STUDIES IN THE NEPHRITIS OF CHILDREN *

FIRST PAPER

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RENAL FUNCTION TESTS

For many years the study of nephritis has attracted a great deal of attention from clinicians. The problems involved are so complicated and so many, the correlation of different anatomic lesions with variations in functional capacity is so difficult, and the stages through which any given case of nephritis may pass are sometimes so varied in the pictures they present, that it is indeed impossible for anyone to feel that he understands nephritis, no matter how much experience he may have had with it. Up to ten or twelve years ago the problem that chiefly interested investigators was a study of the histologic changes produced in the kidney tissue by different types of nephritis, and little attention was paid to changes in the functional capacity of the organ. At present the reverse is true, and studies in kidney function dominate the literature on nephritis in the last decade. Nearly all the work, however, has been done with adults, and nephritis in children has received comparatively little attention.¹ Two years ago, at the suggestion of Dr. John Lovett Morse, I became interested in nephritis, and since then have studied between sixty and seventy cases of acute and chronic nephritis in the wards of the Children's Hospital. During the course of these investigations many interesting questions have arisen, which will be discussed later, and the present paper will take up only functional tests.

There is this great difference between nephritis as seen in adults and in children. In adults there may be recognized, broadly speaking, two great groups of nephritic cases; one dependent on acute infectious processes somewhere in the body, the toxins of which injure the kidneys either temporarily or permanently; the other dependent on slow-going degenerative changes in the blood vessels, which produce so-called "chronic interstitial" nephritis, or "cardiorenal" disease. By far the majority of cases of nephritis in adults fall into the second group, and

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1. For a review of the literature dealing with nephritis in children see Hill, L. W.: Boston Med. and Surg. Jour., 1917, **177**, 313.

it is this group of cases which has been most extensively studied. On the other hand, I do not feel that it is too strong to say that nearly all nephritis in children depends on infection; for practical purposes we can rule out the slow-going "vascular" or chronic interstitial type. (A few cases of "chronic interstitial" nephritis in children have been reported, however.) Thus it may be seen at the outset that in dealing with nephritis in children we are dealing with a far different problem from that of nephritis in older persons, and we must not necessarily expect functional tests to show the same phenomena as in the adult.

Many tests of kidney function have been used in the last few years, some of which have passed into oblivion, some of which have survived. These functional tests may be divided into two broad groups, the first of which comprises those tests that measure the power of the kidney to excrete chemical substances not ordinarily contained in the food, or "körper fremden" substances, as the Germans have put it. The second group comprises those tests which measure the ability of the kidney to excrete substances ordinarily contained in the food. Three of the most important functions of the kidney are to excrete nitrogen, salt and water, and it is these, therefore, that are usually taken as the test substances to determine the kidney's functional power.

Phthalein Test.—A number of tests with substances foreign to the body have been proposed, but the only one which has survived is the phenolsulphonephthalein test of Rowntree and Geraghty. This has been found, after extended use all over the world, to be the most practical test of kidney function for general clinical use.

In this test, which is now familiar to everyone, 6 mg. of the dye phenolsulphonephthalein is injected intramuscularly, and all urine passed for two hours is saved. This is made alkaline with sodic hydrate to bring out the color of the phthalein, diluted to 1,000 c.c., and the intensity of the resulting color is compared with that of a standard solution. The result is expressed in per cent. of phthalein excreted in two hours; the test is therefore one of the rapidity of the kidneys to excrete the dye. A normal adult should excrete from 50 to 80 per cent. of the phthalein in two hours, and any figure above 50 is usually considered normal for an adult. The figures for children vary considerably from this, as will be seen.

The results of this test in twenty-seven normal children are shown in Table 1. These children might not perhaps be considered as strictly normal children, inasmuch as they were all in the hospital for various reasons, but they were all free from any condition which could possibly influence the function of the kidney, such as fever, malnutrition, etc. A Duboscq colorimeter was used.

It may then be said that the average phthalein excretion for normal children is somewhere in the neighborhood of 75 per cent., and that if the function is below 60 per cent. it may be considered as abnormal.

These figures agree fairly closely with those of Tileston and Comfort² and Leopold and Bernhard,³ whose average figures for normal children are 78 per cent. to 81 per cent., and 70 per cent., respectively.

The test was performed on thirty-seven children with nephritis of all degrees of severity. Twenty-one cases were acute, sixteen chronic.

The average excretion of the twenty-one acute cases was 59 per cent., or 17 per cent. below the normal average; 59 per cent. would be a normal phthalein excretion for most adults.

The average excretion of the sixteen chronic cases was 63 per cent., or 13 per cent. below the normal average of 76 per cent.

TABLE 1.—PHENOLSULPHONEPTHALEIN EXCRETION IN NORMAL CHILDREN

Age, Years	Phthalein Excretion, Per Cent.	Age, Years	Phthalein Excretion, Per Cent.
2½.....	64	8.....	77
5.....	77	8.....	79
6.....	80	9.....	66
6.....	71	9.....	70
7.....	69	10.....	80
7.....	90	10.....	74
7.....	77	10.....	65
7.....	77	10.....	100
7.....	66	10.....	76
7.....	66	11.....	80
7.....	74	11.....	77
7.....	80	11.....	80
8.....	87	11.....	90
8.....	87		

High, 100 per cent.; low, 64 per cent.; average, 76 per cent.

DISCUSSION

From the figures in Table 2 it can be said that the phthalein excretion is diminished in many cases of acute or of chronic nephritis in children, and that it is likely to be a little lower in the acute cases than it is in the chronic. The reverse is true in adults. Many chronic "cardiorenal" cases show a phthalein excretion of 5 to 10 per cent., or even sometimes such a slight trace that it cannot be read at all. Most cases of chronic nephritis in children are of a mild type, and even the very severe cases, of which we have seen a number, do not show nearly as much interference with phthalein excretion as one would expect. It is no uncommon thing to see a normal excretion in a child who has had nephritis for two or more years, who is edematous and anemic, and who has an increased blood pressure and a urine loaded with albumin and casts. In dealing with children, then, normal or high phthalein excretion helps us very little, as the test may be high in many cases in which there is unquestionably severe kidney damage. A low

2. AM. JOUR. DIS. CHILD., 1915, **10**, 278.

3. AM. JOUR. DIS. CHILD., 1916, **11**, 432.

TABLE 2.—PHENOLSULPHONEPHTHALEIN EXCRETION IN NEPHRITIS

ACUTE CASES		
Age, Years	Phthalein Excretion, Per Cent.	Remarks
9.....	63	Mild
9.....	62	Severe; bloody urine; blood pressure 140
6.....	62	Severe; bloody urine
4.....	80	Edematous; blood pressure 135
10.....	54	Moderately severe
8.....	50	Moderately severe; considerable edema
5.....	66	Moderately severe
10.....	71*	Severe; much edema
5.....	76	Moderately severe; slight edema
3.....	53, 50	Moderately severe; slight edema
4½.....	66	Mild
5.....	65	Moderately severe
3.....	83	Moderately severe
4.....	30	Moderately severe
5.....	70	Mild
7.....	64, 35	Severe; much edema
8.....	43	Moderately severe
4.....	43	Moderately severe
4.....	75	Severe; much edema
4.....	21	Severe; much edema
5.....	43	Severe; much edema
CHRONIC CASES		
7.....	55	Chronic interstitial nephritis; blood pressure 210
9.....	70	Moderately severe; two years' duration; blood pressure 150
7.....	66	Mild; one year's duration
9.....	80	Mild; subacute
2.....	66	Very severe; much edema; blood pressure 130
12.....	66	Mild
11.....	69	Very severe; much edema
7.....	50, 37, 70	Moderately severe; one year's duration
5.....	33, 60, 54, 30, 44	Very severe; two years' duration
6.....	62, 71, 60	Severe
4.....	87	Mild; subacute
6.....	50	Moderately severe
13.....	71	Mild; two years' duration
4.....	50	Moderately severe
3.....	60	Moderately severe
8.....	59	Moderately severe

* After decapsulation.

The average excretion of the twenty-one acute cases was 59 per cent., or 17 per cent. below the normal average; 59 per cent. would be a normal phthalein excretion for most adults.

function, however, tells us a good deal: in acute nephritis it puts us on our guard, and makes us consider the case a severe one whether or not it appears so clinically; in chronic nephritis it tells us that permanent damage has been done to the kidney, and makes us very guarded in our prognosis.

Added Salt and Urea Test.—Another method of testing renal function which has been in vogue is the addition of a known amount of salt and urea to a standard diet, and then determining how much of the

added salt and urea has been excreted in a given period of time. In adults this test is usually performed as follows:⁴

The patient is put on a constant standard diet containing a known amount of nitrogen, salt and water, and the amounts of salt and nitrogen in the urine are quantitated daily until their excretion has become constant. This usually takes from two to three days. On the third or fourth day 10 gm. of salt is added to the diet and by daily urine analyses it is determined how long the kidneys take to excrete the added salt. Normally it should be excreted in two days. After the ability of the kidneys to excrete salt has been determined, 20 gm. of urea is added to the diet, and the rapidity of excretion of this is determined in the same way.

This test necessitates keeping the patient on a carefully fixed diet and collecting accurate twenty-four hour urine specimens for eight or ten days. Any such procedure as this is obviously impossible in the case of small children, owing to refusal to eat, wetting the bed, etc. It was felt desirable to modify this test in dealing with children, and this was done as follows:

For three days the child was kept on the following standard diet:

Oatmeal, 4 tablespoonfuls	1 orange
Bread, 3 slices	1 small baked potato
16 per cent. cream, 4 ounces	Sugar, 4 drams
Salt-free butter, 2 ounces	Water, 34 ounces
Whole milk, 16 ounces	

This diet contains about 5.7 gm. of nitrogen. On the third day the twenty-four-hour output of salt and nitrogen in the urine was determined, and the next day 10 gm. of urea (containing 4.65 gm. nitrogen) and 5 gm. of salt were added to the diet. (Given together in a little water, early in the morning.)

The nitrogen and salt were then quantitated in the following twenty-four hour urine specimen, and by subtracting the urinary nitrogen and salt of the previous day the amount of these substances eliminated in the twenty-four hours after the addition was determined. I realize that it is better to give the salt and urea on different days than to give them together, and that there are also other objections to this simplified method of procedure, but even with this simple method many failures resulted, owing to the capriciousness of the child's appetite, unwillingness to take the salt and urea, wetting the bed, etc., and the cases reported represent only a portion of many attempted.

Twelve cases of nephritis were studied by this method, six of them acute, six chronic.

DISCUSSION

As may be seen from a glance at the table of normals (Table 3), the salt and urea excretion varied normally within rather wide limits, and it is therefore difficult to establish a normal standard. Age seemed to bear no relation to a large or a small excretion. Inasmuch as normal children vary so much in their reaction to this test, it is valuable only within very wide limits, and the excretion of salt and nitrogen may be said to be abnormal only if it is very much impaired. In six of the twelve cases studied the excretion of salt, of urea, or of both, may be said to be abnormally low (those marked †); in the rest of the cases it may be said to be normal. Marked impairment of salt excretion

4. Frothingham: *Am. Jour. Med. Sc.*, 1915, **149**, 808.

occurred more frequently than of nitrogen, especially in those cases which were, or had been, edematous.

Value of the Test.—The added salt and urea test may be of some value in indicating that the function of the kidneys is impaired, but only if the excretion is very poor, inasmuch as the normal response to the test may vary within such wide limits. If the excretion of both salt and urea is high, it is safe to assume that the kidney's function is

TABLE 3.—RESULTS OF SALT AND UREA TEST OF RENAL FUNCTION
NORMALS

Age, Years	Salt and Nitrogen Above Control *		Remarks
	Salt, Gm.	Nitrogen, Gm.	
11½.....	4.24	3.33	
10.....	1.47	5.00	
8.....	2.90	3.60	
10.....	2.40	3.40	
6.....	3.16	4.12	
11.....	4.22	4.32	
6.....	2.16	3.70	
6.....	3.78	4.55	
NEPHRITICS			
4.....	—0.25	1.96	Severe acute nephritis; no edema†
4.....	2.96	2.80	Mild acute nephritis; slight edema
10.....	3.84	2.88	Mild acute nephritis; no edema
7.....	1.90	3.24	Severe acute nephritis; no edema
8.....	3.90	3.16	Severe acute nephritis; no edema
9.....	3.80	3.00	Moderately severe acute nephritis; no edema
4.....	1.37	2.53	Severe chronic nephritis; considerable edema
9.....	—1.60	—2.86	Severe chronic nephritis; moderate edema†
7.....	3.02	2.40	Mild chronic nephritis
7.....	4.88	5.62	Mild subacute nephritis
11.....	4.22	6.26	Mild chronic nephritis
6.....	5.45	3.85	Severe chronic nephritis after decapsulation (Edcbohls' operation)

* By this is meant the excess of salt and nitrogen excreted on the test day over that of the previous day.

† A minus sign indicates that less salt or urea were excreted on the day after their addition to the diet than on the day before.

Twelve cases of nephritis were studied by this method, six of them acute, six chronic.

not much impaired, as the test is an extremely severe one, for Zondek⁵ has shown that diseased kidneys may be able to eliminate a large amount of urea or of salt *alone*, but not a large amount of both substances when they are ingested together. Even if this test occasionally does yield information of value, it is not at all adapted for general use in children, as the difficulties of carrying it out accurately are well high insurmountable.

5. Zondek: Ztschr. f. klin. Med., 1915, **82**, Nos. 1 and 2.

The "Two Hour" Renal Test.—This test was first proposed by Hedinger and Schlayer⁶ in 1914. In this country it has been used extensively by Mosenthal⁷ in Baltimore, and O'Hare⁸ in Boston. It is performed as follows:

The patient is put on a full diet, containing a considerable amount of protein, of purin extractives and of salt, in order to make a demand on the power of the kidneys to excrete such a diet. The fluid allowance is fixed, and no fluid is allowed between meals. The noon meal is considerably larger than either of the others and is designed particularly to call forth the kidney's power of excretion. The urine during the test day is collected in two-hourly periods, and the night urine in one sample. The amount and specific gravity of each two hourly specimen is noted as well as the amount and gravity of the night urine. The amount of salt and nitrogen and the salt and nitrogen concentration of each specimen are quantitated.

Mosenthal⁷ has well explained the principles of this test as follows:

The kidney expresses its diminished power to functionate by a fixation of its power of concentration. The normal kidney yields a urine of medium, low or high specific gravity according to the proportion of fluids and solids that must be excreted in order to maintain the composition of the body fluids at a constant level. The diseased kidney, on the other hand, loses this flexibility, and the power to answer the demand for a more concentrated or a more dilute urine no longer exists.

The normal response to a test meal is shown by a considerable variation in the amount, specific gravity, nitrogen and salt concentration of the two-hourly specimens, and by a relatively small amount of night urine, of high (1.020) specific gravity, and high nitrogen concentration (1 per cent.). A kidney whose function is impaired excretes a urine which varies very little in specific gravity and nitrogen and salt concentration in each two-hourly period. The gravity may be fixed at a low or a fairly high level. Also the amount of night urine is likely to be large, and the nitrogen concentration and specific gravity low (below 1 per cent. and 1.020, respectively). The fixation of the specific gravity is the most important point to observe, and it is not at all necessary to make salt or nitrogen determinations on any of the specimens. Moreover, it is not essential that the patient consume the exact diet indicated; it is merely necessary that the diet be a full one, containing a considerable amount of purin bases, nitrogen and salt, and that the noon meal shall contain more of these than the other meals. It is essential that the fluid taken with each meal be the same in amount, and that no fluids be taken between meals or at night. The test takes only one day, does not require the patient to be on a particularly rigid diet, and if, perhaps, one two-hour urine specimen is lost, no particular harm is done. *This, therefore, is a test which is very well adapted for ordinary clinical use, as in its simplest form no long drawn out procedure or complicated urinary analyses are necessary.*

6. Schlayer: Arch. f. klin. Med., 1914, **114**, 120.

7. Mosenthal: ARCHIVES INT. MED., 1915, **16**, 733.

8. O'Hare: THE ARCHIVES INT. MED., 1916, **17**, 711.

I have modified the original procedure somewhat, especially for use in children, and have carried it out in this manner.

The child is put on the following diet:

Breakfast	Dinner
Cereal, 2 tablespoonfuls	Chopped meat, 2 tablespoonfuls
Bread, 1 slice	1 egg
Butter, $\frac{1}{2}$ square	1 potato
Apple sauce, 2 tablespoonfuls	Butter, $1\frac{1}{2}$ cubes
Milk, 6 ounces	Milk, 6 ounces
Water, 4 ounces	Water, 4 ounces
Extra salt, 1 gm.	Extra salt, 1 gm.
Caffein sodium benzoate, 2 grains	Caffein sodium benzoate, 2 grains

The caffein is given instead of the tea or coffee which is given to adults to secure diuretic response from the kidneys.

The two-hour urine specimens are then collected in the usual manner, starting at 6 in the morning, and continuing until 6 at night. The night urine is collected from 6 p. m. to 6 a. m.

Then the gravity of each two-hourly specimen, and the amount of night urine is measured, a fixation of gravity in each specimen indicating loss of power on the part of the kidney to vary the concentration of solids in the urine, and hence impaired function. The determination of the specific gravity of each specimen is really all that is essential, but in most cases we have measured the day and night urine, and in some the nitrogen concentration of the night urine.

As controls, fifteen normal children were studied, for as far as we know, no work with this test has ever been done with children, and it is desirable to establish a standard of normality.

NORMALS

	No. 1 Aged 11 Yrs. Specific Gravity	No. 2 Aged 10 Yrs. Specific Gravity	No. 3 Aged 11 Yrs. Specific Gravity
Time			
6- 8	1.018	1.013	1.016
8-10	1.010	1.021	1.022
10-12	1.015	1.023	1.023
12- 2	1.021	1.024	1.020
2- 4	1.017	1.027	1.015
4- 6	1.021	1.028	1.011
6- 6	1.023	1.020	1.020
	Night urine, 260 c.c.	Night urine, 320 c.c.; nitrogen concentration, 88%	Night urine, 165 c.c.; nitrogen concentration, 1.1%
	No. 4 Aged 7 Yrs. Specific Gravity	No. 5 Aged 10 Yrs. Specific Gravity	No. 6 Aged 10 Yrs. Specific Gravity
Time			
6- 8	1.017	1.016	1.015
8-10	1.025	1.009	1.016
10-12	1.025	1.018	1.022
12- 2	1.022	1.009	1.028
2- 4	1.030	1.025	1.020
4- 6	1.026	1.025	1.025
6- 6	1.032	1.027	1.027
	Night urine, 75 c.c.; nitrogen concentration, 2%	Night urine, 210 c.c.; nitrogen concentration, 1.7%	Night urine, 325 c.c.

	No. 7 Aged 6 Yrs. Specific Gravity	No. 8 Aged 9 Yrs. Specific Gravity	No. 9 Aged 10 Yrs. Specific Gravity
Time			
6- 8	1.019	1.018	1.017
8-10	1.022	1.018	1.004
10-12	1.027	1.024	1.019
12- 2	1.027	1.028	1.020
2- 4	1.025	1.027	1.023
4- 6	1.028	1.026	1.025
6- 6	1.030	1.025	1.030
	Night urine, 160 c.c.; nitrogen concen- tration, 2.5%	Night urine, 480 c.c.; nitrogen concen- tration, 1.10%	Night urine, 120 c.c.

	No. 10 Aged 9 Yrs. Specific Gravity	No. 11 Aged 9 Yrs. Specific Gravity	No. 12 Aged 9 Yrs. Specific Gravity
Time			
6- 8	1.018	1.022	1.020
8-10	1.017	1.212	1.012
10-12	1.020	1.018	1.009
12- 2	1.015	1.018	1.020
2- 4	1.015	1.014	1.019
4- 6	1.023	1.017	1.016
6- 6	1.020	1.023	1.020
	Night urine, 350 c.c.; nitrogen concen- tration, 1.1%	Night urine, 290 c.c.	Night urine, 260 c.c.

	No. 13 Aged 6 Yrs. Specific Gravity	No. 14 Aged 6½ Yrs. Specific Gravity	No. 15 Aged 6 Yrs. Specific Gravity
Time			
6- 8	1.025	1.024	1.015
8-10	1.032	1.027	1.025
10-12	1.035	1.024	1.015
12- 2	1.026	1.020	1.020
2- 4	1.027	1.021	1.025
4- 6	1.029	1.028	1.020
6- 6	1.029	1.028	1.010
	Night urine, 70 c.c.	Night urine, 200 c.c.	

DISCUSSION OF NORMALS

Normal children show about the same response to the nephritic test meal that normal adults do. It will be noted as one looks over the results obtained in the normal cases that there is considerable variation in the gravity of the two-hour specimens in each case. *In every normal case there is a difference of at least 8 points between the highest and lowest gravity of the two-hour specimens, and usually there is a difference considerably greater than this.* These tables show very well how in health the concentration of the urine is varied from hour to hour. In every normal case except one, the specific gravity of the night urine was over 1.020. The amount of night urine in the normals varied too much to be able to determine on any definite standard of normality. Sixteen nephritics were studied. These were various types of cases, some acute, some subacute or chronic, some mild, others severe. In most cases the phthalein test was made in addition to the test meal, for purposes of comparison, and in a few the determination of the concentration of blood urea nitrogen. No case was studied which was

edematous, as conditions of urinary excretion are changed in such a way by edema that the two-hour renal test does not apply to this group of cases.

ACUTE NEPHRITIS

CASE 1.—R. M., aged 6 years. Severe acute nephritis. Urine: smoky; albumin, large trace; sediment shows many hyaline and granular casts, and many red blood cells. Time of test, one month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.018	2- 4.....	1.018
8-10.....	1.020	4- 6.....	1.018
10-12.....	1.020	6- 6.....	1.022
12- 2.....	1.018		

Blood urea nitrogen = 21 mg. per 100 c.c. blood.

Night urine 40 c.c.

Interpretation: Fixation of gravity at a moderately high level, characteristic of acute nephritis in the stage of repair; indicates that normal function has not yet returned.

CASE 2.—H. K., aged 3½ years. Severe acute nephritis. Urine: albumin, trace; sediment shows many red blood cells and a rare cast. Phthalein excretion = 33 per cent. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.010	2- 4.....	1.011
8-10.....	1.014	4- 6.....	1.013
10-12.....	1.013	6- 6.....	1.013
12- 2.....	1.015		

Night urine, 180 c.c.; nitrogen concentration, 1.06 per cent.

Interpretation: Fixation of gravity at a low level; phthalein test lower than it should be at this stage, indicating the possible development of a chronic process; night urine of low gravity, but with a normal nitrogen concentration.

CASE 3.—J. C., aged 10 years. Severe acute nephritis. Urine: bright red; albumin, large trace; sediment shows many red blood cells, and a few bloody and granular casts. Blood urea nitrogen 32 mg. per 100 c.c. blood. Phthalein excretion = 40 per cent. Time of test, four days after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.012	2- 4.....	1.014
8-10.....	1.015	4- 6.....	1.015
10-12.....	1.015	6- 6.....	1.015
12- 2.....			

Night urine, 505 c.c.; nitrogen concentration, 0.67 per cent.

Interpretation: Marked fixation of gravity at a low level; low phthalein test; moderately increased blood urea, indicating retention of nitrogen; a decided nocturnal polyuria. All tests indicate a considerable degree of functional impairment.

CASE 4.—J. M., aged 4 years. Severe acute nephritis. Urine: albumin, large trace; sediment shows many casts and red blood cells. Phthalein excretion = 75 per cent. Blood urea nitrogen = 19 mg. per 100 c.c. blood. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.020	2- 4.....	1.020
8-10.....	1.020	4- 6.....	1.022
10-12.....	1.022	6- 6.....	1.022
12- 2.....	1.021		

Night urine 202 c.c.

Interpretation: Fixation of gravity at a high level; normal blood urea

and phthalein; clinically a severe case of nephritis, but with high functional tests. Here the two-hour renal test indicates a damaged kidney when the other tests give no indication of it.

CASE 5.—L. N., aged 5½ years. Moderately severe acute nephritis. Urine: albumin, absent; sediment shows a few casts. Time of test, 1 month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.005	2- 4.....	1.020
8-10.....	1.017	4- 6.....	1.021
10-12.....	1.020	6- 6.....	1.025
12- 2.....	1.020		

Night urine, 200 c.c.; nitrogen concentration, 1.1 per cent.

Interpretation: No fixation of gravity; a normal response to the test meal; high gravity and nitrogen concentration of night urine. Tests indicate a kidney which has nearly recovered, and in which there is no chronic process developing.

CASE 6.—M. P., aged 5½ years. Mild acute nephritis. Urine: albumin, none. Sediment shows rare hyaline and granular casts. Phthalein excretion = 83 per cent. Time of tests, seven weeks after onset; boy clinically well.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.025	2- 4.....	1.024
8-10.....	1.023	4- 6.....	1.022
10-12.....	1.020	6- 6.....	1.030
12- 2.....	1.020		

Night urine, 170 c.c.; nitrogen concentration, 1 per cent.

Interpretation: No fixation of gravity; high gravity and nitrogen concentration of night urine; high phthalein excretion. Tests show, in conjunction with his good general condition, that he has practically recovered, and is in no danger of developing a chronic condition.

CASE 7.—R. I., aged 8 years. Moderately severe acute nephritis. Urine: albumin, trace. Sediment shows large numbers of red blood cells and rare cast. Phthalein excretion = 43 per cent. Time of tests, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.018	2- 4.....	1.015
8-10.....	1.018	4- 6.....	1.015
10-12.....	1.015	6- 6.....	1.018
12- 2.....	1.016		

Night urine, 230 c.c.; nitrogen concentration, 0.77 per cent.

Interpretation: Fixation of gravity at a low level; low concentration of night urine; low phthalein excretion. A damaged kidney, which still shows severe interference with function.

CASE 8.—S. B., aged 4 years. Acute nephritis. Urine: albumin, none. Sediment shows rare red blood cell. Boy clinically well. Phthalein excretion = 43 per cent. Time of tests, one month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.014	2- 4.....	
8-10.....	1.012	4- 6.....	1.015
10-12.....	1.015	6- 6.....	1.018
12- 2.....	1.015		

Night urine, 340 c.c.; nitrogen concentration, 0.70 per cent.

Interpretation: Fixation of gravity at a low level; large quantity of night urine with a low nitrogen concentration; low phthalein excretion. Although the boy is clinically well, and shows no albumin in the urine and little in the sediment, the functional tests indicate that his kidneys are not functioning

normally. This means that it is possible he is developing a chronic process, and would tend to make us watch him rather carefully for the next few months.

CASE 9.—J. M., aged 10 years. Acute nephritis. Urine: albumin absent. Sediment shows a rare granular cast and a rare red blood cell. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.016	2- 4.....	1.011
8-10.....	1.010	4- 6.....	1.018
10-12.....	1.015	6- 6.....	1.020
12- 2.....	1.006		

Night urine 400 c.c.

Interpretation: No fixation of gravity; probably no impairment of function. This boy had a very marked response to the diuretic materials of the test meal, passing 1,260 c.c. of urine in the test twenty-four hours, with a fluid intake of only 900 c.c.

CASE 10.—J. W., aged 2½ years. Mild subacute nephritis. Urine: albumin absent. Sediment shows a rare red blood cell and a rare cast. Time of test, three months after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.016	2- 4.....	
8-10.....	1.005	4- 6.....	1.020
10-12.....	1.015	6- 6.....	1.024
12- 2.....	1.014		

Night urine 160 c.c.

Interpretation: No fixation of gravity. The good general condition of the child, and the normal response to the test meal show that he is developing no chronic process, although his urine has contained a few blood cells for a long time.

CHRONIC CASES

CASE 11.—M. H., aged 11 years. Very mild chronic nephritis. Urine: albumin, slightest possible trace occasionally. Sometimes the urine contains none. The sediment sometimes shows a rare cast. Blood urea nitrogen, 14 mg. per 100 c.c. blood. Phthalein excretion = 70 per cent.

Time	Specific Gravity	Salt Concentration, Per Cent.
8-10.....	1.010	0.60
10-12.....		
12- 2.....	1.010	0.62
2- 4.....		
4- 6.....	1.020	0.70
6- 8.....	1.020	0.94
8- 8.....	1.021	0.88

Night urine, 315 c.c.; nitrogen concentration, 0.92 per cent.

Interpretation: No fixation of gravity; no fixation of salt concentration; reasonably high gravity and nitrogen concentration of night urine; normal blood urea nitrogen and normal phthalein excretion. Functional tests together indicate that the nephritic condition is extremely mild, probably nonprogressive, and that as far as can be told from such tests, the function of the kidney is normal.

It is in just this type of case that functional tests are of the most value. Here is a girl who has had an acute nephritis, and whose urine has not cleared up as it should, still containing a little albumin and casts occasionally. If we can determine by our functional tests that the function of the kidney is normal, it aids us immensely in prognosis and makes us feel that the urine

will eventually clear up, and that the girl will not have a seriously progressive nephritis.

CASE 12.—F. L., aged 5½ years. Chronic nephritis of two years' duration; clinically severe. Urine: albumin, trace. Sediment shows many hyaline and granular casts. Phthalein excretion = 25 per cent.

March 23, 1916		May 7, 1917		May 8, 1917
Time	Sp. Gr.	Time	Sp. Gr.	Sp. Gr.
7- 9.....	1.007	6- 8.....	1.020	1.017
9-11.....	1.005	8-10.....	1.020	1.018
11- 1.....	1.008	10-12.....	1.019	1.019
1- 3.....	1.005	12- 2.....	1.018	1.018
3- 5.....	1.003	2- 4.....	1.020	1.018
5- 7.....	1.005	4- 6.....	1.018	1.019
7- 9.....	1.007	6- 6.....	1.019	1.019
9-11.....	1.007			

Interpretation: Marked fixation of gravity in 1916 at a low level; in 1917 at a fairly high level; very low phthalein excretion. The functional tests indicate a severely damaged kidney in which a permanent and probably progressive nephritis has developed.

CASE 13.—I. C., aged 10 years. Chronic nephritis of three years' duration. Although the child has had albumin and casts in the urine at every examination during the last two years, her general condition is excellent, and at a glance she would be taken for an unusually healthy child. Urine: albumin, slight trace. Sediment shows a few hyaline and granular casts.

Blood urea nitrogen = 9 mg. per 100 c.c. blood. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.021	2- 4.....	1.025
8-10.....	1.021	4- 6.....	1.025
10-12.....	1.022	6- 6.....	1.026
12- 2.....	1.026		

Night urine, 220 c.c.; nitrogen concentration, 1.4 per cent.

Interpretation: Moderate degree of fixation at a high level; night urine of high gravity and high nitrogen concentration; moderately low phthalein excretion; tests indicate moderate functional impairment. Taken in conjunction with the good clinical condition, they indicate a nephritis of mild character, probably not rapidly progressive.

CASE 14.—L. S., aged 7¼ years. Chronic nephritis of two years' duration; acute exacerbation; general condition poor; considerable anemia. Urine: albumin, slight trace. Sediment shows many red blood cells and granular casts. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8.....	1.015	2- 4.....	1.015
8-10.....	1.015	4- 6.....	1.016
10-12.....	1.016	6- 6.....	1.017
12- 2.....			

Night urine 350 c.c.

Interpretation: Marked fixation at a low level; large amount of night urine of a low gravity; moderately low phthalein excretion. In conjunction with the general poor condition the tests indicate a permanently damaged kidney, with an ultimately poor prognosis.

CASE 15.—H. P., aged 3 years. Chronic nephritis of one year's duration. Urine: albumin, trace. Sediment shows rare hyaline and granular cast. Blood urea nitrogen = 14 mg. per 100 c.c. blood. Phthalein excretion = 60 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6-8.....		2-4.....	1.017
8-10.....	1.020	4-6.....	1.018
10-12.....	1.020	6-6.....	1.015
12-2.....	1.020		

Night urine, 210 c.c.; nitrogen concentration, 0.70 per cent.

Interpretation: Fixation of gravity, during the day especially; low gravity and low nitrogen concentration of night urine; low normal phthalein excretion. We can say from the functional tests that the kidney at present is slightly damaged. Whether or not the damage will be permanent and progressive cannot at present be foretold.

CASE 16.—J. G., aged 6 years. Chronic nephritis; acute exacerbation; tests made while he was eliminating edema. Urine: albumin, large trace. Sediment shows many hyaline and granular casts. Blood urea nitrogen = 25 mg. per 100 c.c. blood. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6-8.....	1.011	2-4.....	1.014
8-10.....	1.013	4-6.....	
10-12.....	1.010	6-6.....	1.020
12-2.....	1.014		

Interpretation: Fixation of gravity during the day. The gravity is of little significance in this case as he was eliminating edema. The test diet caused a marked diuresis; his fluid intake was 900 c.c. and his output 1,365 c.c. for the twenty-four hours. With this diuresis he eliminated 10.9 gm. of salt on an intake of about half this.

CASE 17.—F. O'L., aged 8 years. Chronic nephritis secondary to scarlet fever; two years' duration; acute exacerbation. Urine: albumin, large trace. Sediment shows numerous red blood cells and granular casts. Blood urea nitrogen = 16 mg. per 100 c.c. blood. Phthalein excretion = 59 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6-8.....		2-4.....	1.019
8-10.....	1.017	4-6.....	1.018
10-12.....	1.018	6-6.....	1.016
12-2.....	1.019		

Night urine 500 c.c.

Interpretation: Marked fixation of gravity with a large amount of night urine of low gravity. Phthalein excretion very slightly diminished. Blood urea normal. Two-hour renal test shows a diminution of kidney efficiency; other tests do not.

DISCUSSION OF "TWO-HOUR" RENAL TEST

The "two-hour" renal test is a test of kidney function that is particularly well suited for use in children, as it takes only a day to perform, complicated chemical analyses are not needed, and strict dieting is unnecessary. Fifteen normal cases were studied, and in none of them was there a fixation of gravity, or a night urine of low gravity; therefore, there is a good standard of normality. In nearly all the nephritis cases studied there was a definite fixation of gravity, sometimes to an extreme degree, and many cases showed a night urine of low gravity. The test is a very delicate one, probably more so than any other, and it is possible that relatively marked fixation of gravity may mean only slight functional damage. A good deal of caution is

necessary, therefore, in the interpretation of this test, and in stating an opinion on any given case it is best also to take into consideration the phthalein test, the urinary examination, and the general clinical condition of the child.

Blood Urea Nitrogen.—It has long been recognized that end-products of protein metabolism are sometimes retained in the blood in cases of nephritis. The determination of the concentration in the blood of these products is considered to be a valuable diagnostic and prognostic aid. The concentration of urea nitrogen gives us a very good idea of the concentration of the nitrogenous end-products, and the urea nitrogen is the substance that is being used by most observers as an index of nitrogen retention.

Leopold and Bernhard,⁹ studying normal children, found that there was a good deal of variation in the concentration of urea nitrogen in the blood. Their lowest figure was 8 mg. per 100 c.c. of blood, and their highest 21 mg., giving an average of 12 mg. for fifty cases. Inasmuch as only one of their normal cases was over 15 mg., and this one was a cardiac patient, who might well have had urea retention, it is fair to assume that any concentration of blood urea nitrogen over 15 mg. per 100 c.c. of blood is abnormal.

We have made blood urea nitrogen determinations on twelve nephritic children, using the urease method.

TABLE 4.—BLOOD NITROGEN DETERMINATION IN NEPHRITIC CHILDREN

Case	Urea Nitrogen		Remarks
	Per 100 C.c.	Blood, Mg.	
1. J. C.	32.0		Acute nephritis; no edema
2. W. K.	36.0		Acute nephritis; much edema; very scanty urine excretion
3. J. M.	11.6		Severe acute nephritis; considerable edema
4. H. K.	23.0		Severe acute nephritis; much edema
5. M. K.	46.0		Severe acute nephritis; much edema; died the next day
6. R. M.	21.0		Severe acute nephritis; much edema
7. F. O'L.	16.0		Chronic nephritis (mild)
8. M. H.	14.0		Chronic nephritis (mild)
9. H. P.	14.0		Moderately severe chronic nephritis
10. S. W.	24.0		Severe chronic nephritis; died three days later
11. J. C.	25.0		Chronic nephritis
12. J. C.	9.0		Chronic nephritis

DISCUSSION OF BLOOD UREA NITROGEN DETERMINATIONS

Of course, this series of cases is by far too small on which to base any conclusions. From a study of these few cases it would seem that in the severe cases of acute nephritis there may be considerable urea retention, and that a high blood urea warns us to be on the watch for uremia. The same information is given to us by the clinical condition

9. Leopold and Bernhard: AM. JOUR. DIS. CHILD., 1916, **11**, 432.

of the patient. Most of the chronic cases of nephritis in children are so mild and so slowly progressive that there is no urea retention, or at least not enough to give us any information of value. From the little experience that we have had with blood urea determinations we should be inclined to conclude that they have comparatively little value in dealing with nephritis in children, and that they apply more particularly to the hypertensive cases with contracted kidneys, seen in adults.

SUMMARY AND CONCLUSIONS

Four methods of testing kidney function in children have been discussed: the added salt and urea test, the phthalein test, the two-hour renal test, and the determination of the concentration of urea nitrogen in the blood. Of these tests the added salt and urea test is of little practical value in children. The determination of the blood urea is probably of slightly more value. The most valuable of the four tests discussed are the phthalein test and the two-hour renal test, because they are simple to carry out, and because they give us reliable and important information concerning the functional power of the kidney. These two tests supplement each other, and more valuable information can be obtained by using them together than by using either one singly. I feel that these two tests are of unquestioned value, not in diagnosis, not as guides to treatment, but particularly in *prognosis*. The prognosis of nephritis in early life is most difficult, and who can say whether any given child with mild subacute or chronic nephritis will ultimately recover, or whether the nephritis will progress, with a finally fatal termination in a few years? We know that many of these patients recover entirely after one or more years of continuous or intermittent albuminuria, and again, that many of them develop a permanent chronic nephritis and die within a few years.

The tests for function, taken in conjunction with the general condition of the child, help us a good deal in giving an intelligent prognosis, but even with the tests we are often at a loss. In general, repeated *low* functional tests at intervals of a few months mean a poor prognosis. High phthalein excretion alone does not help us one way or the other. High phthalein excretion, normal blood urea, and a normal response to the two-hour test warrant a conclusion that the process is a mild one, that the kidneys are only slightly damaged, and that there is a good chance for ultimate recovery.¹⁰ The diagnosis and treatment of nephritis in children is comparatively simple, but the prognosis is difficult and of great importance, and any simple laboratory tests that can help us in answering this question are worthy of general consideration and use.

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10. The question of prognosis will be taken up more in detail in a later paper.