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Pyelitis in infancy

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PYELITIS IN INFANCY

Senior Thesis
University of Nebraska College of Medicine

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RAYER (1) IN 1837 DESCRIBED FOR THE FIRST TIME THE ENTITY THAT IS NOW KNOWN AS PYELITIS, NAMELY, INFLAMMATION OF THE PELVIS OF THE KIDNEY. HE ALSO POINTED OUT THAT THE INFLAMMATION FREQUENTLY SPREAD FROM THE PELVIS TO THE SUBSTANCE OF THE KIDNEY, OR FROM THE INFECTED KIDNEY TO THE PELVIS SECONDARILY. HUTTENBRENNER (2) IN 1876 WAS ONE OF THE FIRST TO CALL ATTENTION TO THE DISEASE IN INFANCY AND CHILDHOOD, AND MUCH OF THE DESCRIPTION OF THE DISEASE WHICH HE MADE AT THAT TIME MAY BE FOUND IN OUR MODERN TEXTBOOKS.

SEVENTEEN YEARS LATER HIRSCHSPRUNG (3) ALLUDED TO THE AILMENT, AND IN THE FOLLOWING YEAR, 1894, ESCHERICH (4) AGAIN CALLED ATTENTION TO THE COMMON OCCURRENCE OF PYELITIS IN INFANTS AND CHILDREN, PARTICULARLY IN GIRLS. BECAUSE THE COLON BACILLUS WAS FOUND SO OFTEN TO BE THE CAUSATIVE FACTOR, HE CALLED THE CONDITION COLICYSTITIS. FROM THIS DESIGNATION IT IS SEEN THAT ESCHERICH, AND LATER TRUMPP (5), CONSIDERED THE INFECTION TO BE PRINCIPALLY IN THE BLADDER. THIS VIEW, HOWEVER, ON LATER INVESTIGATION, PROVED TO BE ERRONEOUS, AND FROM THE WORKS OF FINKELSTEIN (6), HEUBNER (7), HOLT (8), AND MANY OTHERS, IT HAS BEEN DEMONSTRATED QUITE CONCLUSIVELY THAT, IN THE MAJORITY OF CASES OF
pyuria, there is an involvement of the pelvis of the kidney.

The relatively low mortality rate of pyelitis has made a study of the seat of infection difficult until recent times. With the improvement in cystoscopes, ureteral catheterization of infants became possible, and it has been shown by Hinman (9), Kretschmer and Helmholz (10), and others that in cases of pyuria there is usually an inflammation of one or both of the kidney pelves.

Pyelitis may be defined as an inflammation of the pelvis of the kidney, manifested by the presence of bacteria and pus in the urine. The infection is usually caused by a member of the colon group of organisms, and clinically is marked by fever, pallor, and the absence of other clinical symptoms.

Except for common colds and gastro-intestinal disturbances of infancy, pyelitis is one of the commonest diseases of childhood. In eight years of experience Goppert (11) found that pyelitis made up about 1.2 per cent of his entire practice. Smith (12) estimates that it comprises about 1 per cent of all cases seen by pediatricians.

Pyelitis has been rightly termed as a disease of the diaper age, for beyond this it is usually a more serious disease, although much less common. It is most often encountered during the second and third quarters of the first year and is rather rare in the first six months (13), although there is a very definite type which occurs in the first ten days of life, as described by Smith (12), Kovalesky (14), and Moro and Helmholz (15).
The general frequency of pyelitis makes it difficult to know whether there is a familial tendency to the disease. Helmholtz (16) mentions only one definite instance of a family of six, four girls and two boys. Each of the girls in turn developed pyelitis during the first two years of life; in each instance the disease ran a stormy course and cleared up gradually.

Escherich (4) was the first to point out the great prevalence of pyelitis in girls, and various observers have described from 57-100 per cent of cases in girls; Friedenwald (17), 72 per cent; Abt (18), 95 per cent; Box, 95 per cent; Goppert (11), 89 per cent; Thompson (19), 79 per cent; Still (20), 88 per cent; and Kowitz (21), 57 per cent. Viewing these figures, there can be no doubt that the common colon bacillus pyelitis, during the diaper age, is more common in girls than in boys. The more severe infections often associated with lesions of the kidney (cortical abscesses) are as common in boys as in girls; this is true also for perinephritis.

In congenital cases the equal distribution of sex, and in some instances the predominance of infection in baby boys, is noted in the literature. Conrad (22), in a recent review of the literature, quotes Kovalsky and Moro, R. M. Smith, Helmholtz, Runge, and Finkelstein. He added three cases that he had observed. Sauer (23) reported fifteen cases from six to twenty-eight days of age.
There are two definite periods of the year when pyelitis seems to be more common: in the winter, when it follows infections of the upper respiratory tract, and in the summer, when it is associated with gastro-intestinal disturbances. The infections, whether during the summer or winter, are in most instances due to the colon bacillus (24).

As far as is known at present there is no natural immunity to the disease. Its frequency as a complication of extraneous infection would make it appear that only after the natural immunity of the urinary passages is lowered is infection likely to take place.

Harkness (25), studying pyelitis from the face of infection viewpoint, states that, since there is lacking a definite means of measuring the so-called resistance of an individual and as to whether the child with some form of kidney infection is susceptible to a certain focus, that focus should be removed empirically in the hope of making a break in the chain that is responsible for the faulty metabolic condition. This, he claims, would prevent, to a large extent, secondary involvement of the urinary passages after their natural immunity had been lowered.

The predisposing factors may be considered under two headings (16): (1) pyelitis which is primary in infants and children, and (2) pyelitis which complicates a great variety of ailments affecting practically any of the other systems of the body. It must be assumed that retention is the most important factor in infection. Retention may be due to stones, valves, stricture, phimosis, or it may be functional. Chilling, exposure on
auto rides, sitting on cold floors or in drafts are repeatedly given as possible exciting causes. In the second type of cases, besides the lowering of resistance due to infection, the same factors are evident.

A great variety of organisms have been mentioned as causes of pyelitis. The gonococcus is infrequently the causal agent. The tubercle bacillus occasionally is found to be the sole etiologic factor, but more often the colon bacillus is associated. In certain rare cases, no organisms were isolated by the usual bacteriologic methods. These infections are usually with the tubercle bacillus, but, in rare instances, they may be due to a streptothrix infection as described by Cecil and Hill (26). Soldin and Langer (27) believe that with the onset of pyelitis the streptococcus lacticus, which is normally present in the urine, is replaced by the colon bacillus. Helmholtz and Milliken (28) were unable to confirm these observations, and found the organism in only 8 per cent of specimens of normal urine.

In most of the early work on pyelitis, cultures have been taken only from the bladder. In recent years studies of ureteral cultures have been made by Hinman, Kretschmer, Helmholtz and others, showing that the pelves of the kidney are usually infected. Thus far no serologic studies have been made to show whether the colon bacillus found in the urine is specific to the gastro-intestinal tract of the individual or whether it gains access from the outside. Herrold (29) has shown that colon bacillus from the feces and urine may be serologically and biologically the same. Normally the urethra does not contain bacilli of the
colon group, and the organisms that are present are usually staphlococci, or members of the pseudo-diphtheria group. Schwartz (30), in a study of the urine in eighteen unselected cases of chronic gonococcus vulvovaginitis, found only gram-positive staphlococci and diphtheroid bacilli.

In diseases of the gastro-intestinal tract, gram-negative bacilli are found frequently in the urinary passages. Schwartz (30) found that in 63 per cent of patients suffering from gastro-intestinal disorders there were gram-negative bacilli in the catheterized urine, and in 21 per cent their number was sufficient to indicate a bacilluria, which was twice as common in girls as in boys. Helmholz and Beeler (31) found that in gastro-intestinal disturbances in the first year of life, the colon bacillus was found in the urethra in about one-third of the cases; after this age it was rarely found.

The usual mode of infection in pyelocystitis has not been definitely determined, and the primary seat of infection is not yet known. In only relatively few cases has the inflammatory process in the urinary tract been ascertained. Necropsy findings and ureteral catheterization demonstrate that the pelvis of the kidney is not sufficient to localize the seat of infection. Experimentally it has been shown that the upper urinary passages may be infected by way of the blood and by way of the bladder. Almost all writers have observed that pyelocystitis is more common in baby girls than in baby boys. From 57 to 100 per cent of all cases have been reported by various observers as occurring in girls. Because of the short urethra in the female, infection of
the bladder from without is supposed to occur more readily. This led to the assumption that infections of the urinary tract were by the ascending route. The exposed portion of the female genitalia, and their constant contamination with feces during the diaper age, make it seem likely that the colon bacilli reach the bladder by way of the urethra. In view of this, Smith (12) suggests that microorganisms gain entrance to the blood stream by way of the lymphatics of the external genitalia and thence to the kidney. The same fact may serve as a basis for the theories of the various routes of infection, for example, the ascending and the hematogenous. Another mode of infection, the transparietal mode of Franke (32), is based on the existence of lymphatic anastomosis between the ascending colon and the right kidney, but there is no exact proof that pyelitis can be produced in this manner. Jarrell (33), however, declares this an ideal route to the bladder and ureters.

In favor of the hematogenous route the following evidence is given: In 1896 Biedle and Kraus (16) demonstrated that live colon bacilli and staphylococci could be eliminated from the blood stream by way of the kidney without injury to the urinary tract. It has further been shown by a number of observers that colon bacilli are being absorbed into the gastro-intestinal tract, carried into the blood stream, and either destroyed there or excreted by the kidney.

The excretion of typhoid bacilli in the urine without infection of the urinary tract, and the occasional presence of the tubercle bacilli in the urine without evidence of kidney damage,
are further proofs that organisms are excreted through the kidney during a bacteremia. Brock (34) demonstrated positive cultures of colon bacillus in 7 of 14 cases of bacilluria associated with infectious diarrhea. Cabot and Crabtree (35) demonstrated in the adult positive cultures preceding urinary infections with the colon bacillus. Kowitz (21) found the colon bacillus in the blood and urine in five cases of infectious diarrhea. Soldin and Langer (27) reported the isolation of the bacillus lacticus in the blood of eight patients with severe nutritional disturbances. On the other hand, Levy (16) has shown, in a series of 16 cases, that there may be a definite colon bacillemia without bacilluria. Lepper (36) found that, in the rabbit, bacillemia may persist for a number of days without the appearance of bacteria in the urine. Magoun (37) demonstrated that bacteria enter the blood stream very rapidly from an infected pelvis, particularly if there is a back pressure.

The question of sterility of the urine is also of importance in this connection. If it is true, as Soldin and Langer (27) hold, that bacteria are normally excreted by the kidney, the evidence would be in favor of the hematogenous route. But with their technique it is impossible not to carry in an occasional organism with the catheter. The work of Helmholz and Beeler (31) demonstrated that in the normal infants organisms were only occasionally in the bladder urine obtained with proper precautions, and that the organisms were usually of the coccus or diphtheroid type. Because of their number it was assumed that they were carried in with the catheter. Soldin and Langer (27), in a later study of 136 cases, found the streptococcus lacticus in 128 cases; in
16 associated with colon bacillus. In the 11 remaining cases they found colon bacillus alone, and in four other cases bacillus lactus aerogenes. The difference between their results and those of others, they ascribed to the fact that they used a liquid medium which, they claimed, was essential to the growth of the streptococcus lacticus. Helmholtz and Beeler (28), using the same technique, were able to find the streptococcus lacticus in only 8 per cent, and in only a few instances were able to demonstrate the organism in the liquid media when it could not also be demonstrated in the solid media. Beeler and Helmholtz (38) and Schwartz (39) demonstrated that in parenteral infection and in gastroenteritis the colon bacillus is much more often found in catheterized specimens of urine. Schwartz found that in cases of gastroenteritis 63 per cent revealed gram-negative bacilli.

During recent years there has been a growing conviction among pediatricians that throat infections are often accompanied by pyuria, and that the pyuria disappears soon after the throat inflammation subsides. Children often show repeated attacks of pyelitis following tonsil infections, and the tonsil-adenoid operation is advised (40).

Pyelitis following throat infections would presumably be carried by the blood stream, and might be a streptococcus, unless a lowered resistance would invite some other infection (33).

In favor of the ascending mode of infection is: (1) the frequency in which pyelitis occurs in girls; (2) the incompetency of the ureteral valve in the bladder; and (3) the fact that bacteria can enter the blood stream from an infected pelvis (41).
The production of pyelitis in experimental animals with the colon bacillus was difficult, unless there was an obstruction to the outflow of urine. In the course of their experiments, Beeler and Helmholz (31) found one exception to this, with an organism isolated from a case of spontaneous pyelitis in rabbits. With this organism they were able to produce pyelitis in about two-thirds of the animals injected, both by intravenous and bladder injection.

Histologically, Helmholz (41) pointed out certain differences distinguishing the experimental ascending pyelitis from the hematogenous form. The latter was characterized by cortical and medullary abscesses, and subepithelial infiltration, especially of the papilla. The parietal portion of the pelvis was not inflamed. The ascending form, in many instances, showed peri-ureteral inflammation, marked purulent infiltration around the proximal end of the ureter with extension into the peripelvic fat.

In two recent articles (1929) Helmholz (42, 43) describes his experiments with rabbits and concludes that so far as his study is applicable to conditions in human beings, infections of the urinary tract in infants take place by the ascending route. Cole (1929) (44) also believes the ascending route to be the most common mode of infection since the colon bacillus is the most frequent organism found, travelling through the short female urethra, and by means of the lymphatics from the colon and rectum.

On the other hand, Robertson (45) believes that the evidence available points more to a focal suppurative nephritis as the cause of the symptoms. He states that direct spread of infection
by the urinary passages can take place against the direction of the urinary stream only if reverse peristalsis be present, which, in the obstruction, has never been demonstrated.

The peculiar nature of the circulation through the kidney makes it more liable than any other organ in the body to become the seat of focal infection through the general circulation. The arteries supplying the parenchyma are end arteries. No anastomosis takes place between one blood vessel and another. Also it has been found impossible to reverse the circulation through the kidney (45), so that occlusion of a blood vessel absolutely shuts off a portion of the kidney substance from circulation and provides an opportunity more favorable than can be obtained anywhere else for the growth of microorganisms. The renal artery, however, supplies the pelvis of the kidney as well as the parenchyma, but here the circulation is of a more usual nature; the arteries are not end arteries and anastomosis takes place between the various branches.

There seems to be as yet no evidence that there is a distinctive pathologic lesion for ascending pyelitis, as compared with the hematogenous form, but lesions in the pelvis when associated with cortical abscesses are likely to be of hematogenous origin.

The evidence thus far presented indicates that pyelitis may be caused either by the ascending or the hematogenous route. Knowledge in regard to which infections are limited to the bladder and which involve the entire urinary tract is so insufficient that it may not be decided which is the more likely mode of infection.
Little is known concerning the morbid anatomy of simple pyelitis (16). Often in long continued cases of so-called pyelitis, the pelvis of the kidney may appear entirely normal microscopically. At present these vary from almost complete destruction of the kidney to an organ which appears almost normal at necropsy. In cases of simple pyelitis, in which the patient dies from some other cause, the renal pelvis shows no demonstrable changes.

In a recent article, Wilson and Schloss (46) reviewed the post mortem examination of 49 children and infants whose urine contained pus during life, some as long as two years before death. In only two was there definite evidence of inflammation of the pelvic mucosa. In practically all there was definite evidence of suppurative interstitial nephritis. In those who had recovered from so-called pyelitis, there were scars found showing that there had been suppurative interstitial nephritis.

Jarrell (33) states that recent work on the pathologic anatomy, as found at necropsy, discloses the fact that changes are found in the pelvis and also in the parenchyma in practically all cases, but does not describe these changes. Unless the post mortem examination is made almost immediately after death, the urine destroys, to a considerable extent, the lining mucous membrane. In the more severe cases there may be a thickening of the mucosa and numerous hemorrhages.

The kidneys of patients dying from urinary infection by way of the blood stream may show very marked changes. The lesions are generally due to a damming back of the urine and infection, with infection of the urinary substance (24). The pathologic
picture varies with the chronicity of the obstruction and the time
infection took place. Inflammation of the pelvis superimposed on
hydronephrosis will disclose a markedly dilated pelvis with a
flattening out of the papillae, dilation of the calices, and a
marked involvement of the kidney substance. In the chronic cases
there may be miliary abscesses throughout the cortex and purulent
streaks radiating upward from the papillae. In more acute cases,
the process may manifest itself as a non-purulent pyelonephritis
with great swelling of the kidney, fatty degeneration, and
necrosis (42). Obstruction may be due to calculi, postureteral
strictures, congenital anomalies, or inflammatory in character.

Histologically simple pyelitis is characterized by
slight changes in the lining of the pelvis. Where the cases are
more chronic, there is usually a definite increase in the sub-
epithelial connective tissue, infiltration of the parenchyma with
lymphoid cells, and a tendency for a single layer of epithelium,
rather than the stratified epithelium of the normal pelvis. In
cystitis the evidence of infiltration of the mucous membrane is
usually marked, as is also the subepithelial collection of leuco-
cytes.

Many writers have noted the frequency of relapses in
pyelitis. Goppert (16) gives several instances even after years
of apparently normal health and negative findings in the urine.
Ross (62) claims that these cases are reinfections rather than
relapses. In almost all articles the frequency of relapses is
commented on. This is probably due, to a great extent, to the
fact that the clinical symptoms disappear much earlier than does
the inflammatory condition in the urinary tract, and a sudden rise in temperature in a patient who has been free from fever and other symptoms for some time is usually considered a relapse when, in reality, it is merely a return of symptoms (16).

Almost all pediatricians seem to consider absence of foreign elements in the urine satisfactory evidence of a cure. Before pronouncing recovery in cases of pyelitis it is necessary that at least two sterile cultures be taken at intervals of several days.

When acute pyelitis becomes chronic, it is usually because of (1) severe nutritional disturbance, (2) focal infection elsewhere, (3) inadequate treatment, or (4) urinary obstruction such as stones of the kidney, ureter or bladder, dilated ureters, duplication of ureters, neuromuscular dysfunction of the bladder, and stricture of the ureter or urethra (47).

The disease in the infant, whether severe or mild, is characterized by the absence of any signs localizing the condition in the urinary tract. Even in more severe cases, bladder symptoms are present in less than 3 per cent. The onset is usually acute, with fever. The child may show no other evidence of illness but in many instances an ashen pallor, an unexplained restlessness, and an anxious facial expression characterize the onset. Whether the colicky pains occasionally noted are of renal origin or are due to secondary gastro-intestinal disturbance is hard to determine. The fever may be so slight that, unless a thermometer is used, nothing abnormal is suspected.
Urinary findings alone are pathognomonic. So well established is the clinical entity of high fever, pallor and restlessness, without other findings in the routine physical examination, that the diagnosis of pyelitis is often made before the urine is examined. In severe cases there may be rigidity of the neck, and even convulsions, suggesting a slight degree of infection of the meninges (33).

One type of onset is in association with various infections of the upper respiratory tract, bronchitis, otitis, tonsillitis and adenitis. In such cases persistent temperature beyond the usual period may be due to a complicating pyelitis. There is nothing in the symptomatology diagnostic of the infection, and only the presence of fever not adequately explained by the physical data suggests the urinary infection. In the marantic infant even the fever may be absent.

In the older child symptoms pointing to involvement of the urinary tract may also be absent. Occasionally one patient may complain of low abdominal pain, burning on urination, or tenderness, but usually local signs are absent. In the greater number of cases, pyelitis manifests itself as it does in the younger child, by fever resembling typhoid. With gradually rising fever, and practically negative physical data, except for a possibly palpable spleen and a leucocyte count that may be normal, the picture is suggestive of typhoid and remains so until a negative Widal and a positive culture of the urine establish the diagnosis of pyelitis (48).

Whether the nature of the infecting organism, or portion of the urinary tract involved accounts for the difference in
clinical picture is difficult to determine, but with identical findings in the urine, one patient may be perfectly well except for a high fever, and another may have very marked systemic intoxication characterized by coma, nausea, vomiting, diarrhoea, and rigidity of the neck. This latter group is often mistaken for pneumonia, meningitis, or acute gastro-enteritis. Secondarily there is an involvement of the kidney substance, which can be demonstrated by enlargement of both kidneys.

Various types of fever may accompany pyelitis. As a rule, the temperature is 102, often reaching to 105 and 106 degrees. The fever is usually remittant. There are many variations, the mild form in which the temperature rarely goes over 100, and the septic form in which it varies from 98 to 106 degrees. In this type, at onset and during its course, chills may occur. In certain cases, the temperature is constantly high, much as in pneumonia, and ends with a crisis. The attack may be preceded by a chill, although this is not the rule (44). During the period of fever the child is fretful and uncomfortable but not prostrated. After the fever passes the child is usually weak, but bright, and shows no other signs of having been ill. It is at this point that one is prone to mistake the condition for indigestion or some trivial gastro-intestinal disturbance, and pass it off lightly. However, after two or three days of quiesence the temperature again rises, runs a high irregular course for a few days to again subside. There may be abdominal pains with frequency of urination, but as a rule these symptoms are absent.

A transient blocking of the ureter may cause a sudden rise of temperature when the urine is almost free from pus; with
relief from the obstruction there is a drop in temperature and a shower of pus in the urine. A similar decline in the temperature is occasionally seen in infants who have refused all fluid for a time, and are then given large amounts by stomach tube or intravenously.

Soldin and Langer (27), Langstein and others claim that all cases of pyelitis are secondary. The consensus of opinion, however, seems to be that there is definitely a group of primary as well as secondary cases. The primary group is typified by the well-developed breast-fed infant who is suddenly taken ill with an infection of the urinary tract. The cases in the secondary group follow infections of the upper respiratory tract, and the disturbances of the gastro-intestinal tract. The first group is often overlooked, because the secondary gastro-intestinal symptoms are held accountable for the febrile attack. The secondary group is even more often overlooked because the urine is normal when examined at the onset of the acute illness, and is not reexamined when the complicating pyelitis sets in.

In the newborn infant, pyelitis is more common than is supposed and has been little mentioned in textbooks. It is overlooked at this time, as in later years, because urinalysis has not been performed. An unexplained fever occurring in the first two weeks of life may be due to a pyelitis.

Helmholz (49) reports four cases, three of which were boys. The boys were infected by the colon bacillus, the girl by the staphylococcus aureus, later by the colon bacillus which finally replaced the staphylococcus entirely. Three patients had no
definite symptoms, and the fourth had symptoms entirely referable to the gastro-intestinal tract. The clinical picture was that of an unexplained fever in an apparently normal newborn infant. In two instances the fever gradually increased to 104 degrees. The diagnoses were made by examination of the urine. The infection in the boys cleared up rapidly, the urine becoming sterile in three weeks. The infection in the girl persisted for more than three months. Kovalesky and Moro (14) reported a case of pyelitis due to colon bacillus in an infant aged eight days who died. Smith (12) reported a series of cases with favorable outcome.

The course of pyelitis in patients is usually favorable. The acute symptoms may be very severe and the temperature reach 106 degrees and remain elevated for days. It is very rare, however, that infants die from simple acute pyelitis, it usually being the complicating nephritis which causes death. This may occur either in the form of multiple abscesses of the parenchyma of the kidney, or as a generalized pyelonephrosis with a complete suppression of kidney activity. Renal complications are especially likely to occur if there is obstruction to the urinary flow.

The course of pyelitis is, to a degree, dependent on whether it is a primary infection, or secondary to some extra-urinary infection. As a rule the course of a secondary pyelitis is more favorable than that of a primary, especially in regard to their duration. There is a distinct tendency for the secondary pyelitis to moderate when the primary infection subsides.

At the onset, the symptoms are no indication of the probable course of the disease, nor is there any connection between
the lessening of the general symptoms and the evidences of infection in the urinary tract. The child may appear to be well and still there may be pus in the urine for days or weeks after the temperature has dropped to normal, as when the most severe symptoms are present. As a rule, the acute general symptoms - fever, restlessness, and lack of appetite - persist from 10 days to two weeks. In the severe cases an acute course may last from three to four weeks in spite of all therapeutic measures. Some cases continue for years. There may be pus in the urine constantly and absence of fever with occasional period of irregular fever. Some cases run an afebrile course for weeks and months and then have a return. In these recurrences there may be an extension of the involvement to the kidney substance. The question of recurrent pyelitis is stressed by many authors, but in no series has urine been found to be sterile on repeated examinations. Pyelitis of infancy persisting for more than the second or third year raises the suspicion that there is some anatomic condition interfering with the outflow of urine (16).

The involvement of the kidneys may come on with a relapse, usually associated with violent symptoms, such as hyperpyrexia, convulsions, and early death. Objectively, the only finding on physical examination is a swelling of the kidneys. In infants the infectious process may produce the gradual lessening of tolerance for food, and death from inanition may follow, in spite of the best hygienic conditions and feeding.

The relation of pyelitis in infancy and childhood to that of pregnancy is still disputed. From the lack of evidence of such disturbance in early life, it seems likely that the two
are not related.

As long as the process is limited to the pelvis of the kidney the outlook is good, but with the involvement of the kidney the prognosis becomes dependent on the extent of such involvement. The kidney may be affected primarily or secondarily. If it is acute, the child usually dies in a few days from diffuse pyelonephritis; if subacute, the kidney may be filled with multiple abscesses, which gradually destroy its function, and end finally in multiple sacs of pus, making it difficult to find normal kidney parenchyma. In this group of cases the phenolsulphophthalein excretion, and the blood urea findings help determine the probable outcome.

If pus in the urine is evidence of a general septic condition the prognosis is bad. Involvement of the kidney and malformation of the urinary tract which cannot be relieved surgically make the prognosis bad. The mortality is variable. Helmholz (16) states that in private practice only one patient with uncomplicated pyelitis died. Goppert (11) gives a mortality of 30 per cent.

The diagnosis of pyelitis in almost all instances is made by examining the urine. However, complete diagnosis of infections of the kidney should include: (1) the determining of the presence of an infection; (2) the identity of the infecting organism; (3) the source of the infection; (4) the severity and extent of the lesion; (5) the amount of damage done to the secreting parenchyma, and (6) whether any obstruction is present, and, if present, its nature (50).
With a test tube and adhesive plaster the urine may be easily obtained from the boys, and by using a wide adhesive strip, both front and back, from the girls also. The Spicer urinal is more convenient.

It is always wise never to make a diagnosis of pyelitis which is not based on the finding of bacteria and pus in a catheterized specimen of urine. Even after washing the infant carefully before applying the urinal it is at times difficult to know whether an infection exists. Many so-called cases of pyelitis in girls, complicating extra-urinary infections, are nothing more than the mild vaginitis which may occur with a febrile attack.

All urine in children, especially girls, contains pus in a centrifuged specimen. In health, in the uncentrifuged, in boys, there are not more than four to six cells in a low power field; in girls from six to eight. Unless there are fifteen or more cells to the field, one is not warranted in making a diagnosis. Numerous bacteria in a very fresh specimen is also considered diagnostic (46).

Campbell (1929) (51) decries the tendency to a diagnosis of chronic pyelitis upon the discovery of a chronic pyuria. He states that in nearly all these cases the urinary infection and pyuria are perpetuated by faulty drainage with resultant stasis. A thorough study of the renal disease in these patients shows that the renal pelvis is exempt from inflammation comparable to the clinical manifestations and that the true underlying lesion is a chronic suppurative lesion of the interstitial type. The obstruction in nearly 95 per cent of these patients is either
organic or neurogenic (neuromuscular).

Helmholz (52) reports fifteen cases of neuromuscular dysfunction of the bladder in children whose ages range from a few days to 14 years. Ten of the cases were of the cord-bladder type, four of the atonic type, and in one there was complete relaxation of the bladder sphincter. Diagnosis was made by cystoscope and roentgenogram.

Anomalies of the urinary tract are not uncommon, as shown by Bugbee and Wollenstein's (53) series of 4903 autopsies in infants, 101 of whom were under one year of age. These authors found ten horseshoe kidneys, fifteen rudimentary kidneys, five cases of redundancy of kidney substance, three fused kidneys, one single kidney, and one case of double ureters. These conditions have an important bearing on the diagnosis and treatment of superimposed infections and other accompanying pathology.

When evidence of infection persists longer than four to six weeks in spite of intensive medical therapy, complete urological examination is indicated (51).

The most important feature in treatment is the washing out of the urinary passages (54). The process of flushing is limited by the amount of fluid the child can take. Occasionally infants will refuse to take fluid, or many be so toxic they cannot take it. Then a stomach tube, or better, a nasal tube, may be used. The food intake should be limited considerably in order to utilize the appetite in an effort to increase the fluid intake. An attempt should be made to give an infant at least a
quart of fluid each 24 hours in addition to its food, and as much more as possible. Infants usually prefer water, either plain or sweetened slightly with saccharine, with lemon juice added (46).

When because of vomiting it is impossible to force fluids by mouth, they may be given by rectum. If given this way, they are best administered by the interrupted rather than the continuous method or the Murphy drip. Most infants will absorb from 60-100 c.c. given high in the sigmoid at intervals of from three to four hours. The buttocks should be held together from 5 to 10 minutes after the administration. In this way 450 to 750 c.c. of fluid can be given during the 24 hours. The best solution is 7 per cent glucose to aid in maintaining the nutrition, although physiological salt solution may be given. If alkalies are used, soda bicarbonate may be given this way. When it is impossible to give fluids orally or rectally, the intra-peritoneal route is to be used. Large amounts of fluid - 100 to 400 c.c., depending upon the size of the child - may be given at each injection. Administration is continued until the abdominal wall becomes definitely tense. Absorption is very rapid, and injection may be repeated at intervals of from 6 to 8 hours. If, because of marked distension, it is considered dangerous to give the intra-peritoneal injection, physiological salt solution or 7 per cent glucose may be given subcutaneously or intravenously.

Besides the use of water there are three plans of medicinal treatment: (1) alkaline treatment, (2) the acid-urotropin treatment, (3) the hexylresorcin treatment. The alkaline treatment has given the best results in the acute cases. These are ad-
ministered in the form of sodium citrate and sodium bicarbonate until the urine becomes definitely alkaline. In certain severe cases large doses may be required to obtain this result. As a routine procedure, equal parts of sodium bicarbonate and citrate may be given in 10 grain doses six times in 24 hours to infants under six months of age. This dose may be doubled each day until the urine becomes definitely alkaline. For infants over six months 15 grains are used in the same manner. Usually when alkalinization of the urine is accomplished the temperature drops to normal, although this is not always true. Although the temperature returns to normal, the urinary findings remain practically the same, for it is not possible to alkalinize the urine sufficiently to inhibit the growth of the colon bacillus. The most alkaline urine obtainable has a hydrogen-ion concentration of 8.6 but the colon bacillus does not stop growth until 9.4 is reached. It is likely that the beneficial effect of the alkali, besides its diuretic effect, is by a direct action on the tissues rather than on the bacteria (16). The alkali treatment definitely hastens symptomatic improvement, the temperature drops to normal, and the child's general condition appears improved. The urine alone remains unchanged. It may be difficult, with alkalies alone, to overcome the infection.

Helmholz (1929) (43) reports a series of experiments in which colon bacilli were grown for a number of generations in acid and alkaline broth, finding that in no instance was there any retardation of growth when the organism was transferred from an acid broth of a hydrogen-ion concentration of pH 5.5 to an alkaline broth of a pH 8.4, but that there was almost complete inhibition
of growth for from four to six hours when the transfer was made from alkaline to acid. Moore (55) favors the use of alkalies, followed in four days by urotropin and sodium benzoate, then reverting again to the alkali. He claims better results by this method and declares that the danger of producing an alkalosis is lessened.

Next to the alkalies, the urinary antiseptics are of the most value in the treatment. Of these, urotropin and salol are most commonly used. Urotropin seems to give the best results in chronic cases. Some individuals have an idiosyncracy to it, small doses producing hematuria and vomiting. Its action depends on the liberation of formaldehyde, this occurring in an acid urine. The colon group is particularly susceptible to its action (56). The dosage depends upon the physician, varying from 40 to 90 grains per day (46).

Hexylresorcinal as a urinary antiseptic was first tried by Leonard in 1925 (57). He showed that its bacteriocidal action was equally effective in acid or alkaline urine and that forcing of fluids was a detriment to its action through the reduction of its surface tension. For administration to children it is put up in a 2\(\frac{1}{2}\) per cent. solution in olive oil, making a strength of 1\(\frac{1}{2}\) grains to the dram. The duration of this treatment is from 60 to 150 days, graduating the dosage according to the progress shown by symptoms and urinary findings, being from one to three teaspoonsful three to four times a day. The slowness of the drug's action seems to contraindicate its use in the acute stage, as the acute symptoms may be relieved readily by other methods mentioned. Helmholz (58), in a series of fourteen
cases, carried on treatment with hexylresorcinol for a period of from one to six weeks and was successful in only one case. However, he did not restrict fluids, as was suggested by Leonard, and never carried treatment for longer than 49 days. The use of this drug bears much further investigation.

Local treatments have been used with good results, but catheterization of an infant's ureter is difficult and must be done under general anesthetic. It has been recommended also in acute cases with apparent blocking of the ureter, as evidenced by sudden cessation of pus in the urine. Irrigation of the bladder with silver nitrate, or boric acid solution has not produced a cure with most men, although Hirst (59), and Paulson (60), recently have again advocated its use.

In most instances pyelitis has been uninfluenced by the use of vaccines made from cultures of the patient's urine. Recently Cowie (61) has reported good results with the use of foreign proteins.

The group of cases in which the condition cannot be cleared up by treatment must be carefully studied. The following examinations should be made: blood urea, return of phenolsulphonephthalein, roentgenogram of the kidney ureters and bladder, cystogram, cystoscopic examination and pyelogram. Uroselectin may be given intravenously to aid diagnosis by pyelogram (63). In this way it may be possible to discover the true nature of the urinary anomaly. Close cooperation of pediatrician and urologist will undoubtedly save much valuable time in the treatment of these
cases and prevent much injury to the kidneys (48).

In infancy particularly the general nutritional condition of the patient must be carefully watched and when one considers the large amounts of fluid that must be administered it is easily seen that food may be difficult to give in proper amounts. As soon as the nausea and vomiting have disappeared, small amounts of milk should be given if possible. If this is not available albumin or lactic acid milk, beginning with about a third the required amount of food and increasing up to about two-thirds, may be tried. Milk, diluted alkaline water, some cereal and fruit juice may be given. Older children may have bread and butter, cereals, stewed fruits, cooked vegetables, and pudding. Goppert and Langstein, in addition to the above mentioned foods, give meat and eggs in the afebrile cases. High fever should be combated by tepid packs, or by the administration of 0.25 grains of pyramidon (48).

The child should remain in bed until the fever has entirely subsided, and, in severe cases, seven to ten days longer. Local pain and tenderness should be treated by hot applications and opiates.
CONCLUSIONS

1. Pyelitis comprises about 1 per cent. of all cases seen by pediatricians.
2. It is a disease of the diaper age.
3. Over 57 per cent. of cases are girls.
4. The colon bacillus is the usual causative organism.
5. Hematogenous and ascending routes of infection most common. Not definitely determined which is the more common.
6. Simple pyelitis is rarely fatal, death occurring from the complicating nephritis.
7. Must be 15 or more pus cells to the low powered field in an uncentrifuged specimen for diagnosis.
8. Radiographic examination necessary when ordinary treatment does not cause a cure.
9. Treatment consists in flushing the urinary passages with water; alkalinization of the urine; the acid-urotropin treatment; removal of anatomical defects or obstructions; rest in bed and care of the general nutrition.
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