a tomograph. Tomography, planigraphy, and stratigraphy are names given to those methods of radiography which aim at the sharp radiographic representation of a selected layer of the patient's body, while all the other layers situated in front and behind the selected layer remain diffusely outlined. This is accomplished by moving the tube and film during the exposure in such a manner that the projections of all objects in the selected layer occupy the same positions on the film, while the projections of objects above and below that layer are blurred by movement. The apparatus described by the author consists of a lever mounted horizontally upon a vertical axis, which transmits the motion of the x-ray tube reciprocally to the Potter-Bucky carriage. Its length is equal to the focus-film distance. Its axis is variable along the length of the lever in order to allow the selection of any desired plane of the patient's body. The author describes and discusses experiments demonstrating the accuracy of his apparatus and its applications to clinical radiography.