PROGRESS IN PEDIATRICS

A REVIEW OF THE LITERATURE OF THE PAST YEAR (1918) ON GENITO-URINARY DISEASES IN CHILDREN

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BACTERIOLOGY OF THE URINE

Schwartz¹ investigated the bacteriology of the urine of children with gastro-intestinal disease, and found that urethral and bladder contamination was very common. This was particularly true of girls, which favors the theory of ascending infection in pyelitis. In sixty-three infants with various gastro-intestinal disturbances, thirty-eight, or 60.3 per cent., showed the presence of gram-negative bacilli in the urine. Of those in which the first and second portions of the urine were separately cultured, 21.4 per cent. showed a sufficient number of gram-negative bacilli in the second specimen to constitute a bacilluria. Urethral contamination was almost three times as common in girl babies as in boys, while actual bacilluria was twice as prevalent in girls as in boys.

ALKAPTONURIA

Schochet² discusses alkaptonuria. About seventy cases of alkaptonuria have been reported in the literature. The term "alkaptonuria" was first introduced by Bodeker in 1857 to describe a substance found in the urine, which possessed two chief characteristics: first, the power to reduce alkaline copper solutions, and secondly, the property of absorbing oxygen from the air in the presence of alkali, and as a result turning to a brown black color. The urine may be clear and a normal color when passed, but later becomes dark brown or finally black on exposure to the air. There is no treatment for the condition, and it is of no pathologic significance. It is important, however, in that it may be mistaken for glycosuria. Negative results with fermentation and the polariscope should at once rule out glycosuria. Alkaptonuria must be differentiated from the hemoglobinurias due to drugs (phenol) and diseases (malaria) by the presence of hemoglobin in the urine; from the melanurias and hematurias,

1. Arch. Pediat., January, 1918.

2. Arch. Int. Med. 22:82, 1918.

and from the condition known as "paroxysmal hemoglobinuria" by chemical and spectroscopic tests for the pigments.

RENAL GLYCOSURIA

This interesting condition is discussed in two exhaustive papers by Beard and Grave³ and by Goto.⁴ Beard and Grave say that the condition should not be called "renal diabetes" but "renal glycosuria," as it has nothing to do with true diabetes. It is a very rare condition, and many cases so diagnosed are in reality mild or typical cases of diabetes mellitus. The lesion is renal, and is manifested by a constant excretion of a small amount of dextrose by the kidney. The blood sugar is normal. The tissues can still utilize carbohydrate—on any diet the percentage of sugar does not vary greatly. Most of the patients are apparently in good health. In order to make a diagnosis of renal glycosuria it is necessary to have the following data: (1) a urine containing dextrose, the amount of which is unchanged to any great extent by variation of the carbohydrate intake; (2) a normal blood sugar. (May vary normally between 0.7 and 0.15 per cent.)

Goto⁴ writes as follows:

The general conception now is that anatomic change in the kidney is not necessary for the occurrence of renal glycosuria. The reasons for the permeability of the kidney to sugar are not known.

Since we know that the blood sugar undergoes marked and rapid fluctuation after the ingestion of carbohydrate and that urinary sugar has some relationship to hyperglycemia after meals, it is hardly possible to deny, to a certain extent, at least, the existence of a relationship of urinary sugar in renal glycosuria to the carbohydrate content of the diet. In the case reported by Goto there was no urinary sugar when the carbohydrate in the diet was below 34 gm., because the alimentary hyperglycemia occurring with that diet is under the threshold of the kidney for sugar. The blood sugar was highest after 200 gm. of glucose, but the urinary glucose in that case was less after 100 gm. glucose. Renal glycosuria may depend to a certain extent on the carbohydrate content of the diet:

1. When the renal permeability is but slightly affected, glycosuria may not appear after a carbohydrate poor diet, but when it is severely affected, glycosuria will not disappear even after the entire withdrawal of carbohydrate from the diet.

2. Urinary sugar is not excreted proportionally to the increase or decrease of carbohydrate in the diet. The most important point in the diagnosis of renal glycosuria is the presence of the normal level of

3. Arch. Int. Med. **21**:705, 1918.

4. Arch. Int. Med. **22**:96, 1918.

blood sugar, when sugar appears in the urine. During a long period of time there is apparently, in the few cases reported, no tendency for the amount of sugar in the urine to increase—the patients seem perfectly well, and the condition is usually found during a routine urine examination. No treatment is necessary, and there is no use of decreasing the amount of carbohydrate in the diet, as this is without effect on the glycosuria.

ENURESIS

The literature on enuresis is always interesting, as no two authors use the same methods of treatment. Enuresis is a rather complex condition, which may be a resultant of many causes, and hence the good results reported by different observers with totally different methods of treatment. Many drugs have been used in the treatment of enuresis, some with apparent good results, but it is certain that in any condition where many drugs have been used, no drug is of specific benefit. We believe (see following) at the Children's Hospital that an intelligent regulation of the child's daily life, nervous system, diet, etc., is of more importance than drugs, and Dr. Grover has had excellent results in many cases without using a drug of any sort (see following).

Neave⁵ recommends making the child sit on its chair and hold its water when it wishes to micturate, thus gradually teaching it control.

Fisher⁵ has had good results with sulphonal. He gives 1 grain for each year of the child's age every night for the first week, every other night for the second week, and every third night for the third week. In a considerable number of cases, after this routine has been followed for three weeks the child is permanently cured.

Thompson⁶ has had good results with a widely different method. He inserts a catheter in the bladder, and runs in fluid at a low pressure. At first only that amount of fluid which the patient can hold with comfort (about 3 ounces) is inserted. The fluid injection is repeated three or four times at short intervals, with gradually increasing amounts of fluid. The treatment is carried on for ten days or so until about 10 ounces of fluid can be retained. The fluid used is boric acid solution at a temperature of 100 F. The essential points in the treatment are: (1) passage of a clean catheter; (2) ingestion of gradually increasing quantities, by which the bladder is slowly trained to hold more fluid than it has previously held.

Emerson⁷ reports thirty-four cases of enuresis treated successfully without drugs. Enuresis in children is not a disease, but simply the

5. *Lancet*, London **2**:728, 1917.

6. *Lancet*, London **2**:623, 1917.

7. *Am. J. Dis. Child.* **15**:339, 1918.

persistence of an infantile condition, or habit. Innumerable conditions have been cited as the cause of enuresis, but from their very multiplicity it is evident that the true cause has not been found. In a group study of 100 children reported by Emerson, no special incidence of enuresis was found with adherent prepuce or clitoris, mental retardation, carious teeth or malnutrition. There was, however, marked incidence with nasopharyngeal obstruction. The treatment may be considered to consist of four methods, all or one of which may be used in a given case to establish the "dry habit." The "dry habit" once started must then be continued by careful oversight.

First Method.—Mental suggestion. By arousing the patient's desire to be dry by rewards and other mental suggestions, this is entirely adequate to relieve about 40 per cent. of all cases of enuresis.

Second Method.—By teaching the child to urinate before he wets himself, the urine being voided at regular intervals, and the time between intervals being gradually increased. By such training the act of urination soon comes under the patient's control.

Third Method.—Local irritation. This consists in irritating the vesicular sphincter and the posterior urethra by a bougie-a-boule, so that sensory impulses passing to the brain will become intensified sufficiently to attract the patient's attention, until the habit of control is attained. The bougie is introduced into the bladder, withdrawn, and then passed in and out about four times, enough to cause a sensation of discomfort during the next few urinations. This sensation of discomfort in urinating brings the act into the child's consciousness, aiding him in control.

Fourth Method.—Cerebrospinal irritation. This is produced by the injection into the spinal canal of physiologic sodium chlorid solution, producing such stimulation as to arouse the whole mechanism into consciousness, when habit holds it under control. Ten c.c. of spinal fluid are withdrawn, and 12 c.c. of normal saline introduced. This method is necessary only in extreme cases of enuresis, or in those complicated by mental deficiency, and should be used only after other methods fail.

Grover⁸ has made a study of bed wetting and clothes wetting in a series of 200 cases in the outpatient department of the Children's Hospital, Boston. The ages ranged from 4 to 12 years. He found a history of enuresis in the immediate family in 56 per cent. of the cases. Although adhesions of the prepuce, adenoids, worms and high acidity or alkalinity of the urine are usually considered as of prime importance in the etiology of this disease, Grover has disregarded them and has

8. J. A. M. A. 71:626, 1918.

acted on the assumption that enuresis is due to what he terms a "general fatigue" of a neuromuscular nature. This fatigue is brought about by too much exercise, too little sleep, and more especially by an irregular and poorly chosen diet. After the condition has been going on for several months, a habit of involuntary wetting is acquired, which may persist long after the neuromuscular fatigue is overcome. His treatment is along hygienic and dietetic lines, no drugs of any sort or mechanical or operative means being used.

The child is put to bed at exactly 7 p. m., after urinating. He is then waked at exactly 10 p. m. and 6 a. m. to empty the bladder. In the very active children, an additional rest hour is provided immediately after the noon meal. No exercise is allowed after 4 p. m. Music lessons, moving picture shows, etc., are prohibited. The diet excludes candy, cake, ice cream, soda water, cookies, chocolate, jams, jellies, syrups, coffee, tea, cocoa, meat broths, raw apples, bananas, condiments, pickled and salt foods, frankforts, baked beans and egg-nogs. Meat and vegetables are prohibited at night, and no food of any description is allowed between meals.

The habit of wetting is taken care of by limiting all fluids after 4 p. m., and by the regular urinations at 7 p. m., 10 p. m. and 6 a. m. The habit of clothes wetting and frequent micturition in the daytime is treated by having the patient pass water every ten or fifteen minutes right through the day. This interval is lengthened by five or ten minutes every week, until the interval is two and a half hours. A large percentage of patients were cured in from one to thirty days. A conscientious mother, and an obedient, interested child predispose to a rapid cure. The hygienic and dietary measures outlined not only help the enuresis, but also relieve the nervousness and habit-spasms that so often accompany the condition.

CALCULUS, PYONEPHROSIS, ETC.

Tuberculous Obstruction.—Thompson⁹ in a discussion of the surgical aspects of genito-urinary disease in children, says that occasionally tuberculous peritonitis may be a cause of urinary symptoms by causing a constriction of the ureter, which may bring about symptoms of renal colic. The child is brought in with a history of severe radiating pain in one loin and occasional hematuria. Roentgenograms may reveal a shadow in the region of the upper urinary tract, which suggests stone. An exploratory operation is performed, and no stone found. In such cases a very careful examination of the ureter should be made, and not infrequently it will be found that there are peritoneal bands binding the ureter down to the posterior abdominal

9. Brit. J. Dis. Child, April-June 15:6, 1918.

wall, or even kinking it, or there may be a small mass of tuberculous glands pressing on the ureter and leading to obstruction. In the Guy's Hospital necropsy reports there were found twenty cases of tuberculous peritonitis in which there was evidence of obstructive conditions in the ureter. Cystoscopy, the passage of a ureteral catheter, and the injection of some opaque material into the pelvis of the kidney, with roentgen-ray examination, should enable a diagnosis to be made between a calculus situated within the upper urinary tract and tuberculous glands, producing pressure on the ureter from without.

Pyonephrosis.—This may occur from calculus or from aberrant vessels. Calculi may occur at an early age. For the ultimate cause of their formation we may have to go back to very early life. From many autopsies at Guy's Hospital the following is apparent: in the pelvis, and in the kidney substance, uric acid, sand, concretions or even very small calculi may be found after death from marasmus, or an acute infectious disease with which considerable wasting has been associated. It is not unreasonable to assume that these concretions may be the origin of larger stones and may bring about the formation of definite calculi. It is important to note that in children the symptoms of renal stone may occur on the side which is not affected.

Collins¹⁰ discusses the diagnosis of renal stone in infants and children. At first the child may simply cry a little on urinating, when no external evidences of irritation are visible. Frequency of urination is likely to occur. As the trouble progresses bladder pain becomes evident, especially when the child is active. Greater pain on urination, leading to tenesmus and rectal prolapse, may occur. Sudden cessation of the urine flow may be a common symptom in some cases.

PYELITIS

Helmholz¹¹ reports three cases of pyelitis in the new-born; all were boys; all showed the colon bacillus in pure culture. The most effective treatment was found to be 5 grains of sodium bicarbonate with 5 grains of sodium citrate every three hours.

In another paper Helmholz¹² discusses pyelitis. Pyelitis is characterized by the absence of local and the presence of general symptoms. General symptoms are chills, fever, pallor, loss of appetite and prostration. The younger the child the less likelihood there is of being local symptoms. The infrequency of local symptoms makes it absolutely essential to examine the urine repeatedly in any obscure febrile condition in infancy and childhood. Pyelitis frequently com-

10. Arch. Diag. **10**:259, 1917.

11. Med. Clin. N. Am. March, 1918.

12. Illinois M. J. **32**:311, 1917.

plicates acute infections and gastro-intestinal disturbance, and also gastro-intestinal disturbances frequently occur secondary to pyelitis, and are wrongly considered the sole cause of the fever. One must distinguish between primary and secondary forms of pyelitis.

In the first, the illness begins acutely in a child that is perfectly well; the child suddenly becomes sick with high fever and an absence of physical signs.

The second form may develop during a gastro-intestinal disturbance (summer type) or after infections of the upper respiratory tract (winter type). As a result of temporary plugging of a ureter, the pus may disappear from the urine for from twelve to twenty-four hours. The variability of the clinical picture is such that the only manifestation may be a slight fever, or again, the picture may be so severe as to suggest an acute meningitis. Severe complications are usually due to involvement of the kidney substance. There is a marked tendency to recurrence. The most important single point in the therapy of pyelitis is the free administration of liquid. In the drug treatment we must differentiate between the infant and the older child. The infant usually does best on the alkaline treatment. To an infant of 2 months or over, 90 grains of potassium citrate may be given every twenty-four hours, and this may be increased by 60 grains every day until the urine is alkaline. The urine must be kept alkaline at least two weeks.

It is doubtful exactly what the action of potassium citrate is. It has no antiseptic effect; the bacteria are just as numerous in the alkaline as in the acid urine (?)—although the clinical symptoms have gone. It appears, therefore, that the action of the citrate is largely a diuretic one. If the acid treatment is to be used, from 3 to 5 grains of hexamethylenamin four or five times in the twenty-four hours may be given to a child over 6 months old. If plenty of fluid is given, the danger of producing hematuria is very slight. In older children the potassium citrate treatment is often ineffectual, so that if after three days of treatment the child is no better, it is better to change to hexamethylenamin.

R. M. Smith¹³ says that pyelitis is a common disease, and comprises 1 per cent. of all cases seen. The youngest case he has seen was in a boy 2 days old. After the fourth month it is more common in girls; before this the incidence is about equal. It may begin with gastro-intestinal symptoms such as vomiting and diarrhea, which may mask the real trouble. Urinary symptoms are usually slight or absent. In 75 per cent. of all cases colon bacilli are found. The course is variable, but in general, children with acute and severe symptoms

13. *Med. Clin. N. Am.* 1:1165, 1918.

do better than those with a less vigorous onset. The tendency is to become chronic, and relapses are frequent. The blood is the most probable source of infection. The probable course is somewhat as follows: the organisms enter the blood from the intestinal tract or other parts of the body. Entering the blood directly or through the intermediary lymphatic route, they pass with the blood into the kidney through the glomeruli, down the tubules and out at the pelvis. During the passage through the kidney they may or may not cause an infection. What happens depends on the virulence of the bacteria and on the general resistance of the patient, and the local resistance of the kidney. Colon bacilli have a low pathogenicity; therefore, they rarely cause infection in the kidney. In being excreted at the pelvis, an inflammatory process, causing the disease pyelitis, occurs. There may be an infection of the kidney by extension inward from the pelvis via the lymphatics, but it is not directly associated with the primary condition. A large amount of experimental evidence has been collected to substantiate this mode of infection, and all the various steps in the process have been shown possible of occurrence.

NEPHRITIS

Etiology and Classification.—Ophüls¹⁴ believes that lesions of the glomeruli play a most important part in nephritis and often form the one connecting link in a "bewildering multiplicity of other developments."

"The differences that have been so carefully studied by the pathologists and have given rise to our complex and often confusing nomenclature, naturally remain, but as purely descriptive subdivisions. They should be relegated to that point of relative importance to which they may still lay claim, and should not be permitted to cloud the real picture by the introduction of a mass of perhaps interesting, but evidently subsidiary detail."

It is very likely that the glomerular lesions are embolic, and due to the rapid lysis of the bacteria within the vascular loop of the glomeruli. Streptococci are by far the most common organism concerned in nephritis. The most dangerous forms of nephritis are those associated with streptococcic infections of the tonsil, in which cases the persistence and recrudescences of the renal disease are probably due to the persistence of a septic focus in this locality.

Ophüls recognizes the following groups of nephritic cases due to streptococcic infection:

1. *Acute Glomerulonephritis.*—This is usually due to some septic infection. The glomeruli are intensely inflamed, permitting the escape

14. J. A. M. A. 69:1223, 1917.

of blood, albumin and leukocytes into the capsular space and the tubules. There may be a moderate or a very large amount of blood in the urine. There may or may not be edema.

2. *Subacute*.—This may develop insidiously, and it may be impossible to ascertain the date of onset. The necrotic spots in the diseased glomeruli gradually become replaced by connective tissue, which eventually destroys the glomeruli entirely and converts them into inert masses of fibrous connective tissue. In some cases the blood vessels begin to develop serious lesions. Sometimes these patients are well for a long time, and the condition is discovered only accidentally, or in the last stages, when severe symptoms begin to arise.

3. *Chronic Form*.—In eight cases investigated there was chronic disease of the tonsils, with multiple pus pockets. The tonsil condition may be present without any knowledge on the part of the patient, and is difficult to discover clinically. Why such a condition, which is common in many people who do not have nephritis, should cause nephritis in some persons and not in others is hard to explain. The development of the chronic cases is very insidious, and the course extends over many years. The original lesion in many of them undoubtedly dates back to childhood. The clinical history usually begins only a few months, or at best a few years, before death, when there is often quite a sudden change for the worse from a condition of apparent well-being. The kidneys at necropsy are always much shrunk and show the characteristic microscopic picture of an advanced renal sclerosis. "The patients in this last group vary so much in their rate of development, in the gross and microscopic appearance of the kidneys, and in their symptomatology, that one can readily understand why, both from an anatomic and a clinical point of view, numerous efforts have been made to subdivide this group into subgroups according to whether the disease of the blood vessels in the kidneys plays an important rôle, or whether clinically the signs of cardiovascular disturbance predominate over those of renal origin, or vice versa." Such a subdivision does not seem feasible.

SUMMARY

"1. There is a well defined disease of the kidneys caused by general sepsis arising from some infected focus, and often made progressive by the persistence of such a focus.

"2. Since the glomeruli in this disease show the most characteristic and constant lesions we may speak of it as glomerulonephritis, and as the lesions are so distinctly of an inflammatory character, as true nephritis.

"3. The disease occurs in three forms; acute, subacute and chronic.

"4. Characteristic glomerular lesions may be produced in animals by injection of bacteria into the blood stream.

"5. Many of the chronic cases seem to be caused by a peculiar form of chronic suppurative tonsillitis due to diplostreptococcic infection."

Stengel¹⁵ discusses the classification of nephritis.

The pathologic changes in damaged kidneys may be grouped under three heads:

1. Glomerular change, which may present itself as hemorrhage or exudation in the space between the capillary tuft and the outer limiting epithelial lining of the sac, proliferation and degeneration of the epithelia, hyalinization, atrophy or sclerosis of the malpighian body, thrombosis of the capillaries of the tuft, and in later stages sclerotic thickening of the outer wall of the capsule.

2. Tubular changes, manifested by swelling and degeneration of the epithelial cells lining the tubules.

3. Sclerosis in the form of concentric layers of fibrous tissue surrounding the diseased malpighian bodies, or as fibrous thickening and condensation of the intertubular tissues, is a late result of either the first or second group of changes.

"It is obvious that in a complicated glandular structure such as the kidney, a pathologic lesion is not likely to confine itself to one of the histologic elements to the exclusion of the adjacent parts, and clinico-pathologic experience shows that combinations occur in renal disease which make a rigid classification of definite forms untrustworthy."

We may classify the fundamental forms of nephritis as: (1) tubular nephritis; (2) glomerulo nephritis; (3) renal sclerosis.

It must always be remembered, however, in dealing with any classification of nephritis, that transitional forms are very frequent.

The clinical manifestations of the three broad types into which nephritis may be divided, are as follows:

1. *Tubular Nephritis*.—Very mild tubular nephritis occurs in a great many infectious diseases, and it is hardly worth while to attempt to separate those conditions which are merely toxic degenerations of the epithelium from those which are frankly inflammatory. The milder cases have few symptoms, in the more severe cases oliguria and anemia may occur. Edema is usually marked, but there is little tendency to uremia, nor is the blood pressure usually high. The urine contains a heavy trace of albumin with many casts.

2. *Glomerulonephritis*.—This form is likely to occur in connection with scarlet fever, or streptococcus infections. In the acute stages

15. Med. Clin. N. Am. 1: 1918.

the symptoms are oliguria, with marked albuminuria and abundant casts, often considerable blood, high specific gravity of the urine, edema, moderate elevation of the blood pressure, and a tendency to uremia. The greater albuminuria, the microscopic findings in the urine, the higher blood pressure, and the tendency to uremia differentiate it from tubular nephritis.

In chronic glomerulonephritis the patient is pale and pasty looking, with digestive disturbances, coating of the tongue and general weakness, with circulatory disturbances. The blood pressure is high, often considerably over 200 mm., and there is usually distinct cardiac hypertrophy. There is usually polyuria, and a low gravity urine, usually rather definitely fixed between 1.011 and 1.013. An occasional examination of the urine may show neither albumin nor casts. Toxic symptoms significant of uremia appear sooner or later, and a large proportion of these patients die of uremia.

3. *Renal Sclerosis*.—This term means simply an end stage in some other form of renal disease. This may occur secondary to tubercular or glomerulonephritis or to widespread arterial disease involving the smaller arterioles of the kidney.

The following is a brief summary of the important features of the foregoing types:

1. *Tubular Nephritis*: (*a*). Mild, with practically no symptoms except albuminuria and cylindruria; is likely to occur in most acute infectious diseases; (*b*) severe, with characteristic urinary findings and edema.

2. *Glomerulo Nephritis*: (*a*). Acute form with dropsy, mild or severe hematuria, as well as a tendency to uremia; (*b*) subacute or intermediary form, with scarcely any renal symptoms, but with pronounced elevation of blood pressure; (*c*) chronic form, with excessive blood pressure, marked fixation of the specific gravity of the urine, tendency to uremia, disturbances of vision, and suggestive appearance of the patient.

3. *Renal Sclerosis*: (*a*) possibly primary renal sclerosis following acute interstitial nephritis; (*b*) secondary renal sclerosis following glomerulonephritis and mixed nephritis; (*c*) arteriolar nephritis or benign sclerosis, with high blood pressure, but with little impairment of renal function; (*d*) arteriosclerotic atrophy of the kidney.

Van Zant¹⁶ calls especial attention to nephritis as a result of focal infection. Hemorrhage occurs into the glomerular capsule and tubules as a result of lesions in the glomerular capillaries, creating a hemorrhagic type of nephritis. It is believed by most investigators that bacteria from the primary focus plug up the glomerular capillaries.

16. Colorado Med., 1917, p. 325.

It is interesting and instructive to note that sometimes numbers of cases seem to spring up in a community in quick succession. This would seem to indicate the endemic presence from time to time of a form of streptococcus possessing a special affinity for the tonsils, and secondarily for the kidneys. It is not unlikely that many cases of so-called "idiopathic" acute nephritis, or nephritis from cold, may have an overlooked tonsillar origin (the reviewer wishes to emphasize this point, and believes it to be especially true as regards children). The great symptom of most of these cases is hematuria, not transient or mild, but pronounced in its degree, prolonged in its presence, and disproportionate to the other urinary features. Blood in the urine is often so abundant as to be visible macroscopically for several weeks. The nephritis does not ordinarily appear at the same time as the tonsillitis, but is more likely to show itself in from one to three weeks after the initial tonsillitis has subsided. The prognosis is usually good, and it is of great importance to remove the tonsils as soon as the acute throat symptoms have subsided.

Cross¹⁷ reports four cases of nephritis following sore throat, and attaches especial importance to the streptococcus as a cause of renal disease. He believes that not enough attention is paid to the relation of acute infection of the nasopharynx to nephritis. With the causative organism incarcerated in the tonsillar crypts, buried in the nasopharyngeal tissue, or at the apex of a tooth, what is the mode of assault on the kidney? If we grant that it remains fixed in its *locus* and only its toxin circulates in the blood stream, exercising a special chemical affinity for the renal epithelium, we may think of an acute degeneration of the cells of the kidney tubules. Rather more likely is the probability that the process is one of hematogenous infection, bacterial emboli being carried direct to the kidney, and establishing a true glomerulonephritis. Kidney involvement may appear at any time during or after the local infection. The average period is from seven to fourteen days. The latent reserve power of the kidney is the most important consideration in prognosis. With a severe acute toxemia we may lose our patient; with a continual influence at work, the kidney condition may go on to a diffuse nephritis with permanent damage, anatomic and functional, with all that that implies. In most of the cases, however, the outlook is favorable. The offending tonsils should be removed, but not too early. It is usually best to wait for two or three weeks after the onset of the nephritis.

Butterworth¹⁸ discusses syphilitic nephritis. Not infrequently there are seen in infancy and childhood cases of nephritis that can be

17. Long Island M. J. **12**:15, 1918.

18. Arch. Pediat., June, 1917.

explained in no other way than on a syphilitic basis. In one group of cases the clinical symptoms of nephritis may be wanting, and so insignificant as to pass unnoticed; repeated examinations of the urine may be necessary in order to make a diagnosis. If the child survives the early period of life, then the clinical manifestations are those commonly associated with a chronic interstitial nephritis. Fetal syphilis may result in various kidney changes, such as congenital malformations, cystic kidneys, etc., but the most common syphilitic manifestations may be classed as follows:

1. Acute parenchymatous nephritis, which may be hemorrhagic.
2. Acute interstitial nephritis.
3. Chronic interstitial nephritis.
4. Amyloid degeneration.
5. Gummas of the kidney.

Fowler's¹⁹ classification of syphilitic nephropathies is as follows:

1. Secondary syphilis: (a) Transient albuminuria; (b) acute and subacute nephritis.
2. Tertiary stage: (a) Chronic interstitial and parenchymatous nephritis; (b) amyloid kidney; (c) gumma.
3. Hereditary syphilis: (a) early nephropathies; (b) late lesions.

In hereditary syphilis all varieties of nephritis are met with, but as a rule the kidney changes are overshadowed in importance by other manifestations of the disease. The kidney lesions may occur at two distinct periods: in early life, associated with other visceral lesions, and as a late complication. As a rule, there are few or no symptoms referable to the kidney. The pathologic changes most commonly found give rise to no symptoms aside from depressed renal function. These children are usually underdeveloped, undernourished and anemic. To the naked eye the kidney may appear normal, although under the microscope definite histologic changes may be seen. The kidney may show hyperemia and punctiform hemorrhages. Occasionally whitish or yellowish nodules are found in the deeper layers. They are composed for the most part of connective tissue, but may show caseous degeneration.

As regards prognosis, it is probable that many unrecognized cases are cured by antisyphilitic treatment. Fowler feels that the prognosis is not so bad as the literature would suggest.

MISCELLANEOUS

Rubow²⁰ remarks that the three main groups of medical kidney diseases are those due to epithelial degeneration, to glomerular

19. *Med. and Surg.*, St. Louis **2**:54, 1918.

20. *Hospitalstidende*, **61**: No. 24, 1918; Quoted from *Abstr. in J. A. M. A.* **71**:695, 1918.

nephritis, and to sclerosis of the vessels in the kidney. The blood pressure is inclined to go up as soon as the glomeruli become involved. He warns that if the blood pressure naturally is low, as frequently happens in the young, there may be a considerable rise in the arterial pressure while it still is within apparently normal range. In certain cases the high blood pressure is almost the only certain sign of pathologic conditions in the glomeruli, and he queries whether from this alone, along with the following hypertrophy of the heart, we can draw the conclusion as to serious damage of the glomeruli and sclerosis of the vessels. Functional tests of the kidney may prove misleading with negative responses, as the normal range of functioning in human organs is so great. Healthy kidneys are capable of at least three times the work ordinarily imposed on them. This explains the long latent stage with chronic kidney disease, and shows that ordinary functional tests may give apparently normal findings for a long time even with encroaching disease. Only when the test is applied up to the maximal limit of normal functioning, can the findings be depended on to reveal slight degrees of functional deficiency, and therewith the beginning disease. It is difficult and possibly dangerous to apply a maximal test of this kind.

Even the determination of the residual nitrogen in the blood may prove misleading, if the residual nitrogen happens to be anchored in the solid tissues; in the liver, for example, and is not circulating in the blood. Some deny the possibility of this, but Monakow's research in 1914 on this historetention of residual nitrogen not only confirmed it but showed that the residual nitrogen in the blood is an unreliable index of the amount retained. He had a patient with reflex anuria for five days, and the fifth day the blood showed 50 mg. percentage of residual nitrogen in the blood, corresponding to about 3 gm. nitrogen. When the anuria stopped, it was found that there had been retention of 62 gm. nitrogen, in addition to 7.5 liters water. There must have been 55 gm. of nitrogen retained in the solid tissues; that is, the tissues were able to retain eighteen times as much as the blood. Determination of the residual nitrogen has proved useful in many ways, but it cannot be counted on to reveal incipient disease of the glomeruli. It is possible that applying the test in connection with maximal overburdening of kidney functioning may prove instructive. For example, one man of 53, with high blood pressure and hypertrophy of the heart, had residual nitrogen in the blood, in the morning, 34 mg. per cent., but twenty-four hours after intake of 20 gm. urea the figure was 62 mg. per cent.—a figure essentially higher than would be presented by a normal person under the same test. In a second case with apparently the same high pressure and enlarged heart,

twenty-four hours after the intake of 20 gm. urea, the blood showed a residual nitrogen content only at the upper limit of normal.

The same conditions are inherent in the determination of chlorids. Only with extreme degrees of renal insufficiency is the chlorid content of the blood very high; the surplus is anchored in the solid tissues. When the glomeruli are unable to eliminate as usual, the consequent retention of urea and salt acts as a stimulant to extra functioning on the part of the glomeruli still capable of functioning, as these substances have a diuretic action. Another means by which the organism seeks to compensate the deficient glomeruli is by sending the blood through the kidneys under greater pressure. The rise in blood pressure, and consequent hypertrophy of the heart, occurs early, and in many cases this alone answers the desired purpose of keeping renal elimination within practically normal range. The high blood pressure and hypertrophy of the heart, in combination with slight albuminuria, are therefore the bases for the diagnosis. Polycythemia may complicate kidney disease, and in the one typical case that has come to necropsy, chronic glomerular nephritis was found. The high blood pressure with kidney disease persists unmodified by repose in bed and dieting. The numerous transitional cases between glomerular nephritis and renal angiosclerosis show that there is no essential difference between them. The cardiovascular form may be regarded as a more or less protracted phase of a compensated stage of kidney sclerosis, while the uremic form is the stage of insufficiency when compensation is failing, or when from the first it has been inadequate. Death may occur from hemorrhage in the brain or from heart failure while the kidney trouble is still in the compensated phase. The findings in the kidney then will be quite different from those with death from uremia.

Meara²¹ reports a case of unexplained high blood pressure in a boy 8½ years old. The systolic blood pressure was 210 mm., the diastolic 150. The boy appeared healthy and well, but had been subject to intense headaches ever since he was 5 years old. The heart was much enlarged, and the aortic second sound accentuated. There was a transitory edema of the legs, and the eye grounds showed arteriosclerosis of the retinal vessels, with some hemorrhagic exudate. The urine had a gravity of 1.010 and a trace of albumin, but no casts. The phenolsulphonephthalein test was 63 per cent., and the urea nitrogen of the blood 20 mg. per 100 c.c. blood, both within normal limits. The boy developed a severe hematuria, with intestinal hemorrhage, and finally died from mesenteric thrombosis.

This case corresponds exactly to the cases of "chronic interstitial nephritis" that have been reported before in children, with the excep-

21. *Med. Clin. N. Am.*, July, 1918, p. 5.

tion of the fact that Meara's patient was a well developed, robust boy, who did not show the condition of the infantilism that usually goes with the condition. The etiology is unknown; the prognosis bad.

Foster²² believes that there are three distinct and basic types of what is called "uremia." Clinically, it is rare to see one type uncomplicated by the others.

1. Simple retention of nitrogenous waste. A urinary poisoning, which occurs with complete anuria. In this type convulsions and other nervous symptoms are lacking. The essential positive symptoms are progressive asthenia and anorexia; later stupor and death.

2. The second type occurs with defective water and salt metabolism, resulting in cerebral edema. Convulsions are usually absent, and the blood pressure is not high. There is no marked nitrogen retention. At necropsy the conspicuous condition is edema, especially of the brain and meninges. The cerebrospinal fluid is under increased pressure, and after lumbar puncture there is temporary improvement.

3. The third, or convulsive type of uremia is due, Foster believes, to an abnormal catabolism. It is from such cases that he has isolated a very toxic crystalline substance which kills a guinea-pig with convulsions and coma. He believes that this is not a normal excretory product, but a product of abnormal metabolism.

Sailer²³ has investigated the composition of the sweat in nephritis. He admits that it was shown years ago by Austin and Miller that the blood nitrogen of a nephritic patient was not altered by sweating. But is it not possible that the urea in sweat is drawn from the tissues and not from the blood? Sailer investigated several cases with this in view, and found that usually the percentage of urea in the sweat of a nephritic was greater than that in his blood, which supports his hypothesis that the urea is drawn from the tissues.

Frissel and Vogel²³ discuss the value of the various renal function tests. The functional tests which are now being used may be divided into the following groups:

1. The determination of the rate of excretion in the urine of known amount of a chemical substance, injected or ingested.

2. Determination of the degree of retention in the blood of various normal metabolic products.

3. Comparison in a patient on a known test diet of the ingestion and excretion of nitrogen, salt and water.

4. A determination of the ratio between the concentration of various metabolic products (ordinarily urea) in the blood, and their excretion in the urine, the result being expressed as a ratio or coefficient of excretion.

22. J. A. M. A. **67**:927, 1916.

23. Pennsylvania M. J. **21**:245, 1918.

Frissell and Vogel consider as abnormal a phenolsulphonephthalein excretion below 50 per cent. in two hours, a nonprotein nitrogen of the blood above 35 mg. per 100 c.c. of blood, or a urea nitrogen above 25 mg. per 100 c.c. blood.

They arrive at these conclusions:

1. Kidney function tests have a real prognostic value, particularly if the results are constantly abnormal on repeated examinations.
2. The higher values for the blood retention products are found mainly in the terminal stages of nephritis.
3. By plotting the curve of a very large series of cases it should be possible to arrive at an average expectation of life as indicated by any individual determination.
4. The value of diet and drugs may in the future be shown more clearly by these methods than by any other means now available.

Atchley²⁴ has made an intensive chemical study of eight cases of acute nephritis. A phenolsulphonephthalein excretion below 20 per cent. in acute nephritis is likely to carry with it a serious prognosis; higher value than this need not cause any worry. Urea retention was found in only three cases on admission. Three of the other patients showed no urea retention all the time that they were in the hospital. Two patients retained urea constantly even on a low salt and nitrogen intake. The highest figure for blood urea was in the only fatal case, the only other high urea was in the next most severe case. A high blood urea is probably of serious import in acute nephritis. Atchley doubts the value of the Ambard coefficient, and believes that even moderately rigid interpretation of it as a real index of the exact degree of impairment of urea function may lead to the gravest error. Edema was present in every one of the eight cases studied. While a patient was losing edema there was also a great sweeping out of salt and water; but after reaching a constant weight there is likely to be no abnormality of salt or of water function in the daily balances. It seems clear that the salt function is the first to be regained, followed at varying intervals by the pouring out of water with a coincident decrease in weight.

The first step in the treatment of acute nephritis should be the restriction of salt. The caloric requirement should be maintained from the very beginning, though it is wise to give a low protein intake to all cases of acute nephritis. When there is no retention of urea, 8 to 10 gm. of nitrogen (roughly 60 gm. protein) is a safe intake for an adult, but if there is nitrogen retention 6 gm. (roughly 40 gm. protein) should be the upper limit.

24. Arch. Int. Med. **22**:56, 1918.

Frothingham²⁵ has made studies of renal function in various acute infectious diseases, such as pneumonia, rheumatic fever, typhoid, etc., and arrives at the following conclusions:

In the acute infections in which there is no clinical evidence of serious renal involvement, there is no constant impairment of renal function, as shown by the various functional tests, either during or after the acute stage of infection has passed. In some cases of infectious disease certain suggestions of impairment of function occur, but not constantly enough to draw any definite conclusions. The most striking thing in all groups studied was the frequency of an abnormally high index of urea excretion during the course of the fever. As this increase in the index was not associated with an increase in the phenolsulphonephthalein excretion or an abnormally low blood urea, in most of these cases it seems more likely that some factors peculiar to fever affect this test, rather than that the kidneys themselves are hyperactive during fever. It may be concluded that the various tests for kidney function failed to show any consistent evidence of impaired renal function during the course of or following these acute infections in which the clinical picture or the urinary examination by the older clinical methods showed nothing suggestive of renal damage.

Williams²⁶ believes that diuretics are useless in the treatment of nephritis. If a patient is dyspneic and edematous it is quite likely that he has a disturbance of salt metabolism. Such a patient should be given no other food than one quart of milk plus one pint of water daily for a week or two weeks (few authorities believe in restricting the diet as much as this, even in the most severe cases. L. W. H.). Later, starchy foods, and vegetables rich in iron and calcium may be added. Protein food is given according to the ability of the body to handle it. It is Williams' plan to put these cases on low diets, cautiously building them up as above suggested. At the same time a record is kept of the patient's muscular vigor by means of a dynamometer. As a result of the studies which have thus far been made, Williams feels that a patient gains in muscular vigor on a diet which his body can care for, even though it be much below his normal needs, and he will lose in muscular tone if he is fed ever so cautiously beyond his metabolic limitations. There is no value in persistent purgation with salts or in the use of hot packs.

As a summary, he concludes that kidney disease is probably a constitutional disease with kidney manifestations. In many cases the liability is commonly associated with nephritis and may bear a causal

25. Arch. Int. Med. **22**:74, 1918.

26. Med. Rec. **92**:624, 1917.

relationship to it. The best functional test for the general practitioner is the two-hour renal test.²⁷ Tests for albumin and casts are much less valuable. The phenolsulphonephthalein test is also extremely valuable. Blood studies for nonprotein nitrogen, urea, creatinin, and the determination of the Ambard-McLean coefficient are of considerable importance, but can be done only in a well equipped hospital laboratory. The Karrell (milk) diet is the best treatment for advanced cases with edema and dyspnea. Death is caused by acidosis (not always, certainly, L. W. H.) probably due to retention of phosphates. Calcium and iron both favor the elimination of phosphates and are the best medicines for the disease. Packs, purges and diuretics are probably of little value.

As regards prognosis, blood chemical studies furnish the most reliable evidence of the condition of the patient, and afford a better prognostic guide than does the two-hour renal test. The blood chemical methods are, however, too complex, and are far beyond the laboratory means of the general practitioner, and indeed the majority of hospitals. The two-hour renal test, on the contrary, is much simpler. Important and valuable parts of it can be done by the general practitioner without any technical training or laboratory experience. Merely measuring the urine excretion and determining its specific gravity every two hours during the day, and estimating the amount and gravity of the night urine, are extremely valuable guides in diagnosis, prognosis and treatment.²⁸

PROGNOSIS

Christian²⁹ believes that functional tests have helped us a great deal in prognosis. Several of the methods yield results which are expressed numerically, and this makes it easy to compare results from time to time. It is of the utmost importance, however, to consider the patient as a whole, and not to place too much reliance on any one test or group of tests. Certain extrarenal factors may influence kidney tests a good deal; that is, severe anemia or cardiac decompensation. Under such conditions some functional tests may indicate advanced nephritis, and yet the kidneys may be really sound. Repeated tests are of the most value in prognosis, as we must know how rapidly any given condition is progressing. When renal function is fairly good, the chance for prognostic error is greatest. It may be said that there are two fairly distinct groups of nephritics as regards prognosis: (1) Progress slow and steady; (2) progression by sudden exacerbations.

27. Mosenthal: *Arch. Int. Med.* **16**:733, 1915.

28. Hill, L. W.: *Am. J. Dis. Child.* **14**:267, 1917.

29. Pennsylvania M. J. **21**:233, 1918.

Four functional tests are used at the Peter Bent Brigham Hospital:

1. Phthalein test.
2. Blood urea and Ambard coefficient determinations.
3. Mosenthal test meal (called elsewhere "two-hour renal test").
4. The amount of diuresis produced by such a diuretic as theophyllin.

As a summary, Christian says that tests of renal function give us additional facts on which to base a prognosis as to renal lesions. "They will, if used with such limitations as are indicated above, greatly improve prognosis, but they will only reduce, not eliminate, our prognostic errors. Too many factors play a part in the human organism to permit perfection in prognosis. Properly interpreted tests of renal function aid us much in the management of nephritic patients. Often they enable us to determine serious conditions not previously suspected. Frequently they enable us to bring to our patients a far more cheerful outlook than seemed justified from the data obtained by other methods of examining the patient."

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