PROGRESS IN PEDIATRICS

A REVIEW OF RECENT LITERATURE ON THE GENITO- URINARY DISEASES OF CHILDREN *

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VOLUME OF URINE

Addis and Watanabe¹ studied the daily volume of urine in adults on a standard diet and found that the volume of urine in any individual for any one day or part of a day is extremely variable in spite of constant water intake. They found that not less than 38 per cent. of the twenty-four hour volume was excreted during the first eight hours of the day, and not less than 53 per cent. in the first twelve hours. The night urine was never more than 47 per cent. of the total twenty-four-hour amount. Of course, the volume of urine excreted varies a good deal with the temperature, with the humidity, and with the number and character of the bowel movements, for if much fluid is excreted through these channels, there will be less excreted through the kidneys. Such studies are extremely valuable, as it is often necessary to know what the ratio between intake and output should be. As far as I know, no such work has been done with children, and it is rather difficult to decide sometimes in dealing with nephritic children, whether the urine output is as high as it should be in relation to the fluid intake.

CHEMISTRY OF URINE

C. U. Moore² discusses phenol excretion in the new-born and arrives at the following conclusions:

1. An increase in the number of stools per day is associated with a decrease in the total phenol output in the urine.
2. In a series of fifteen infants the phenol excretion per kilogram of body weight is less in the breast fed than in the artificially fed infant.
3. In infants and in adults, so far as it is possible to determine from the limited number of cases now at hand, there is an interrelation

* Submitted for publication Dec. 17, 1917.

1. Addis and Watanabe: *Jour. Biochem.*, 1916, **27**, 267.

2. Moore, C. U.: *JOUR. DIS. CHILD.*, 1917, **13**, 15.

between the total phenol excretion and the protein intake as measured by the total nitrogen excreted in the urine. This relation can be expressed in the general term "trebling the protein intake doubles the phenol excretion."

4. Contrary to the earlier findings, phenol is quantitatively present in the urine of every new-born infant, the average of nineteen cases being 11.2 mg. for the first three days of life.

5. As phenol is present during the period of starvation, it must originate in part through endogenous metabolism.

Johnson and Veeder³ have studied the nitrogen partition in the urine of normal children.

Urea nitrogen makes up from 80 to 85 per cent. and ammonia nitrogen from 3 to 5 per cent. The combined figure for the two is less than 90 rather than above 90 as in adults.

Creatin is constantly present, as is creatinin. The two combined form a smaller percentage than the creatinin alone in the adult. "The amount of undetermined or "rest" nitrogen is high in children.

Torres⁴ discusses the relation between the diet and the acidity of the urine, and proves that a suitable regulation of the diet is a most valuable adjunct to the various drugs which have been used for the purpose. He arrives at the following conclusions:

1. The difficulties which one often encounters in changing the reaction of the urine in children are very much diminished when a suitable diet is prescribed.

2. Diminishing the amount of protein in the diet to 2 gm. and sometimes to 3 gm. per kilogram will often in itself render the urine alkaline without using a drug.

3. In cases in which the amount of protein reaches the lowest physiologic limit without turning the urine alkaline, one may continue to diminish the acidity by adding vegetables to the diet.

4. In cases in which vegetables are used to turn the urine alkaline, one must use, if possible, vegetables in which the amount of protein is smaller in proportion to the salts, like fruits, rice, wheat, etc., rather than those which have a large amount of protein, as peas, beans, etc. Substances which contain purins, like coffee, tea and cocoa, may increase the acidity, because they may produce uric acid.

5. In cases of infection, especially in infections of the urinary tract, and in cases of starvation, the urine tends to become more acid than in other conditions; therefore, it is more difficult to render it alkaline.

3. Johnston, M. R., and Veeder, B. S.: *AM. JOUR. DIS. CHILD.*, 1917, **13**, 404.

4. Torres, C.: *AM. JOUR. DIS. CHILD.*, 1917, **14**, 365.

6. When drugs are used without the proper diet, the doses necessary to make the urine alkaline are much larger than is ordinarily believed.

7. The action of drugs (either acid or alkaline) is very fleeting; therefore, they should be given in large and frequent doses.

ANURIA

Clough⁵ reports a case of prolonged anuria in a boy of 7. The boy had scarlet fever, and during the attack passed very little urine. When he came under the writer's care, soon after the attack, the anuria persisted, and for over a month he passed only from 2 to 6 ounces of urine a day. He never had any edema, nor any albumin, and on only one occasion were casts found in the urine. He made a good recovery.

CALCULUS

Lazelle⁶ reports a kidney stone in a child of 7. The symptoms consisted of attacks of abdominal pain, acute in character, passing off usually in a few hours. The roentgen ray showed a stone in the kidney, and at operation two stones were successfully removed.

While ureteral and kidney stones are by no means so common in children as they are in adults, they are not so rare as has been generally believed, and a number of cases have been reported of late years, particularly by English writers.

TUMORS

O'Neil⁷ says that bladder tumors in infants and children are distinctly rare. The great majority appear before the fifth year. They are of the connective tissue type, and are clinically and pathologically malignant, except in rare cases. Disturbances of micturition, shown by sudden retention or incontinence, are usually the earliest symptoms. Abdominal pain is a common symptom. The urine at first may show no abnormality; later signs of cystitis develop. As they do not tend to ulcerate at first, hematuria is often absent.

Early diagnosis and operation offer the only means of recovery.

Friedlander⁸ reports a sarcoma of the kidney treated by roentgen ray. The tumor occurred in a boy of 4 and was so large that no surgeon was willing to attempt its removal. Roentgen-ray treatments were started and for a while the tumor grew smaller, but later increased in size. The child finally died of bronchopneumonia occurring during an attack of measles.

5. Clough, F. E.: *AM. JOUR. DIS. CHILD.*, 1916, **11**, 367.

6. Lazelle: *Northwest Med.*, 1916, **15**, 403.

7. O'Neill: *Boston Med. and Surg. Jour.*, Dec. 9, 1915.

8. Friedlander: *Tr. Am. Ped. Soc.*, 1916, **28**, 59.

The tumor examined at necropsy showed extensive degenerative lesions due to the roentgen ray, proving that the treatment was not without its effect on the tumor tissue.

ENURESIS

But little of importance has been written about enuresis recently. The very multiplicity of drugs and other measures that have been suggested to control this disorder show how little is really known about it.

Dunham¹¹ is an advocate of suggestion as a therapeutic measure in nocturnal enuresis. The condition, he believes, is not so common as is generally thought. Among 800 nervous children admitted to the Phipps Psychiatric Dispensary, ranging in age from 5 to 16 years, only 7 per cent. were bed wetters.

Many cases are due to pure nervousness and no abnormality of the urine or of the genito-urinary tract can be shown.

Dunham reports good results with his suggestive treatment, which he carries out as follows:

These four sentences are printed on a card.

1. I am not going to wet the bed.
2. I am going to wake up at midnight.
3. I shall get up and pass water.
4. I shall not wet the bed any more.

PYELITIS

R. M. Smith¹² discusses the mode of infection.

In favor of the ascending theory are the clinical data. Against it are the facts that colon bacilli have never been shown to pass up the normal unobstructed ureter, and that they have frequently been introduced into the bladder without causing any damage. He believes that the ascending theory has not been proved, and that the facts, experimental and otherwise, are against it.

The usual mode of infection is through the lymphatics, the colon bacilli invading the lymphatics from the intestinal tract, or from some focus elsewhere (particularly the vulva, in girls). From thence they pass into the blood, and from the blood to the kidney. After reaching the kidney they pass through the glomeruli and are excreted at the pelvis. They may be excreted without any damage, or may cause a pyelitis. Smith cites the case of a child who had a severe pyelitis secondary to a few impetiginous pustules on the neck. The cultures from the neck and from the urine showed *Staphylococcus aureus*.

11. Dunham, F. L.: AM. JOUR. DIS. CHILD., 1916, **12**, 618.

12. Smith, R. M.: AM. JOUR. DIS. CHILD., 1916, **12**, 103.

When the original focus of infection cleared, the pyelitis cleared up also. Smith explains the greater frequency of pyelitis in girls than in boys by the fact that the vulva, urethra and vagina are fine culture grounds for bacteria, which enter the lymphatics, blood, and finally the kidney, but that the infection does not ascend through the urethra.

Huet¹³ likewise supports the theory of descending infection. He reports an epidemic of pyelitis which started in a child who had pyelitis secondary to a bronchitis. Four other children who were cared for by the same attendant later developed pyelitis. He believes it was transmitted by milk: that the attendant in changing the babies' diapers infected her hands and then the milk. The colon bacilli recovered from all the cases were of the same type, and Huet believes that this series of cases proves that occasionally, at any rate, infection may be per os.

Helmholz and Beeler¹⁴ injected sixty-six rabbits with various strains of colon bacilli, and only two showed a typical pyelitis. Eleven rabbits were injected with a mixed culture of pneumococci and colon bacilli; of the eleven animals, six showed focal lesions of the kidney: three had pyelitis, one had cortical abscesses and two had diffuse hemorrhages into the cortex. Their conclusions follow:

1. It is possible to produce typical pyelocystitis in the rabbit by the intravenous injection of colon bacilli isolated from human cases.

2. If a mixture of organisms is injected, the relative number of kidney infections can be greatly increased.

Abt¹⁵ brings up the point that sometimes in a case of pyelitis several specimens of urine have to be examined before any pus can be found. He tends to favor the ascending theory of infection, because it is so well supported by the clinical facts. *Fever* and *restlessness* are the two main symptoms. Forcing water is the most important single thing in the treatment. Abt recommends using very small doses of hexamethylenamin and believes the patient should be watched very carefully while taking it. He does not favor the vaccine treatment.

Levy and Strauss¹⁶ find that the strength of formaldehyd necessary to inhibit the growth of the colon bacillus is a concentration of 1 to 5,000 or greater. Under a dose of 7 grains of hexamethylenamin three times a day (in adults) formaldehyd is never present in a concentration greater than 1 to 5,000. The only organism destroyed or inhibited by this concentration is the typhoid bacillus. For the destruction or inhibition of other organisms a high acidity of the urine is necessary, and this high acidity in combination with formaldehyd may produce injury of kidney tissue.

13. Huet: *Jahrb. f. Kinderh.*, December, 1915.

14. Helmholz, H. F., and Beeler, C.: *AM. JOUR. DIS. CHILD.*, 1917, **14**, 5.

15. Abt, I. A.: *Med. Clinics of Chicago*, 1916-1917, **2**, 895.

16. Levy and Strauss: *Arch. Int. Med.*, 1914, **14**, 730.

Graves¹⁷ discusses pyelitis with special reference to its occurrence in boys. He believes in the descending theory of infection. In the treatment of all cases of pyelitis in boys the intestine is to be recognized and dealt with as the potential source of the disease. The alkaline treatment is the best to follow in most cases. In all obstinate cases, autogenous vaccines should receive a trial.

Summary.—I believe at the present time it is fair to state that most authors favor the descending theory of infection. Opinions differ a good deal as to modes of treatment. Most agree that forcing fluid is of a good deal of value, and that vaccines may help somewhat in occasional chronic cases, but the relative virtues of the alkaline and of the acid-hexamethylenamin treatment have by no means been decided. A man of as great experience as Still recommends the alkaline treatment unreservedly, and barely mentions hexamethylenamin, and yet we know there are many cases of pyelitis which do not respond at all to alkalies. From what various men have written, it would seem that the alkali method of treatment will cure a good many cases, and that it is probably to be preferred to *small* doses of hexamethylenamin. Large doses of hexamethylenamin will, however, clear up many cases that have not responded well to small doses or to the alkali treatment. Such large doses are not entirely without danger, however, although by no means as dangerous as many writers state. The most reasonable method of treatment usually to follow, would, therefore, be to start with alkalies, and if good results are not apparent in two or three days, to use large doses of hexamethylenamin.

ORTHOSTATIC ALBUMINURIA

Jeanneret¹⁸ thinks that "postural" albuminuria is the best name for the condition, as other factors besides orthostasis enter into its production. He studied the effect of lordosis and of various postures in causing albuminuria in 204 children. His results may be summarized as follows:

1. Many children with a fixed lordosis have no albuminuria.
2. In only 3 per cent. of the children studied could albuminuria be induced by causing the patient to be in an artificially lordotic position, and then only if the child was kept motionless.
3. Orthostasis alone caused albuminuria in only 1.3 per cent. of the children, and then only when the child was kept motionless. Therefore neither lordosis *alone*, nor the erect posture *alone* is enough to produce albuminuria.

17. Graves: Am. Jour. Med. Sc., 1917, **154**, 548.

18. Jeanneret: Arch. de méd. d. enf., 1915, **18**, 46.

4. Lordosis and orthostasis combined, accompanied by movements of the legs, produced albuminuria in only 1.6 per cent.

5. The combination of the factors lordosis, orthostasis and immobility caused albuminuria in 49 per cent.

6. Sex, age and tuberculosis were found to have no etiologic significance.

Therefore, postural albuminuria is due not to a single factor, but to a combination of several.

When a child with a lordosis stands erect there is caused considerable venous stasis in the region of the kidney. Muscular contractions compensate for this by compressing the veins and helping the blood along with the aid of the valves, which are particularly numerous in the veins of the lower leg. If the muscular contractions are not vigorous enough, they do not suffice to compensate for the venous stasis that is caused by the lordosis and orthostasis, and albuminuria results.

These considerations are important in treatment. Nephritic albuminuria tends to disappear under the influence of rest; postural albuminuria tends to disappear under the influence of exercise, particularly of walking. This same exercise will exaggerate a nephritic albuminuria. Jeanneret believes, therefore, that children with postural albuminuria should be taken out of school for a few weeks, should be sent to the country, if possible, and made to exercise a great deal: in a word, exercise should be the specific remedy for postural albuminuria. The diet need not be restricted. The prognosis is excellent, and postural albuminuria never develops into nephritis. This is the most comprehensive study of the subject since that of Jehle, whose elaborate monograph appeared in 1909. Jehle believed that lordosis was the cause of albuminuria; Jeanneret seems to have proved that other factors are of equal importance.

Achard¹⁹ calls especial attention to the fact that orthostatic albuminuria often first appears after infections which may have affected the kidneys. He believes that in orthostatic albuminuria the lordosis and the orthostasis are acting on an already damaged kidney. In the normal subject the erect attitude diminishes the ease with which the blood returns by the inferior vena cava and the renal veins. There results from this the passage of a certain amount of fluid from the vessels into the lower part of the body, and an increased concentration of albumin in the blood, which can be demonstrated by the refractometer. At the same time there is a transitory diminution of the arterial pressure, and of the volume of urine. Lordosis facilitates venous stasis and the transudation of albumin, but something else is necessary in order to

19. Achard: *Rev. gén. de clinic et de therap.*, 1916, **30**, 625.

bring about albuminuria, and this additional factor is a slightly damaged kidney. The therapeutic indications follow these etiologic lines. Achard recommends neglecting the damaged kidney and treating the lordosis. It is the weight of the head and of the trunk which causes lordosis, because they are insufficiently supported by feeble muscles. The following measures he believes of value in treatment:

1. Resting in a prone position two hours after dinner each day.
2. Avoiding attitudes that provoke lordosis.
3. Special exercises designed to strengthen the back muscles.
4. Massage and hydrotherapy for the general circulation.
5. Diet and general hygiene.

Janeway²⁰ discusses especially the diagnosis as follows:

First put the patient to bed for a considerable period, to make sure that the urine becomes free from albumin after a reasonable length of time. The second specimen passed after going to bed ought to be albumin free, or we are not dealing with a case of postural albuminuria. After determining that the urine is free from albumin while the patient is flat on his back, we can have him stand in a markedly lordosed position against a wall for half an hour. This will usually produce extreme albuminuria, and on going to bed again the albumin will promptly disappear. Lordosis is an important, but not an essential factor; a considerable degree of lordosis may exist without albuminuria, and the albuminuria may exist without lordosis.

One interesting diagnostic point, according to Janeway, is that the majority of nephritics show only albumin coagulable by heat; orthostatic cases often show protein precipitated by acetic acid in the cold, which may be euglobulin.

The treatment consists in a correction of the posture, invigorating exercises and a full diet.

Barber and Smith²¹ made phenolsulphonephthalein tests on six patients with orthostatic albuminuria. In four cases it was quite normal. In one case it was 5 per cent. lower than the usually accepted standard. In the other case it was 14 per cent. lower with the patient standing than it was when made in the recumbent position.

Hempelman²² likewise investigated kidney function in orthostatic albuminuria by means of the phenolsulphonephthalein test. He found that the percentage of phenolsulphonephthalein excreted in two hours by normal individuals was not affected by position. In seven cases of orthostatic albuminuria the phenolsulphonephthalein test was from 58 to 86 per cent. When these patients were put in a lordotic position, producing a marked albuminuria, the total output of phenolsulphonephthalein in two hours was reduced on an average of 12.9 per cent.

20. Janeway: *Med. Clin. North America*, 1917, **1**, 21.

21. Barker and Smith: *Am. Jour. Med. Sc.*, 1916, **151**, 44.

22. Hempelman, T. C.: *AM. JOUR. DIS. CHILD.*, 1915, **10**, 418.

Beifeld²³ reports a case of orthostatic albuminuria cured by tonsillectomy and believes that chronically infected tonsils may occasionally be a contributing factor in causing the condition.

NEPHRITIS

The literature on nephritis in the adult in the last few years is enormous, but comparatively little has been written about the condition in children. Certain of the papers which have been written with especial reference to adults apply equally well to children, and for that reason a few of the more important ones are included here. Two things especially have interested investigators of nephritis in recent years, the functional capacity of the organ, and the classification of the different types of the disease. It is beginning to be realized that an accurate knowledge of the function of the kidney as a whole is more important to the clinician and to the patient than a knowledge of the particular type of damage that has been done to the various unit structures of the kidney as seen under the microscope, and for this reason pathologic studies have largely given way to chemical studies concerned with the power of the kidney to do its work.

The classification of nephritis has always been a most perplexing problem, and has never been very satisfactory. At present, authorities on the subject seem to be departing further and further from the old anatomic classifications, which recognized several types of both acute and chronic nephritis, and are tending to simplify the classification more and more, recognizing particularly clinical types of the disease rather than histologic types as shown under the microscope. This puts a complicated subject on a much simpler and clearer basis.

ETIOLOGY

Loeb²⁴ calls especial attention to tonsillitis as an important cause of nephritis.

1. Acute nephritis results from acute tonsillitis far more often than is usually believed.
2. The symptoms are not manifested until some time after the inception of the disease.
3. There are probably many cases in which a mild nephritis occurs incident to a tonsillitis, which goes on to resolution without the patient or physician being conscious of its presence.
4. It is incumbent on practitioners to examine the urine of every patient with tonsillitis, not only during the height of the disease, but for some time afterward as well.

23. Beifeld: *Jour. Lab. and Clin. Med.*, 1917, **2**, 638.

24. Loeb: *Tr. Am. Laryngol., Rhinol. and Otol. Soc.*, 1910, p. 146.

5. Spontaneous, or "idiopathic" nephritis is probably often due to a tonsillitis that has not been considered as an etiologic possibility.

6. Chronic affections of the kidney may very well owe their origin to unrecognized acute attacks of nephritis of tonsillar origin.

7. Much light may be shed on this subject by a study of the urine in a large number of cases of acute tonsillitis.

Grulee and Gaarde²⁵ discuss involvement of the kidney as a result of focal infections, with especial reference to tonsillitis. They report six cases of acute hemorrhagic nephritis in children, following several days after an attack of acute tonsillitis. The urine is very bloody, almost as to suggest a hemorrhage into the bladder. There may also be a good many pus cells present, the pus cells tending to appear as the reds diminish in quantity. There are no uremic symptoms, no edema, and the condition is usually much improved or entirely cleared up in two or three weeks. Cultures from the throat agree in many cases with the urinary cultures (hemolytic streptococci or staphylococci). In some cases the removal of a focus of infection such as the tonsils is followed by an immediate clearing up of the urine.

Baxter²⁶ reports five cases of acute hemorrhagic nephritis secondary to infection of the post nasal space. Symptomatically, the children became well in about four weeks, but the ultimate clearing up of the urine took from two to four months in some cases.

Dick and Dick²⁷ made urine cultures from a number of cases of chronic nonsuppurative nephritis, with the following results:

In all cases examined the urine contained numbers of bacteria, mostly anaerobes. In one case the bacterial flora of the urine was the same as that of a focus of infection in another part of the body. The bacteria isolated from the urine readily produced experimental nephritis. These facts lead us to believe that bacteria multiplying in the foci of infection frequently gain entrance to the blood stream and are excreted in viable condition through the kidneys, and that the excretion of bacteria in this way by the kidneys may be a common cause of nephritis.

The same authors²⁸ investigated a number of patients with evident focal infections to learn how frequently bacteria found in the focus of infection could be isolated from the urine, in what number they occurred in the urine, and whether excretion of bacteria might occur to any extent without clinical evidence of injury to the kidneys.

Eighteen patients were studied. In six of these the bacteria found in the urine did not correspond to those found in the focus of infection. In four cases a partial correspondence was found between the bacterial

25. Grulee and Gaarde: *Jour. Am. Med. Assn.*, 1915, **65**, 312.

26. Baxter: *Arch. Pediat.*, 1916, **33**, 729.

27. Dick and Dick: *Jour. Am. Med. Assn.*, 1915, **65**, 6.

28. Dick and Dick: *Arch. Int. Med.*, 1917, **19**, 493.

flora of the urine and that of the focus of infection. In eight cases the correspondence was more striking.

Staphylococci and gram-positive anaerobic diphtheroids are common inhabitants of the urethra. In eight cases, aside from these organisms, one or more of the kinds of bacteria found in the urine were isolated from the focus of infection.

Such studies indicate the very great importance to the kidney of focal infections.

Frank²⁹ believes that most nephritides in childhood are secondary to acute infection of some sort elsewhere in the body. There are, however, types of nephritis in infancy that are apparently primary, and are not dependent on previous infection. In babies, gastro-intestinal disease is often a cause of nephritis. Frank calls especial attention to the fact that of twenty-two cases investigated by him pathologically, many were of the hemorrhagic type, which is a particularly common sort of nephritis in childhood.

CLASSIFICATION AND GENERAL CONSIDERATIONS IN NEPHRITIS

Langstein and Benfey³⁰ adhere closely to the earlier classification of Heubner. They recognize the following types of chronic nephritis in children:

1. Chronic hemorrhagic nephritis is particularly characteristic of children. It is characterized by occasional exacerbations of hematuria, and nearly always is accompanied by edema.

2. A second form is first shown by edema, but is accompanied by no blood in the urine. The urine contains a great deal of albumin and many casts. Infectious processes are likely to be the cause of the nephritis in the first group, and not so likely in the second.

3. Contracted kidney, or "interstitial" nephritis (very rare).

4. A parenchymatous nephritis secondary to pyelitis.

5. A form of nephritis coming on very insidiously and manifested by general debility of the child, called by Heubner "paedo nephritis levis." The urine contains a small amount of albumin, a few casts and leukocytes, and from time to time a few red blood cells. It is very likely to be a sequel of scarlet fever or tonsillitis.

6. "Intermittent" albuminuria. Rare and of little practical importance.

Christian³¹ discusses the classification of chronic nephritis in adults. It is especially instructive to observe how he has done away with the old complicated anatomic classification. He says:

29. Frank: *Arch. f. Kinderh.*, 1914, **11**, 202.

30. Langstein and Benfey: *Med. Klin.*, 1914, **23**, 5987.

31. Christian: *Cleveland Med. Jour.*, 1917, **16**, 223.

As our knowledge stands today, it is wiser to drop the terms "interstitial," "parenchymatous," etc., very largely from our clinical classification, and to use instead simple descriptive terms which indicate with the chronic nephritis the presence or absence of hypertension or myocardial insufficiency. The old type of kidney classification has been based on a study of the end-result of the diseased process.

Porter³² discusses the condition known as renal infantilism. This is a most interesting condition, which has been described by the English writers particularly. It is dependent on a contracted kidney with high blood pressure, of the same characteristics as so-called "interstitial" nephritis in the adult. Coexistent with the kidney condition is a state of infantilism. Porter's patient was 7 years old and weighed only 32½ pounds (should be about 49 pounds). There was incompleteness of calcification in all diaphyses, ossification was absent in the wrist bones, and the mental development corresponded to the stature of the child rather than to his age. He was very thirsty and passed a large quantity of urine of low gravity, containing a small amount of albumin and a few granular casts in the sediment. The bladder was of enormous capacity and he often voided 16 to 18 ounces at once.

The most striking symptoms in all the cases previously reported (looked up by Porter) were polydipsia, polyuria, enuresis and dry skin.

Parkinson³³ reports a case of nephritis without albuminuria. The child was 3½ years old, and had pneumonia, after which edema appeared. The urine showed no albumin, but microscopically showed a few red blood cells and casts.

He brings up the point that "latent" nephritis may be more common than is suspected.

It is doubtful whether such a condition should be called true nephritis. It corresponds rather to the condition spoken of as "acute renal irritation" which may occur in any acute fever. The pathologic text-books speak of it as "acute degenerative" nephritis.

H. Wessler³⁴ found that in nearly all of his nephritic cases in children, both acute and chronic, there was a distinct cardiac hypertrophy, often coming on as soon as two weeks after the onset of the nephritis. This was shown by percussion, by the fluoroscope and by roentgenograms.

Berkley and Lee³⁵ after a study of ninety-three cases of acute and chronic nephritis in children, have settled the question of blood pressure, which is one that had previously been in dispute. They found:

32. Porter: *Arch. Pediat.*, 1915, **32**, 85.

33. Parkinson: *Brit. Jour. Child. Dis.*, 1916, **13**, 138.

34. Wessler: *Arch. Int. Med.*, 1914, **14**, 516.

35. Berkley and Lee: *AM. JOUR. DIS. CHILD.*, 1917, **13** 354

1. The blood pressure is elevated in the nephritis of childhood, and occasionally to a marked degree. This applies to both acute and chronic nephritis.

2. Systolic and diastolic pressures are not increased to the same extent, the former averaging about 20 mm. Hg, and the latter about 10 mm. above normal.

3. The pulse pressure is increased, but the factor is not constant.

4. The blood pressure in chronic nephritis shows no constant elevation above that in acute nephritis.

5. The blood pressure may, in rare instances, be of prognostic value.

6. No relation has been found to exist between the blood pressure and the urinary findings.

7. Patients having marked edema showed a slightly higher average blood pressure than those with little or none. The difference is not great enough to warrant any definite conclusions.

8. Albuminuric retinitis is probably not common, even in cases showing a marked increase in blood pressure.

FUNCTIONAL TESTS

Kidney function in children has not been investigated so extensively as it has in adults.

Leopold and Bernhard,³⁶ in a series of children free from renal disease, found that the phenolsulphonephthalein excretion for two hours varied between 50 and 96 per cent., with an average of 70 per cent. Five cases of acute nephritis and five of chronic nephritis were studied. In both the acute and chronic cases the phenolsulphonephthalein excretion was diminished. The same authors found in normal children the following apportionment of the nonnitrogenous constituents of the blood. The total nonprotein nitrogen varied between 19 and 40 mg.; the urea nitrogen varied between 8 and 21 mg., the average being 12 mg.; the uric acid varied between 6 and 3.2 mg., the average being 1.8 mg. The creatinin varied between 0.5 and 4 mg., the average being 1.5 mg. The blood of sixteen children with renal conditions was examined. In acute nephritis the nonprotein nitrogenous constituents were found to be within normal limits, and in chronic nephritis they were usually increased.

Leopold and Bernhard arrive at the following conclusions:

1. Figures for the nonprotein nitrogenous constituents of the blood, as well as for the phenolsulphonephthalein excretion of children free from renal disease, are practically identical with the figures obtained from adults, and vary within the normal limits as the adult figures vary.

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

2. The changes in these figures in children the subjects of renal disease corresponded with the changes observed in adults.

3. The importance of the tests for diagnosis and prognosis, amply demonstrated in adults, will in all probability hold true for children, although a more comprehensive series of cases is required definitely to establish this view.

Tileston and Comfort³⁷ found that the phenolsulphonephthalein excretion for normal children varied between 78 and 81 per cent., while the nonprotein nitrogen of the blood varied between 22 and 26 mg. per 100 c.c. of blood. They investigated three cases of acute nephritis, the phenolsulphonephthalein tests being 39 per cent., 56 per cent. and 54 per cent. The nonprotein nitrogen of the blood in these cases was, respectively, 64, 34 and 24 mg. per 100 c.c. blood. They arrive at the following conclusions:

1. The determination of the total nonprotein nitrogen and urea of the blood is of great assistance in the diagnosis of uremia, and as a guide to the treatment of nephritis, a marked increase in these substances indicating actual or impending uremia, and calling for a diet low in protein. In the diagnosis of nephritis it is inferior to other methods, because many cases of nephritis show no retention of nitrogen.

2. The phenolsulphonephthalein test is very valuable in the diagnosis of nephritis, showing probably better than any other one method the degree of impairment of renal function. In the diagnosis of uremia and as a guide to diet it is inferior to blood analysis, for a low phenolsulphonephthalein output may occur without retention of nitrogen.

3. These investigations of the blood and of the phenolsulphonephthalein excretion would appear to indicate a better secreting capacity of the child's kidney as compared with that of the adult.

Hill³⁸ investigated four different types of tests for kidney function in children.

Phenolsulphonephthalein Test.—In twenty-seven normal children the highest phenolsulphonephthalein test was 100 per cent., the lowest 64 per cent., thus giving an average of 76 per cent. The figures for children are therefore somewhat higher than those for adults. 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. The average excretion of the sixteen chronic cases was 63 per cent., or 13 per cent. below the normal average.

37. Tileston and Comfort: AM. JOUR. DIS. CHILD., 1915, 10, 278.

38. Hill: AM. JOUR. DIS. CHILD., 1917, 14, 267.

Added Salt and Urea Test.—This consisted in adding a weighed amount of sodium chlorid and urea to a standard diet, and then determining how much of the added substances could be excreted in twenty-four hours. This test was found to be of little practical value.

"Two-Hour" Renal Test.—The "two-hour" renal test of Hedinger and Schlayer was performed in sixteen cases of nephritis and was found to be of considerable value in determining the degree of damage to the kidney. The principle of this test is that a normal kidney can vary the concentration of the urine from hour to hour; a nephritic kidney is likely to lose this ability. This is an extremely delicate test, and very easy to perform; hence it is of considerable practical value.

Blood Urea Nitrogen.—The concentration of blood urea nitrogen was determined in twelve nephritic children and was found to be slightly increased in some, normal in others. In general, the more severe the case appeared clinically, the more retention of urea was there likely to be. This is not a very valuable test for use in children.

The most valuable of the four tests are the phenolsulphonephthalein and the two-hour renal test, and they are valuable not especially in *diagnosis*, but more particularly in *prognosis*.

Zondek³⁹ believes that in considering kidney function it is not correct to look on salt and nitrogen as two separate factors without influence on each other.

Many times we see a kidney which may retain salt and put out nitrogen well, but when we cut down the nitrogen intake the salt excretion improves remarkably. Also, by adding a large amount of nitrogen to the diet, we can diminish the kidney's power of putting out salt. Occasionally we can even make a normal kidney hold back nitrogen by adding an excessive amount of salt to the diet. A salt-free diet is beneficial in reducing blood nitrogen. The question of fluid intake comes in as a third factor, to which a similar rule to the two other factors (sodium chlorid and nitrogen) is attributed. This rule seems to make an exception in the case of Schlayer's vascular hyposthenuria during the stage of regeneration of an acute nephritis, where, on account of the decreased power of the kidney to concentrate solids, there is copious diuresis due to the large amount of salt that is being excreted (getting rid of edema), for there is also increased nitrogen output with this increased salt excretion.

The salt concentration of the urine is greater during the daytime, the nitrogen concentration during the night. Normally, Bowman's capsule cares for salt, water and nitrogen excretion. This does not hold, however, for an injured kidney. Damaged kidneys function in an entirely different manner from healthy ones. It is not at all pos-

39. Zondek: Ztschr. f. klin. Med., 1915, **82**, 78.

sible to say that any given part of a diseased kidney excretes any given substance or substances. In a damaged kidney, if the damage is particularly to the glomerulus, let us say, the work of excreting salt and nitrogen falls on the tubules, and they might perhaps be able to excrete a fair amount of salt or of nitrogen *alone*, but not of both together. If in feeding a patient with nephritis, little or no salt is given, the tubules can concern themselves with nitrogen excretion alone and do it efficiently.

Zondek has found a diminution in the concentration of nonprotein nitrogen of the blood even when a nephritic child was taking as much as 120 gm. of protein daily, if the diet was salt-free. This is a rather new conception of kidney function, and Zondek in closing his paper makes a special plea for more individualization and less of routine in prescribing the diets of nephritic children.

TREATMENT

Hutinel,⁴⁰ in 1910, summed up in a few words most succinctly the principles to follow in treating nephritis in children. He said:

Let me insist that in dealing with these nephritic children it is especially important to pay attention to careful nursing and hygiene. It is by these measures that the malady is cured, or in the more serious forms, that life is prolonged. Use drugs as little as possible. Especially is it important not to irritate the kidney and to forbid the patient eating any substances whose end-products he cannot eliminate. It is necessary, moreover, to do away with any coexisting infection, however insignificant it may appear, and to watch carefully the mouth, digestive tract, respiratory apparatus, skin, etc. In a word, one must remember that the kidney is delicate, and spare it as far as possible.

This was written seven years ago, but it holds equally well for the principles of treatment today.

Janeway⁴¹ believes that often in dealing with chronic nephritis the protein intake is cut down unnecessarily. He says:

To tell every patient with albuminuria or hypertension to stop eating red meat, or still worse, as I have actually seen done, to go on a milk diet, is evidence either of colossal ignorance or of inexcusable mental laziness. If the phenolsulphonaphthalein test is normal I see no reason for restriction of the protein, either qualitatively or quantitatively, below a moderate normal intake.

Epstein⁴² discusses the type of nephritis ordinarily called "chronic parenchymatous," with especial reference to treatment. This is the type of nephritis which is usually associated with the "large white kidney" spoken of in the textbooks, and one of the most striking clinical manifestations of it is the development of edema, which may often

40. Hutinel: Bull. méd., Paris, 1910, **24**, 95.

41. Janeway: Am. Jour. Med. Sc., 1916, **151**, 158.

42. Epstein: Am. Jour. Med. Sc., 1917, **154**, 638.

reach an extreme degree. It is in this condition that the salt-free diet first advocated by Widal and his co-workers has been so successful, and the most generally accepted view of the causation of the edema is that the kidney is unable to excrete salt, and that the water retention is secondary to this. Epstein believes that other factors are perhaps of more importance than salt retention. He has proved that there is a considerable diminution of the protein of the blood serum which is caused by the continuous albuminuria, and that sometimes a nephritic of this type may lose over 20 gm. of protein a day in the urine. As a result of the decrease of protein in the blood serum there is caused a decrease in the osmotic pressure of the blood, which favors the absorption of fluid by the tissues. Therefore, in this particular type of kidney disease, a high and not a low protein diet is indicated. A diet containing a large quantity of protein with a minimum of carbohydrate and fat is the most efficient. The carbohydrate is restricted to promote a maximum assimilation of protein, and to exclude the greater production and retention of water which is incidental in the metabolism of carbohydrates. The fats are excluded because of the marked increase of fatty substances in the blood. The fluid allowed is restricted to the quantity present in the food, plus that which is necessary for the comfort of the individual patient. Enough salt is allowed to make the food palatable.

The diet is made up largely of the following articles: Lean veal, lean ham, whites of eggs, oysters, gelatin, lima beans, lentils, split peas, green peas, mushroom, rice, oatmeal, bananas, skimmed milk, coffee, tea and cocoa.

Christian⁴³ has studied extensively the use of diuretics in nephritis. In most patients with acute nephritis the kidneys will not respond to diuretics and diuretics are likely to do more harm than good. In chronic cases in which edema is of renal origin, diuretic drugs have very little effect in increasing urine output; in the group in which most of the edema is due to cardiac insufficiency, diuretics may work wonders. Theophyllin (theocin) is the best diuretic, but is likely to produce nausea. In nephritis, reduction of fluid intake salt poor diet, sweating and purging are the best methods of removing edema.

Harris⁴⁴ reports several cases of nephritis treated with epinephrin. Ten minims of a 1 to 1,000 solution injected subcutaneously once a day were found to diminish albuminuria and edema. Often a marked diuresis was caused by it.

Ercolani⁴⁵ likewise discusses the use of epinephrin in nephritis. He believes that the adrenals suffer injury in nephritis as well as the

43. Christian: *Dominion med. Monthly*, 1917, **49**, 25.

44. Harris: *Liverpool Med. and Chir. Jour.*, 1916, **36**, 85.

45. Ercolani: *Gazz. d. Osp.*, 1917, **38**, 321.

kidney itself, and that disturbances of the myocardium or of the nervous system in nephritis may be due to a lack of adrenal secretion. According to Ercolani, epinephrin is detoxicating and vasoconstricting in nephritis, both of which processes counteract the infection and ward off injury from the kidneys.

Morse⁴⁶ discusses the Edebohls operation as a therapeutic measure in the nephritis of children and carefully analyzes twenty-three cases in which it was performed. He concludes:

Edebohls' operation is of much value in properly selected cases of nephritis in childhood. It may save life and result in permanent cure in acute nephritis. No child ill with acute nephritis should be allowed to die, therefore, without giving it the advantage of the chance afforded by this operation. It may prolong life for considerable periods in a not inconsiderable number of cases of chronic nephritis, and may possibly, in rare instances, result in cure. It should, therefore, always be considered in all cases of chronic nephritis in childhood which are not responding reasonably well under medical treatment.

99 Commonwealth Avenue.

46. Morse: *Jour. Am. Med. Assn.*, 1917, **69**, 525.