THE VALUE OF RENAL FUNCTION TESTS IN CLINICAL MEDICINE.

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The trend of medical research to-day is towards the study of function in the living subject in health and disease rather than the study of merely pathological material. I feel that it is to the biochemist that we are to look for further advances in the art of medicine, and that in time the art will approximate more nearly to a science.

The pathologists have given us tests which have revolutionized clinical medicine; to mention only a few: the Wassermann reaction, Widal's reaction, and the identification of the tubercle bacillus in sputum. There are many other tests which are most helpful, but perhaps not quite so certain. The biochemist is following on, and is perfecting tests of function that in time will be almost if not quite as indispensable as those tests I have mentioned.

The pathologist has tended to retire more and more into his laboratory aloof from clinical medicine, owing in a great measure to the lack of helpful co-operation on the part of the clinicians. The ultra-modern doctor, ignoring the clinical side, expects the laboratory to do all his work for him, and seems to consider the proper equipment for a doctor to be a hypodermic syringe and a few test tubes. The ultra-conservative clinician, on the other hand, ignores the pathologist. "A murraim," says he, "on the biochemist and all his gimcrack tests; give me a stethoscope and my ten digits and all is well."

Between these groups the pathologist has been starved clinically. It is often forgotten that full clinical details, in addition to being of intense interest to the pathologist, are often essential if he is to arrive at a correct interpretation of his findings. Now, while the pathologist has been able to carry on and help us without our help in return, the biochemist cannot do so as interpretation of findings is so dependent upon associated clinical observations. My object in this paper is to put before you the possibilities of one biochemical test, and to beg your interest in a more or less new branch of medicine, and to ask you to remember that the biochemist and the clinician must go forward hand in hand if the great possibilities of the new work are to be perfected. In the great teaching centres this co-operation is accomplished by teams or units where the biochemist, himself a clinician, sees the cases, and also has the assistance of most skilled physicians and surgeons in correlating biochemical observations.

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with clinical findings. Here in the provinces we have all got to be members of the team if we are to get results.

Now, after this rather uncalled-for preamble, I will proceed to the subject matter of my paper.

Renal function has been measured, or I should say that attempts have been made to measure it in various ways. The functioning of the kidney is a subtle business, and we are not perhaps always sure what function or part of a function we are measuring. There are, however, several tests which are of vital importance, and which give most valuable information when taken in conjunction with the clinical aspects of the case. The surgically-minded will all know the tests for permeability of the kidney necessarily undertaken to implicate the diseased kidney before excision. One of these tests depends upon the excretion of a dye which can be easily distinguished in the urine withdrawn from each ureter separately. This test is invaluable but is of supreme importance only to the surgeon and perhaps incidentally to his patient. We have the rough tests which we have all used for years, and which are still essential—I mean the routine examination of the urine—its specific gravity, the presence of protein, sugar, pus and blood. Nowadays these essential tests are only preliminaries, and if any variation from the normal be found we must proceed to one or other of the more modern tests of function. Considerable work has been done on the blood, and while blood-tests are on the whole more accurate and occasionally essential, it has been found that almost as much information is obtainable from the urine as from the blood. The blood-tests too are more complicated, require more elaborate apparatus and demand more skill on the part of the investigator. The test on which I place most reliance, and of which I have most experience, is the urea concentration test. This test was launched by Professor McClean, and most valuable results were achieved. Recently a modification has been put forward by Calvert, of St. Mary's Hospital, and it is this modification which I practise, and which I claim to be of such great assistance in diagnosis and prognosis, and to have such a wide sphere of application.

Broadly speaking, the test is useful:

(1) In surgical cases.
(2) In obstetric cases.
(3) In medical cases.

(1) SURGICAL CASES.

Here the test is of assistance in two ways. First, suppose a case of damaged kidney, pyonephrosis, tuberculosis or other unilateral lesion. You first of all implicate the offending kidney by a dye test. Now the question arises, "Is the other kidney sufficient to support life?" The function test will give you the answer.
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Now take the second group. This group comprises cases of obstruction to the flow of urine best exemplified by cases of enlarged prostate. Here the test is of the very greatest value, in many cases it is essential and determines the possibility or otherwise of prostatectomy.

In all such cases a renal function test should be performed, and where the function is found to be seriously impaired a preliminary suprapubic drainage should be done, and after the lapse of ten days or so a second function test will often show that the kidney function has improved sufficiently to allow the prostatectomy. I wish to mention here that in these cases of obstruction to the flow of urine, the blood urea or the total non-protein nitrogen of the blood gives rather more satisfactory results than the urea concentration tests. Why it is so I do not know; that is one of the subtleties of the renal function which I mentioned in my preamble.

(2) Obstetric Cases.

These cases are most interesting. An enormous amount of work has been done recently and a great deal remains to be done, but the renal function test furnishes one certain definite and compelling indication.

We may divide our obstetric cases roughly into three classes:—

(1) Simple Albuminuria of Pregnancy with or without Symptoms.—Here the renal function is unimpaired or little impaired, as shown by this test. I am not sure whether Calvert's method will show more than McClean's original method, as I have not had the opportunity of performing the test in these cases and other observers have used McClean's original method.

(2) True Nephritis complicated by Pregnancy.—By expressing myself in this way I am treading on rather debatable ground and am allying myself with those who deny the existence of a true renal toxæmia of pregnancy. Whichever view you take, the group is a most important one, and the point of view is immaterial to my purpose to-night, as in my second class I wish to include cases of severe renal toxæmia if such exist.

In these cases the test shows definite impairment of renal function, and in such cases, unless there are very strong reasons against such a course, pregnancy should be terminated, as if allowed to go to term the renal disease becomes rapidly worse and often the foetus dies in utero.

(3) Pre-eclamptic and Eclamptic Conditions.—Whilst in eclampsia the renal function is usually found to be impaired, the test is unnecessary. In the pre-eclamptic state the renal function usually shows no impairment, and we have to rely on other tests such as blood-pressure observations and especially upon the test of liver function.

(3) Medical Cases.

It is here that I claim the greatest value for the test to the general practitioner. It is of value in diagnosis and prognosis in the following types of case:—
(1) Nephritis.—In acute nephritis at first renal function is practically in abeyance. As the patient recovers the state of the renal function may be ascertained and the stages watched. If permanent damage to the kidney persists the extent of the damage and the type of the lesion may be worked out.

In chronic nephritis the test distinguishes clearly between the so-called parenchymatous or hydræmic nephritis and the chronic interstitial type of nephritis.

(2) Hyperpiesia.—The test clearly distinguishes this condition from chronic interstitial nephritis. Personally I feel that if the test did no more than this it would deserve the attention of every practitioner, as without this test I find it often very difficult to make a diagnosis in these cases, and the diagnosis is so important both from the point of view of treatment and prognosis.

(3) Functional or orthostatic albuminuria may be distinguished from nephritis.

(4) It is useful in the differential diagnosis of cases of ascites and oedema when seen late. Recently I saw two cases of ascites and the test in each case reversed the diagnosis, and the new diagnosis was upheld by the clinical course of the disease.

Now for the test itself. It consists essentially in giving fifteen grammes of urea and obtaining later as concentrated a specimen of urine as possible. Then a quantity of fluid is given and as dilute a specimen as possible is obtained. The urea in these two specimens is estimated and the difference between the two readings, that is, the range of urea concentration, constitutes the criterion of efficiency. In efficient kidneys this range is always over two per cent and usually about three per cent.

This test is little trouble to the practitioner, little trouble to the patient, and very little trouble in the laboratory.

Here are the instructions I give to the patient:

(1) Do not eat or drink anything after 6 p.m.
(2) Empty the bladder at 10 p.m., keep a specimen, mark it A.
(3) Then drink the medicine given.
(4) Empty the bladder one hour later, i.e., at 11 p.m. and throw the water away.
(5) Keep all water passed between 11 p.m. and 7 a.m., measure it, save a specimen and mark it B.
(6) Between 7 a.m. and 8 a.m. drink slowly two pints of fluid such as weak tea, water, barley water, etc. Keep all water passed between 7 a.m. and 9 a.m., emptying the bladder at 9 a.m., measure it, keep a specimen and mark it C.
(7) Send note of amounts of water passed and the specimens A, B, C, for examination.

B and C specimens are used for the test proper; I use A for the routine examination, protein, pus, blood, etc.
Now for results. Calvert gives the following figures as typical findings:

<table>
<thead>
<tr>
<th>Condition</th>
<th>B. Urea per cent</th>
<th>C. Urea per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>3.82</td>
<td>0.40</td>
</tr>
<tr>
<td>Parenchymatous (hydræmic)</td>
<td>2.60</td>
<td>2.40</td>
</tr>
<tr>
<td>Ob. Interstitial (azotæmic)</td>
<td>1.32</td>
<td>1.12</td>
</tr>
<tr>
<td>Hyperpiesis</td>
<td>4.40</td>
<td>0.90</td>
</tr>
</tbody>
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You will see from these figures that there is a very definite type of reading for each type of disease.

In the normal the concentrating power is high, i.e., over three per cent and the range of concentration is also high.

In the hydræmic type the concentrating power is also quite good, but the range is negligible.

In the azotæmic type the concentrating power is poor, and again the range is negligible.

In hyperpiesis the type of reading obtained is normal, but tends if anything to be rather exaggerated.

Now I will show you some results of tests carried out by me during the past twelve months; you will see that Calvert’s findings are followed very closely.

**Chronic hydræmic nephritis:**

- (B) Sp. gr. 1020 Urea per cent 2.90
- (C) 1020

Blood-pressure.—Systolic, 195; diastolic, 105. Urine contained protein but very few casts.

**Chronic interstitial nephritis:**

- (B) Sp. gr. 1010 Urea per cent 0.90
- (C) 1009

Blood-pressure.—Systolic, 225; diastolic, 135. Died three months later from renal failure.

**Pure hyperpiesis:**

- (B) Sp. gr. 1023 Urea per cent 4.10
- (C) 1006

Blood-pressure.—Systolic, 205; diastolic, 120. Only symptom was epistaxis.

**Double renal calculus:**

- (B) Sp. gr. 1010 Urea per cent 1.25
- (C) 1009

Blood-pressure.—Normal. Trace of albumin, few pus cells, no blood.

**Case of albumuria:**

- (B) Sp. gr. 1020 Urea per cent 3.50
- (C) 1004

Two cases of ascites:

1. (B) ... ... ... ... ... 2.45 per cent urea
   (C) ... ... ... ... ... 0.85 ...
2. (B) ... ... ... ... ... 3.15 ...
   (C) ... ... ... ... ... 3.15 ...

The first of these cases had been diagnosed nephritis and the second cirrhosis! As this test plainly showed, the diagnosis was wrong in each case. The former is either an unusually chronic case of cirrhosis or chronic peritonitis. The second case died with uraemic symptoms.

Two cases of haematuria.

1. Haematuria with albumin and pus—
   (B) ... ... ... ... ... 3.50 per cent urea
   (C) ... ... ... ... ... 0.60 ...

This is probably a unilateral renal lesion. Diagnosis not yet settled.

2. Haematuria—
   (B) ... ... ... ... ... 2.25 per cent urea
   (C) ... ... ... ... ... 0.85 ...

This was obviously not nephritis. It later turned out to be carcinoma of the bladder.

Now, finally, I have a confession to make. One does not always obtain such clear-cut typical findings as those I have shown, and the reading of results in such cases is sometimes difficult. The atypical readings given in definite cases of nephritis during the transition stage are easy enough when one has a good clinical history. Difficulty arises in cases of heart failure and in vague undiagnosed cases of illness where the kidney is possibly the offender. Here I think there is a future for this test. I am not yet certain whether one can obtain any useful information as to the state of the kidneys in a condition of heart failure. I have not yet investigated a sufficient number of cases to give an opinion, though if one could obtain reliable evidence of the renal condition in such cases it would be of considerable assistance.

Calvert says that in cardiac failure, "the B and C values are raised, and that their approximation varies directly as the degree of heart failure." If this is the last word the test is not going to help us much here.

I will just show you a few charts from cases such as I have mentioned, and which I cannot read at present, but which I hope to be able to read later on, as I intend to try out the test thoroughly in this type of case. I hope that by close clinical observation, and perhaps by the addition of another function test, these atypical findings will be capable of a rational translation and help one to a diagnosis.

1. A case where the only diagnosis so far has been "debility." This man gives a history of certain attacks which suggested the possibility of some renal lesion. He also gave a history of urethral stricture which had to be dilated. Urine except for the fixed specific gravity is normal. A catheter specimen was sterile. Blood-pressure is normal.
Range of function test:—

(B) Sp. gr. 1014 Urea per cent. 1.72
(C) 1012 1.63

There is obviously impaired renal function possibly due to back pressure at the time of the stricture; there may be dilated renal pelvis not quite amounting to a hydronephrosis.

(2) A case of recovering cardiac failure. (Aortic disease.)
Range of function test:—

(B) Sp. gr. 1012 Urea per cent. 1.92
(C) 1010 1.70

Blood-pressure.—170/70.
I suspect renal disease of interstitial type, but am not yet sure.

Range of function test:—

(B) Sp. gr. 1030 Urea per cent. 4.26
(C) 1040 3.05

No albumin, sugar, casts, pus, or blood.
Clinically I took this case for an ordinary chronic hydremic nephritis. I am now inclined to look upon it as a case of hyperpiesia with cardiac defect.

All the above cases are still under observation.

REFERENCES.
[2] HUGH MACLEAN. "Modern Methods in the Diagnosis and Treatment of Renal Disease."