

A STUDY OF URINARY INFECTION IN CHILDHOOD,

WITH REFERENCE TO ITS INCIDENCE AS

▲ COMPLICATION OF OTHER DISEASES

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INTRODUCTION

In the routine examination of the urine of children under treatment in hospital for a variety of conditions, pyuria was found so frequently that it was decided to make a study of a large group of these patients in order to ascertain :-

- (a) The incidence of infection of the urinary tract
- (b) Its nature
- (c) The factors which precipitate it
- (d) Its duration and influence on prognosis
- (e) The prophylaxis and treatment.

Until recently, lesions of the kidney in children, associated with the passage of pus and organisms in the urine had been considered to be due to inflammation of the pelvis of the kidney. The observations of Chown (1927) and Wilson and Schloss (1929) have shewn that the lesion most commonly present is a bilateral suppurative interstitial nephritis. The term "Pyelonephritis" will therefore be used here in preference to the term "Pyelitis".

HISTORY

Infection of the urinary tract has long been known as a disease of adults, but the condition as it occurs in children was barely recognised until the end of the nineteenth century. At this time diseases of children were becoming the object of special study, and the growth of bacteriology at the same time supplied the medical man with a new weapon for their further investigation.

Von Hüttenbrenner's account of urinary infection in infancy in 1876, aroused practically no interest, many physicians denying the existence of such a condition, and for nearly a quarter of a century no further cases were reported.

Osler in 1891 recorded a case in a four year old boy, associated with phimosis, which was eventually, after some months, treated by circumcision, no specific treatment being known at this time. Two years later Monti, who had formerly failed to recognise the disease in children, wrote a paper on "Pyelitis in Childhood", referring to it as a complication of "alimentary catarrh" and of infection by "such parasites as entinococcus, strongylus and gigas,

which often afflict the pelvis of the kidney and cause pyelitis".

The following year Escherich's paper on "Colicystitis in Infants" stressed the relationship between gastrointestinal and urinary disorders. In the same year Holt reported three typical cases and was the first to employ alkaline therapy. One is not surprised to read that the cases, which occurred in a malarial district, were first treated by large doses of quinine, which had no effect in controlling the pyrexia.

In 1896 Finklestein published the results of eight autopsies performed upon children who had died from urinary infections. Trumpp, the next year, made a study of "Colycystitis in Children" showing that bacilluria frequently occurred in gastroenteritis. Four further cases of "pyelitis" were described by Baginsky in the same year.

In 1902 Thomson read a paper before the Obstetrical Society of Edinburgh, giving an account of eight cases of "pyelitis" which he had treated in baby girls. He was the first to draw attention to the significance of a rigor in the diagnosis of this condition, and made the statement that he had not been able "to find an account of any case in which this symptom occurred in a child under two years,

who had not malaria, without there being pus in the urine". A further case was described at the same meeting by Ritchie.

A fatal case of anaemia, secondary to chronic pyelonephritis in a child of a year old was reported in 1907 by Carpenter, who performed the post-mortem examination. In the same year Abt's paper on "Cystopyelitis" was published and Knox described a case secondary to ileocolitis.

Until this time the condition had been regarded as sufficiently rare to warrant the publication of any case which was diagnosed, but in 1908 Goeppart gave an account of ninety-seven cases, some of which had occurred as early as the neonatal period.

Morse in 1909 studied the possible routes of infection and decided that the organisms sometimes reached the kidneys through the blood stream and sometimes through the urethra. His was the first series of cases which included a large number of boys, it having previously been considered that the condition was practically limited to small girls. He was also the first to employ an autogenous vaccine in treatment.

Two years later a great advance was made by Beer (1911) who showed that it was possible to perform cystoscopy and ureteral catheterisation upon young children. This

procedure had been considered impossible before, and even catheterisation of the bladder of infants had been severely criticised. Kretschmer, and Lowsley and Butterfield reported further cases in 1916 which had been investigated by these means. Examination of the urinary tract of young children by intravenous pyelography was described by Kretschmer in 1927. These methods of investigation are now routine in cases which prove resistant to treatment, and since their advent many of the chronic cases, previously considered incurable, have been cured or greatly improved.

Neale in 1931 reported a series of over a hundred cases of urinary infection in children and concluded that the condition occurred more frequently than had hitherto been supposed, but that the child ~~case~~ was rarely admitted to hospital and often got better without treatment. He advocated nephrectomy in unilateral chronic cases.

Since 1931 two new methods of treatment have been successfully employed. Helmholtz and Clark (1931) introduced the ketogenic diet, as a result of their observations upon epileptic children. Mandelic acid therapy was substituted for this in 1935 by Rosenheim, at first being used only in adults suffering from pyuria, but later being found to give equally good results in children.

As a result of the increased knowledge on the subject, and the better facilities now available for diagnosis, cases of pyelonephritis in children are more readily recognised. Treatment is consequently begun earlier than formerly and is more likely to be successful in the acute case, while the prognosis is improved in the chronic and recurrent cases. A further study of the condition is however still necessary.

CRITERIA OF INFECTION

The number of pus cells present in the urine during infection of the urinary tract shows considerable variation. Thomson (1910) who has made an extensive study of the condition states that in "pyelitis" of children one or more pus cells per high power field of the microscope, in an uncentrifuged urine, is sufficient evidence of infection upon which to make a diagnosis. Griffiths and Mitchell (1927) however consider that a healthy boy may excrete as many as six leucocytes per high power field, and a girl double this number. Parsons and Barling (1933) are of the opinion that more than six white cells per high power field is abnormal. Still (1927) has noted that the urine of a child suffering

from "pyelitis" contains on an average six to thirty pus cells per high power field.

From the above statements it is seen that considerable diversity of opinion exists as to the number of leucocytes present in the urine of children in health and disease. A group of 310 children was therefore studied, among whom 43 were admitted to hospital with pyuria, or developed it while in hospital, in order to determine the variation of the urinary constituents, in the presence and absence of urinary infection.

Technique

On admission of the children to hospital, and at weekly intervals, a specimen of urine was obtained for examination. In boys the glans penis was cleaned with 2% dettol, followed by normal saline and the urine collected in a sterile receiver. In the case of very young infants a sterile test tube was strapped to the penis, after cleansing in the usual manner. The specimen was obtained from girls by swabbing the external genitalia in the same way, but if pus cells were found on examination of the urine a catheter specimen was taken to confirm their presence and for cultural purposes.

The usual laboratory tests were employed to determine the reaction of the urine and the presence of abnormal constituents. The sulphosalicylic acid method was used when testing for the presence of albumen, partly because it was considered a more accurate method than boiling, and partly because the amount of urine obtained from young children was often very small. The specimen was well shaken, so as to mix the contents thoroughly and was examined microscopically for pus cells, which if present were counted per high power field, at least twelve fields being counted and the average taken. The centrifuged deposit was then examined under the microscope, the presence of pus and epithelial cells, red blood corpuscles, casts, organisms and crystals being noted. Where definite urinary infection was present a stained film was examined for tubercle bacilli by Ziehl-Neelsen's method, and in cases which were resistant to treatment, a culture was made to exclude the presence of this organism. Finally a MacConkey plate was inoculated and if there was a question of organisms other than coliform bacilli being present a culture was also made on a blood agar plate. The plates were incubated, and inspected twenty-four and forty-eight hours after inoculation. Cultures were

not repeated in subsequent examinations unless there was some indication for doing so.

The urine of every child admitted to hospital over a period of six months was examined by the methods described, 1100 specimens being investigated. An examination of 900 specimens from children free from urinary infection was made, and the following facts were noted :-

- (a) Reaction - this was usually found to be acid, the pH. ranging between 5.4 and 6.0.
- (b) Deposit - The "brick-dust" deposit of urates was usually present in febrile conditions. White urates were less common and phosphates were rarely seen.
- (c) Albumen. - A trace of albumen was frequently present during fever, especially in pneumonia. In severe gastro-enteritis a larger amount of albumen was usually found.
- (d) Acetone bodies. - These were found during a febrile illness, after anaesthetics and during gastrointestinal upsets.

Microscopical examination of the shaken-up specimen and the centrifuged deposit was made with the following results :-

- (e) Leucocytes. - In urine collected under ideal conditions leucocytes were scanty. Among the boys examined the

count was almost invariably less than one cell per high power field, ten to twenty fields being counted, and in many cases cells were entirely absent. In specimens from girls a few cells were usually found, a count of one or two per high power field being a normal finding in non-catheter specimens. Where urine was obtained by catheterisation the same low count as for boys was found to occur.

- (f) Red blood corpuscles. - A few red blood corpuscles were commonly found upon microscopical examination during a febrile illness. They were abundant in the specimens from three cases of acute focal nephritis. Apart from these conditions they were rarely observed.
- (g) Epithelial cells. - A few epithelial cells from various parts of the urinary tract were usually seen if a large enough number of fields were inspected.
- (h) Casts. - In specimens from children with a severe illness, especially in pneumonia and enteritis a few granular tube casts could usually be found, but were never present in large numbers.
- (i) Crystals. - On microscopical examination of the centrifuged deposit crystals of calcium oxalate were found

with great frequency, especially in children who were recovering from their illness. As already stated urates were frequently present during fever. The presence of phosphates was not often noted.

- (j) Organisms. - Urine collected under aseptic conditions was usually sterile, though a scanty growth of staphylococcus albus was a common finding in phimosis, and of coliform bacilli in urine of girls where a catheter specimen was not employed. A heavy growth of B.Coli was obtained in several cases of gastroenteritis.

Two hundred specimens of urine from children who were suffering from urinary infection due to B.Coli were examined, the findings being as follows :-

- (a) Reaction. - A strongly acid reaction was always noted in untreated cases, which became more acid on standing.
- (b) Appearance. - The specimen obtained was often opalescent or turbid, but in some cases was quite normal in appearance.
- (c) Odour. - A characteristic fishy odour was sometimes noted, which was not observed in any other condition.
- (d) Deposit. - A deposit of pus was occasionally present after standing, but in many cases the amount of pus was too small to be observed without the aid of the micro-

scope. Urates and pus cells were never found in the same specimens. A deposit of mucus was frequently seen.

- (e) Albumen. - A trace of albumen was a frequent finding, but was by no means an invariable one. Albuminuria was more marked in some of the severer cases particularly those following gastroenteritis.
- (f) Blood. - In two specimens blood was found to be present by laboratory tests. On microscopical examination a few red blood corpuscles could usually be found in acute cases. In three acute cases a large number were present.
- (g) Leucocytes. - Pus cells were always found at some stage of the illness, but varied in number and in their time of appearance. Early in the disease they were often scanty or absent and appeared in large numbers as the temperature fell. (Chart II.). The number of cells varied from one to two, to a hundred or more per high power field, the average number in sixteen acute cases being twenty-two. Clumping together of ten or more cells was sometimes a characteristic feature.
- (h) Epithelial cells. - A number of epithelial cells from various parts of the urinary tract were usually noted,

which appeared to increase in number as the condition improved. A large amount of epithelial débris was a common finding after the acute stage of the illness was over.

- (i) Casts. - A few granular tube casts were found in the severer cases, but were never numerous and were absent in the majority of cases.
- (j) Organisms. - Coliform bacilli in large numbers could almost always be seen microscopically before cultures had been made.
- (k) Crystals. - Pus cells were sometimes seen, together with calcium oxalate crystals, and occasionally with phosphates or uric acid.

These observations have led me to believe that :-

1. The urine of children who are not suffering from infection of the urinary tract does not contain more than two leucocytes per high power field, if collected under aseptic conditions, the count being the same for the two sexes.
2. The finding of as few as two pus cells per high power field when associated with other symptoms of the disease and a growth of organisms on culture is consistent with a diagnosis of infection of some part of the urinary tract.

Bacteriology

The great majority of cases of pyelonephritis in children are due to infection of the kidney by the bacillus coli communis.

Among the forty three children under treatment for urinary infection this organism was present in forty-two cases. In the remaining one, a fatal case of ascending purulent pyelonephritis, following circumcision, a bacteriological examination was unfortunately not made, but it is probable that this isolated case was due to staphylococcal or streptococcal infection as the symptoms were of greater intensity and the lesions more widespread than in any of the cases where the infecting organism was the coliform bacillus. This case has been referred to in greater detail in a later section.

Observations by Kretschmer (1927) and White (1933) have shewn that tuberculosis of the kidney is more frequently the cause of chronic pyuria than had hitherto been supposed. Routine examination of the urine for tubercle bacilli, and its culture in resistant cases failed to reveal the presence of this organism in the urine of any of the children under observation.

In the cases of urinary infection occurring in the

neonatal period, bacillus coli is not found so constantly. Graham (1925) in a study of six cases found the infecting organism to be staphylococcus aureus, streptococcus and bacillus coli twice each. Craig (1935) found that bacillus coli was present in the majority of cases but in seven of these another organism was also present. In a series of six infants who were found to have infection of the urine during the first few days of life, staphylococcus aureus was isolated three times and bacillus coli in the remaining three cases.

With the exception of these neonatal cases the symptoms and urinary findings which are described in this paper refer only to cases of bacillus coli infection of the urine.

INCIDENCE OF URINARY INFECTION

A study was made of 310 children, admitted to hospital with a variety of conditions, in order to ascertain :-

1. The absolute incidence of urinary infection among them.
2. Its occurrence in the various age groups.
3. Its distribution between the sexes.
4. Its incidence as a complication of other diseases.

The term "primary infection" is used to define those cases in which the symptoms developed spontaneously in children who were apparently in good health before their onset. The term "secondary infection" indicates that the condition developed during the course of another disease.

Of the 310 children under observation, 150 were boys and 160 girls, the ages varying from four days to fourteen years.

TABLE I.

Incidence of urinary infection in 310 cases

	Cases under Observation	Total No. of Cases of Urinary Infection.	Percent- age of admissions to hospital	PRIMARY CASES	Percent- age of admis- sions.	SECONDARY CASES	Percent- age of admis- sions.
Total	310	43	13.8	20	6.4	23	7.4
Boys	150	8	2.5	2	0.65	6	1.9
Girls	160	35	11.3	18	5.8	17	5.4

In Table I are set out the figures showing the incidence of infection of the urinary tract in 310 children, admitted to hospital over a period of six months. Among a

total of 43 cases of urinary infection (13.8% of all admissions), 20 (6.4%) were primary, and 23 (7.4%) were secondary to another condition. 6.4% is a high figure as compared with the findings of others, but may be accounted for by the fact that the hospital in question is able to accommodate a number of children who would not be considered ill enough for admission to the average hospital, and who would normally be treated in the out-patient department, where a mild infection might be overlooked.

Of the 43 cases of urinary infection under treatment 8 (2.5% of all admissions) were boys and 35 (11.3%) were girls. A study of Table I shows that of the 20 primary cases 2 (0.65%) were boys and 18 (5.8%) were girls. Among the 23 secondary cases there were 6 (1.9%) in boys and 17 (5.4%) in girls. These figures are indicated in Table ~~1~~.

Table 2

Incidence of urinary infection among boys
and girls of the series.

	Cases of urinary infection	Percentage for Sexes	PRIMARY Cases	Percentage for Sexes	SECONDARY Cases	Percentage for Sexes
Total	43		20		23	
Boys	8	18.6	2	10	6	26
Girls	35	81.4	18	90	17	74

It will be seen from a study of the figures in Table 2 that urinary infection was more than four times as frequent in the girls than the boys of the series. A greater preponderance among the girls is found in the primary group, the cases occurring in a proportion of nine to one. In the secondary group, although the girls are still in the majority the difference is less marked, the proportion being three to one.

Table 3
Incidence of urinary infection at different
ages

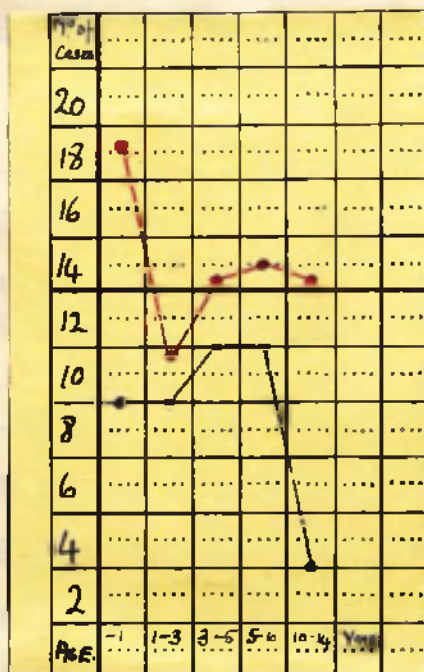
AGE GROUP (Years)	Total Cases for each Group under observation	Urinary Infection Total No.	Percent-age for Group	PRIMARY CASES	Percent-age for Group	SECONDARY CASES	Percent-age for Group
Under 1	49	9	18.3	3	6.1	6	16.8 12.2
1 - 3	82	9	10.8	3	3.6	6	16.8 7.2
3 - 5	79	11	13.9	5	6.3	6	16.8 7.5
5 - 10	78	11	14.0	8	10.2	3	14.0 3.8
10 - 14	22	3	13.5	1	4.5	2	16.8 9.0
Total	310	43		20		23	

Table 3 shows the incidence of infection of the urinary tract at different ages, the cases being divided into five groups according to the age of the child. A study of these figures shows that the largest number of actual cases occurred between the ages of three and ten years. When the number of children under observation in each group is taken into consideration however, the incidence of infection is found to be highest in the group of children below one year, being 18.3%, and lowest in the 1-3 year group, being 10.8%.

The incidence of primary infections is highest in the 5-10 year group, being 6.1%, and lowest in the 1-3 year group, being 3.6%.

The high incidence of cases in the group of children under one year is due to the number of secondary cases, of which six (12.2%) occurred. In Table 4 are tabulated the actual number of cases in each group, and the absolute incidence, expressed as a percentage of the total number of children in each group.

Table 4



_____ Actual number of cases in each age group.

_____ Percentage of cases in each group

In Table 5 are set out the diseases to which pyuria was secondary and the number of cases of urinary infection which occurred in each condition. A study of these figures shows that the largest number of cases of secondary infection followed gastrointestinal disorders, a third of the total number of cases occurring in this condition. This will be discussed in detail in a later section.

Table 5Incidence of urinary infection in various diseases

DISEASE	Number of Cases	Percentage
Gastrointestinal disorders	8	34.7
Diseases of the Ear, Nose and Throat	4	17.4
Skin diseases	4	17.4
Rheumatic conditions	3	13.0
Local conditions	3	13.0
General Debility	1	4.3

Route of Infection

The work of former observers has suggested that there are four possible routes through which infection of the urinary tract may occur. These are as follows :-

1. Ascending through the lymphatics.
(Ascending lymphatic)
2. Through the blood stream. (Haematogenous)
3. From the intestine. (Transparietal)
4. Ascending through the urinary passages.
(Ascending direct)

Previous Work

Experiments by Blandini (1909) and Walker (1922) suggest that the infection may reach the kidneys from the urethra or external genitals by the lymphatics. They have shewn that free intercommunication exists between the lymphatics of the posterior urethra, bladder and lymphatic plexus in the peri-urethral sheath. They have further shewn that the lymphatics of the upper end of the ureter communicate with those of the subcapsular plexus of the kidney, which in its turn is connected with the lymphatics in the kidney substance. Blandini's experiments shewed that *B. Prodigiosus*, placed in the posterior urethra of a guinea pig could be recovered from the upper end of the ureter and kidney substance in twelve hours. Walker confirmed this, and by using certain dyes was able to show that these were carried to the upper end of the ureter by the periuteteral lymphatics. He was also able to demonstrate the close connection which exists between the lymphatics of the genital organs and those of the urinary tract.

In support of the haematogenous route of infection are the findings of Escherich (1894) and Finklestein (1896) who found organisms in the blood stream of children suffering from gastroenteritis, and in their organs after death.

Kovalesky and Moro (1901) reported two fatal cases of *B. Coli* septicaemia in infants, accompanied by pus in the urine. Lepper (1921) shewed that organisms injected into the blood stream would infect a kidney already damaged by stasis. Chown (1927) and Wilson and Schloss (1929) have found that in fatal cases the lesion present is a suppurative pyelonephritis. Helmholtz (1929) shewed that although infection of the kidney was difficult to produce experimentally by injection of organisms into the blood stream, when it did occur the resulting lesion was a pyelonephritis, whereas if infection occurred from the bladder a pyelitis was found. These findings therefore support the haematogenous route in children since a pyelitis is rarely if ever discovered.

The evidence in support of the transparietal route is less convincing. Wreden (1893) stated that injury to the mucous membrane of the colon in a rabbit resulted in a cystitis. Réymond (1893) shewed that in adults salpingitis and metritis was often followed by cystitis, and that the area of the bladder which was first infected corresponded to the part which was in contact with the inflamed organs. Knox (1907) reported a fatal case of pyuria complicating chronic ileo-colitis in an infant, in which at autopsy a

piece of inflamed and thickened colon was found in close contact with one kidney. Walker (1922) has shown that free communication exists between the lymphatics of the colon and those of the urinary organs. Burnett (1927) advanced the theory that the preponderance of right-sided cases of pyelonephritis was due to the fact that a free lymphatic connection exists between the ascending colon and right kidney, whereas on the left side these are few or undeveloped. Posner and Lewis (1894) however stated that they had never been able to find organisms in the tissues between the colon and urinary organs.

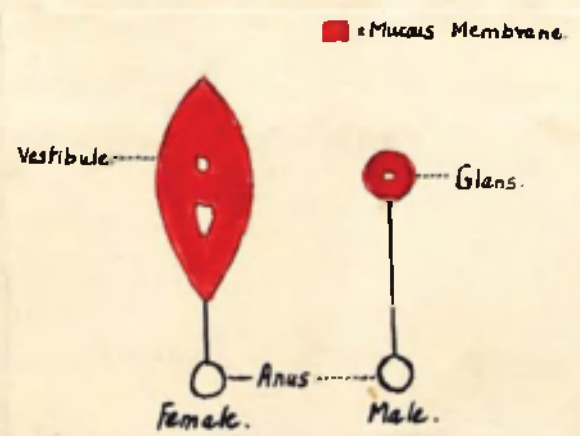
There is little to support the theory that infection takes place by a spread of organisms along the urinary passages from below. The preponderance of cases occurring in girls has been explained in this way, organisms being supposed to gain access to the bladder through the short wide urethra of the girl. Trümpp (1897) and Schwartz (1918) have shown that the urine of children suffering from gastro-enteritis frequently contains coliform bacilli, the contamination being more frequent in girls. Caccia (1907) proved that organisms injected into the bladder of puppies did not produce infection of the urinary tract unless the

bladder was damaged or there was obstruction to urinary outflow. Bauereisen (1910) and Draper and Braasch (1913) stated that organisms could only ascend to the kidneys along the lumen of the ureter under conditions of urinary stasis or incompetence of the uretero-vesical valve.

Discussion

My own opinion is that in a large number of cases infection spreads upwards along the lymphatics. This would help to explain the number of cases following enteritis and the preponderance in girls. Schwartz (1918) found that organisms frequently entered the urethra during diarrhoea, especially in girls. Walker (1922) proved that certain organisms and dyes were carried from the posterior urethra along the lymphatic channels to the kidney. It seems reasonable to suppose that coliform bacilli may be conveyed to the kidneys in the same way. This does not however explain the high incidence of primary cases among girls. If the area of mucous membrane covering the external genitals and its distance from the anus is compared in the two sexes it will be seen that in girls there is a relatively large area of mucous membrane covering the labia and vestibule which is in close proximity to the anus, while in boys there

is only a small area of mucosa covering the glans penis, which is separated from the anus by the scrotum. (See diagram).



Comparison between the amount of mucous membrane covering the external genitals in the two sexes, and its proximity to the anus. (diagramatic)

Faecal contamination of the mucous membrane of the external genitals must therefore be more frequent in girls than boys, and it is possible that absorption of infected material may take place through the lymphatics from the relatively large mucus surface of the vulva. It is well recognised that urinary infection is a frequent sequel to gynaecological operations, particularly on the vagina and external genitals, and to infected tears of the perineum and vagina in the puerperium, and it would appear from the rapidity with which urinary symptoms occur that the spread of infection is through the lymphatics in these cases.

The same thing may presumably take place in small girls, particularly where excoriation of the external genitals is present.

This path of infection does not explain every case, and in boys and those cases occurring immediately after birth there is presumably some other route. It seems probable that infection through the blood stream occurs in a number of cases of both sexes. The sudden onset with rigors, the character of the pyrexia, the appearance of the child and in rare cases the finding of an enlarged spleen are suggestive of a blood borne infection. Blood cultures are not often positive but this does not exclude the possibility of a few organisms entering the blood stream and settling in the kidney. The fact that a bilateral suppurative pyelonephritis is the lesion most often found post-mortem is in favour of this route. It would appear that as a result of an attack of enteritis, constipation or active purgation the mucous membrane of the bowel becomes damaged and a few organisms enter the blood stream. If the child's health is good and no abnormality of the urinary tract exists these are destroyed or excreted without any damage resulting. If the resistance of the child is poor, urinary excretion obstructed by some

abnormality in the urinary tract, or dehydration is severe, a pyelonephritis may result. The following case suggests that infection was blood borne :-

A male infant, born spontaneously at term, developed pyrexia four days after birth. On examination he was found to be drowsy, jaundiced and to have lost considerable amount of weight. He vomited several times and refused his feeds. The urine was scanty and high coloured and was found to contain a few pus cells, and a heavy growth of staphylococcus aureus was obtained in repeated cultures. The infant improved with treatment, but the general condition was not satisfactory until a week after the onset of symptoms, when an axillary abscess appeared from which staphylococcus aureus was obtained in pure culture. From the time of opening the abscess the condition of the child improved. All symptoms rapidly subsided and he was discharged from hospital in good health seventeen days after the onset of the illness.

The transperietal route has its supporters, but its existence is difficult to prove. One would expect pyelonephritis to be a more frequent complication of appendicitis and intussusception, but my own observations have not led me to believe that this is the case, and even when peritonitis develops it is rare to find pus in the urine.

The direct ascent of infection through the urinary passages has little to recommend its existence and need not be considered further.

The Site of Infection

In fatal cases the usual finding is a bilateral suppurative pyelonephritis without involvement of the renal pelvis.

Cabot and Crabtree (1916) reported a fatal case in an infant of four months, in which the post-mortem finding was a true pyelitis, without involvement of the kidneys. I have been unable to find a record of any similar case.

Chown (1927) as a result of thirty autopsies upon children who had had pyuria during life states that the lesion present is a multiple focal suppurative interstitial nephritis without involvement of pelvis, ureters or bladder. Wilson and Schloss (1929) made the same statement as a result of 49 autopsies upon children. Craig (1935) found that the infection was limited to the kidney substance in five out of six fatal cases occurring in the neonatal period. In the sixth case some involvement of the renal pelvis was also present, but was apparently secondary to the kidney lesions.

It appears, therefore, that infection limited to the pelvis of the kidney is rare in children. It has been said

that cases of pyelitis always recover while those of pyelonephritis usually die. Wilson and Schloss (1929) were, however, able to demonstrate scarring of the kidneys in three cases, which died from another cause some time after they had recovered from pyuria. In none of these instances did they find any evidence of a healed lesion in the pelvis. They also record a case where a kidney was removed from a child during an acute infection and showed multiple abscesses in the interstitial tissue without involvement of the pelvis. The child recovered.

Among 43 cases which came under observation for pyuria there were: Seven fatal cases, a post-mortem examination being made in three of these. In the first case urinary infection had followed measles and gastroenteritis and was a terminal condition in a severely debilitated child. No changes were found in the kidneys. The second case, a male infant which had died at the age of fourteen days following a ritual circumcision was found to have extensive changes. The glans penis was gangrenous and the penile ^{veins} ~~was~~ thrombosed. The bladder, ureters and renal pelvis were acutely inflamed and multiple abscesses were scattered throughout the substance of the kidneys. Pyaemic abscesses were found in the shoulder joints. Microscopic examination confirmed the diagnosis of

ascending purulent pyelonephritis. I have been unable to find a record of any similar case in a young child. The third case, a female infant aged ten days, had had rapid loss of weight from birth with the development of typical symptoms two days before death. Pus cells and B.Coli were present in large numbers in the urine. At autopsy the kidneys were found to be congested and the seat of marked cloudy swelling. Microscopically small areas of leucocytic infiltration between some of the collecting tubules were found. The pelves, ureters and bladder were normal. This finding, is therefore, consistent with the findings of Chown, Wilson and Schloss, that the pathological lesion present is a bilateral suppurative interstitial nephritis, without involvement of the rest of the urinary tract.

THE FACTORS PRECIPITATING INFECTION

1. The pH. of the urine

In view of the rapid improvement in symptoms which takes place, in acute cases, on the administration of alkalis, it was decided to study the pH. of the urine in a series of children under observation in hospital.

The following technique was adopted. The reaction of the morning specimen of urine was estimated every third day,

the undermentioned indicators being used for the purpose :-

- (a) Bromo-Cresol Purple
- (b) Bromo-Cresol Green
- (c) Bromo-Thymol Blue
- (d) Bromo-Phenol Blue
- (e) Phenol-Red
- (f) Congo-Red

The results obtained were compared with a standard series of colours and by this method readings were available ranging from a pH. 3.0 to pH. 8.5. Comparisons with standard solutions showed that the method gave accurate results within a pH. of 0.2.

In 800 estimations of the urine of children who were free from urinary infection and were not under treatment with alkalines or acids the pH. of the urine was found to range between 5.4 and 6.0 with an average reading of 5.7, which did not vary with the age of the child.

A study was now made of a group of children to find whether any notable change in the pH. of the urine preceded the development of a urinary infection. Observations were carried out in 120 cases of which seven subsequently developed pyuria. The diseases under treatment will be noted later. No constant change was found in the reaction of the urine in any of these cases, either before or after the development of pyuria. (Chart I)

four hours. As the condition improved the desired reaction was more easily maintained and smaller amounts of alkali could be given. (Chart 3)

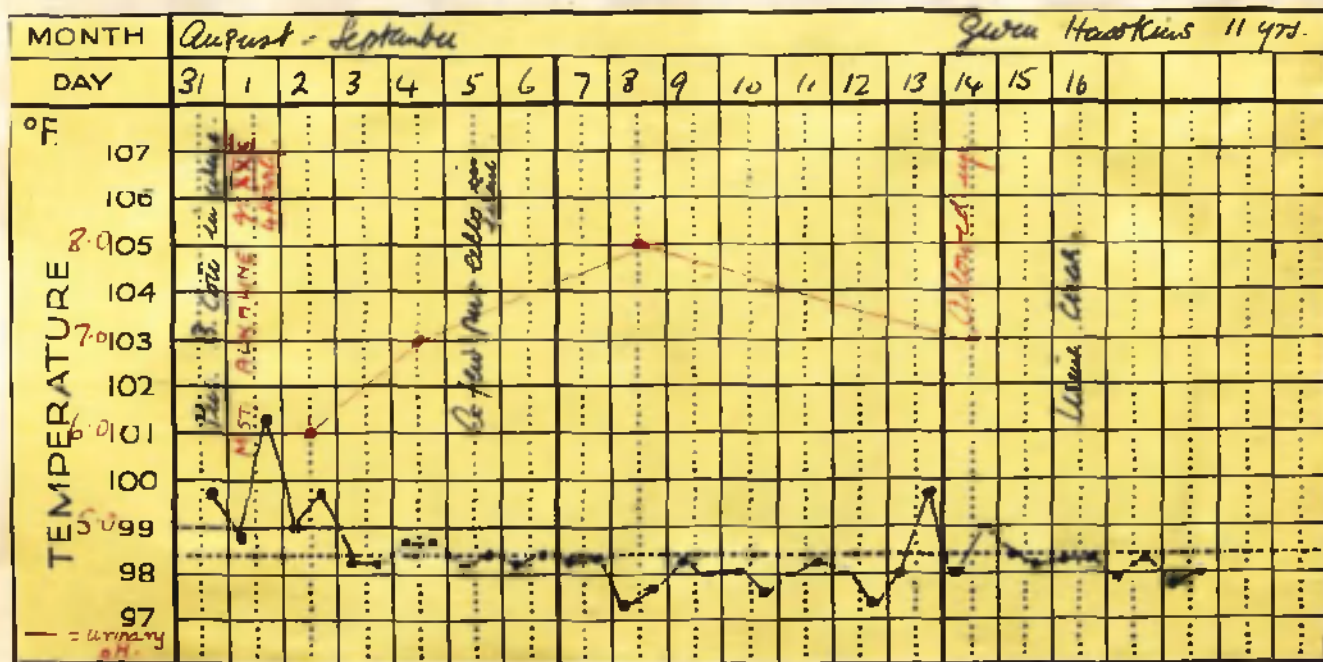


Chart 2. Showing ease with which the urine can be alkalinised in a mild case

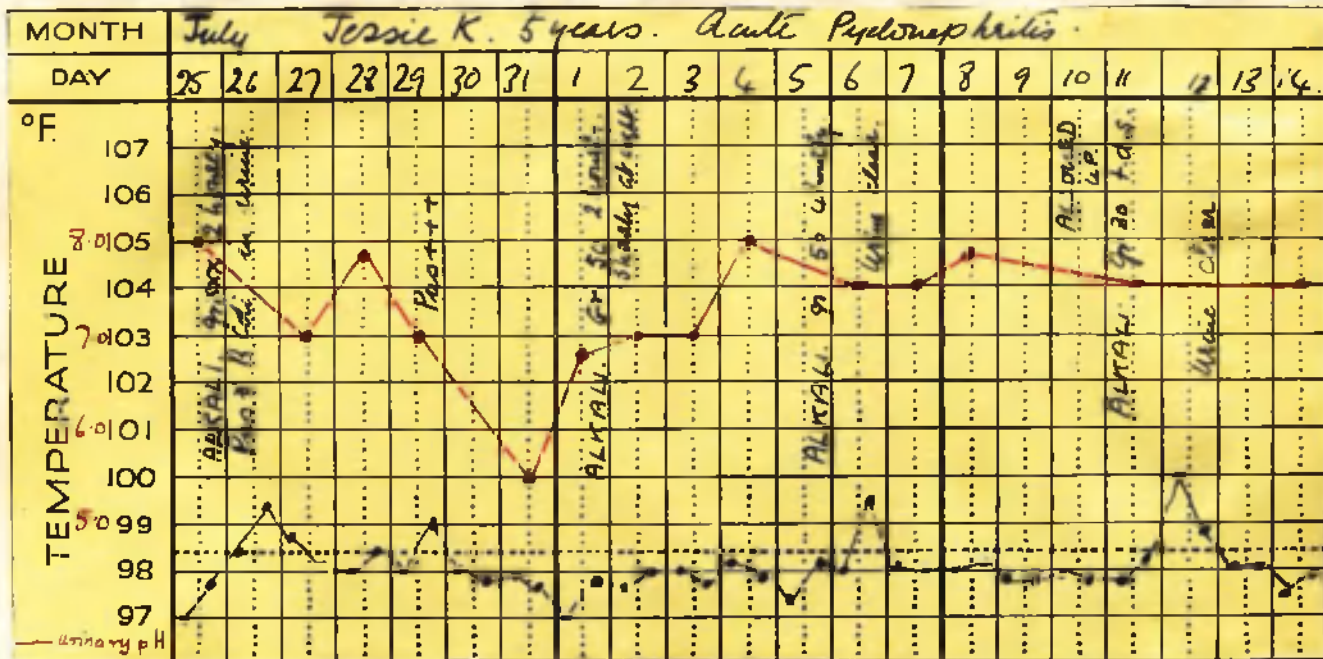


Chart 3. Showing difficulty in keeping urine alkaline in a more severe case, and later the ease with which the alkalinity can be maintained as the urine clears.

Observations upon children undergoing alkaline treatment for reasons other than urinary infection showed that a small dose was sufficient to keep the pH. of the urine at 7.5 or over and to maintain it at this level.

(Chart 4).

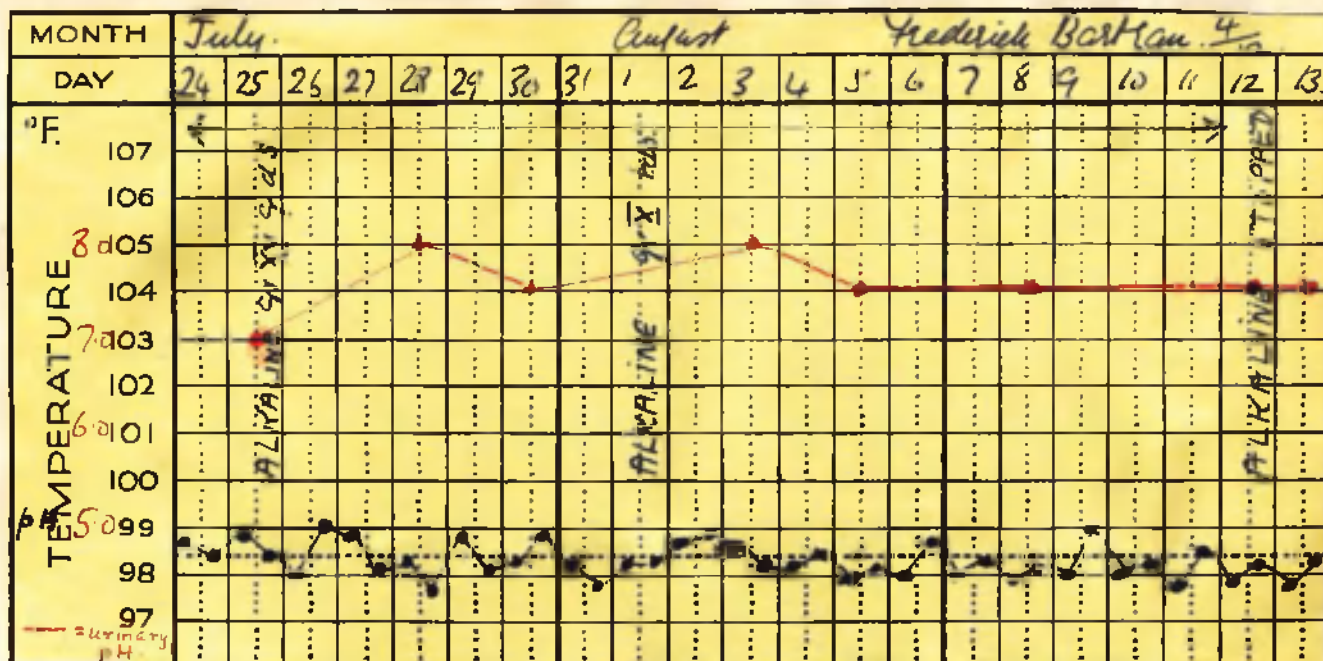


Chart 4. Effects of alkaline treatment in a child free from urinary infection

It was therefore found to be a useful method of differentiating between cases of mild pyelonephritis and those in which the pus was due to vaginitis or some similar condition, especially in cases where it was not considered desirable to take frequent catheter specimens of urine.

2. Duration of disease and confinement to bed

It seemed probable that the child which had a long illness would be liable to develop infection of the urinary tract, as a result of stasis, particularly if he were kept in a recumbent position for any length of time.

Among the children under observation the duration of confinement to bed varied from a few days to many months. The longest stay in hospital was that of a boy aged six years, suffering from rheumatic carditis, who was in bed for ten months, several of which were spent in a recumbent position. In spite of this fact, the urine, examined at frequent intervals, was never found to contain a single pus cell.

A girl aged thirteen years, admitted with sacroiliac arthritis was confined to bed for three months and was not encouraged to move about during this time. At no time was pus found in the urine.

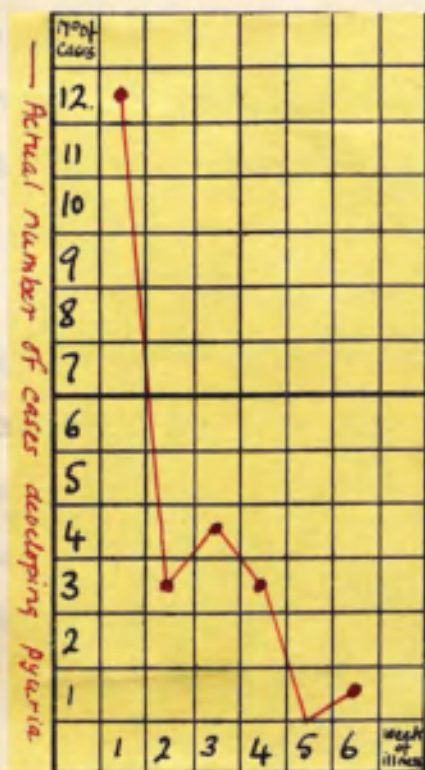
A girl of two years, suffering from pneumonia and empyema, remained in bed for nine weeks and during this time she showed no inclination to stand up or run about her cot. The urine remained free from pus during the whole illness.

Twenty-three children who were already under treatment for other conditions developed urinary infection. The diseases to which it was secondary will be mentioned in a later section. The time of onset of pyuria is shown in Table 6. Twelve children (52%) developed this condition during the first week of the initial disease, three (13%) during the second week, four (17%) in the third week and three in the fourth week. In one case only was the onset delayed until the sixth week of illness.

It appears, therefore, that the duration of the stay in bed has no influence upon the development of urinary infection. The susceptible child becomes infected early while the others remain free from infection over a prolonged period.

Table 6

Showing the time of onset of pyuria during the course of other diseases in twenty-three cases.



3. Constipation and the administration of aperients

There is no doubt that constipation and the subsequent administration of aperients plays some part in the production of urinary infections.

Morse (1909) obtained a history of chronic constipation in three of his cases. Thomson (1910) noted this and found that out of twenty-five cases of "acute pyelitis" there was a history of habitual constipation in twelve. Walker (1922) states that in chronic cases, pyuria frequently recurs after the administration of cascara. Albee (1927) considers intestinal stasis and putrefaction are of such importance in chronic pyuria that he advocates high colonic lavage in the treatment of all cases.

Among the twenty cases of primary infection which came under observation there was a definite history of constipation in five. This is not a very high figure but as a number of the cases were over five years old it is probable that habitual constipation was present in a larger number of children, but had not been observed by the mothers.

Among the twenty-three cases of secondary infection, constipation was an outstanding feature in six, and had in all these cases so definitely preceded the onset of pyuria as to make it appear extremely probable that the two conditions were associated with each other.

4. Severity of the original disease.

In Table 5 are set out a list of the diseases in which urinary infection occurred as a complication. With the exception of six cases of gastroenteritis, one of which followed measles and pneumonia, the conditions to which pyuria was secondary were all of a mild nature.

Observation of two girls, each aged two years, suffering from pneumonia and empyema, failed to reveal any evidence of urinary infection, although in both cases a long febrile illness occurred. A boy aged three years, admitted to hospital with generalised peritonitis following appendicitis had continuous pyrexia for four weeks and ultimately developed a pelvic abscess. The urine remained free from pus and sterile throughout the illness. A three year old boy developed acute focal nephritis during the course of bronchopneumonia. Despite the fact that the original disease was a severe one and damage to the kidneys, as indicated by albuminuria, and the passage of casts and red blood corpuscles, had occurred neither pus nor organisms were found on frequent examinations of the urine.

The majority of conditions which were followed by the development of urinary infection were of a mild nature. It seems probable that a severe illness is not in itself

sufficient to render the patient prone to infection of the urinary tract, but that some other factor must be present, and this is as liable to occur in the mild illness as in the more severe condition.

5. Age and sex

In every account of pyelonephritis in childhood stress has been laid on its preponderance in girls, and the typical case is described as occurring most frequently below the age of one year. Morse (1909) in a series of 50 cases found that 60% were girls. Thomson (1910) in a description of 25 cases found this figure to be as high as 84%, all his cases being below the age of two years. Gärter (1926) reported 114 cases, 83 of which were girls, but noted that if the 61 cases which had occurred below the age of one year were alone considered, the distribution between the sexes was almost equal. In Still's account of 40 cases (1927) there were 36 girls and 30 of the children were under two years. Graham (1933) in a study of 435 cases found that below the age of six months the incidence of urinary infection was almost the same for the two sexes, but thereafter it was higher in girls. Among 20 fatal cases referred to by Sheldon (1936) in which the diagnosis was confirmed by post-mortem examination there were nine boys.

The incidence of urinary infection among boys and girls in a series of 43 cases has already been referred to and is shown in Tables 1 and 2. 35 of the total cases were girls and 8 were boys. In the group of primary cases the preponderance among girls was more marked, being 9 : 1, while in the secondary group it was 3 : 1.

Five cases, occurring in the neonatal period have been omitted, since they did not come under observation until the above series of cases was completed. Four of these were however boys. The observations of Goeppert (1908), Sauer (1918), Paterson (1931) and Craig (1935) have shown that urinary infection in the neonatal period is more frequent in boys.

The age at onset of symptoms in 43 cases is shown in Tables 3 and 4. The children under observation in hospital have been divided into five groups according to their ages, and the cases of urinary infection occurring have been expressed as a percentage of the total number of children in each group. A study of these tables shows that the percentage for all cases was highest in the group of children under one year. When the primary infections are alone considered, however, the highest incidence is found to be in the 5 - 10

year group, while in the secondary cases it is again highest below one year. Table 4 shows that the incidence of infection in the cases under observation fell between the ages of one and three years and then rose again up to ten years of age.

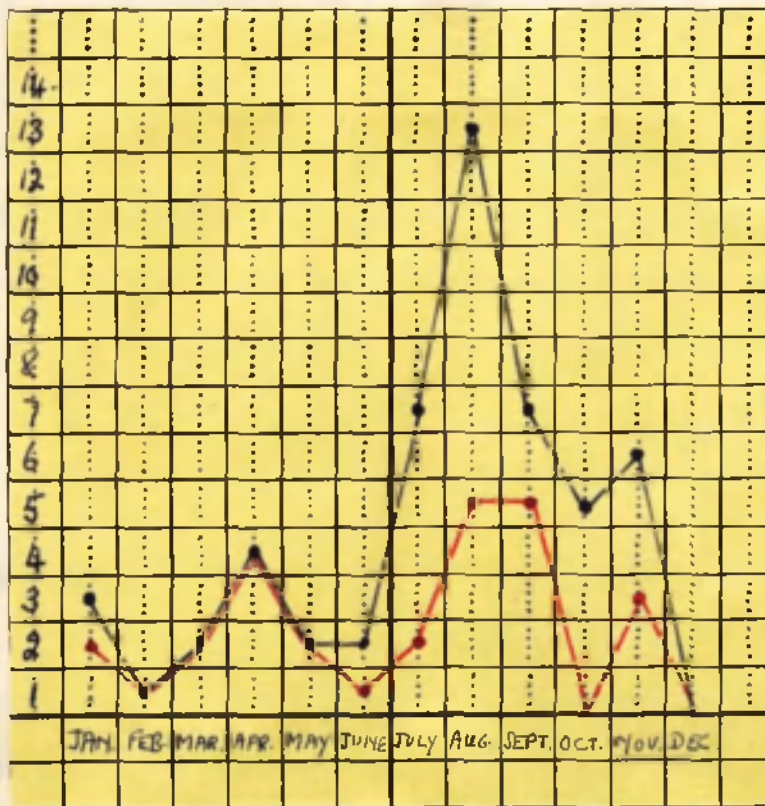
It would appear that the high incidence of cases below the age of one year, noted by many observers, is due to the frequency with which urinary infection occurs as a complication of other conditions at this age and it will be seen later that gastrointestinal disorders are a frequent precursor of urinary infection in infants.

A possible explanation of the preponderance of cases in girls is discussed elsewhere.

6. Seasonal Incidence

Investigations were mainly carried out between June and December and the figures for the earlier months have been obtained from the hospital records and, therefore, only include cases in which the principal disease was pyelonephritis.

Table 7 shows the total number of cases of urinary infection under treatment each month, and the number of primary cases admitted to hospital.

Table 7Cases of urinary infection under treatment

— Total cases under treatment

— Primary cases admitted.

A study of this table shows that the total number of cases of urinary infection under treatment was highest during the month of August and remained high throughout the Summer and Autumn months. It will be seen later that this rise in the number of cases corresponded to the increased number of cases

of gastroenteritis admitted. The number of primary cases remained highest in August and September, fell to nil in October and rose again in November to correspond to the increase in the total number of cases for this month. These figures show an actual increase in the cases under treatment, and not an apparent one, since the total number of children in the wards remained almost constant throughout the year.

There does not appear to be any explanation for the increase of primary cases in August and September, and in only one of these cases was a history of diarrhoea obtained.

7. System diseases

System diseases, particularly those of the gastrointestinal and upper respiratory tracts have been frequently considered to be factors in the production of urinary infection. Acute infectious diseases are also said to predispose to the condition, a fact which was noted by Monti (1893) and Abt (1907).

Among 50 cases described by Morse (1909) urinary infection followed gastroenteritis on two occasions and upper respiratory infection on one. Thomson (1910) in a study of 25 cases, noted the occurrence of this condition after scurvy three times, rickets four, abdominal tuberculosis once, and severe anaemia once. It is possible that in the last case the anaemia was in reality secondary to chronic pyuria, as in the

case reported by Carpenter (1907). Schwartz (1918) found pus cells and coliform bacilli in the urine of 29.2% of girls and 22.7% of boys ill with gastroenteritis. More recently King (1931) has stated that in his opinion 90% of the cases follow upper respiratory tract infection and the remaining 10% occur after gastrointestinal disorders.

The diseases which were complicated by urinary infection have been shown in Table 5. A study of this shows that in 23 cases of secondary urinary infection the initial diseases were gastroenteritis eight times, upper respiratory infection and skin diseases four, rheumatism and genitourinary conditions three times and anaemia and debility once. 34.7% of the cases of secondary infection followed gastroenteritis, pyuria occurring twice as frequently in this condition as in any of the other diseases.

Table 8

Comparison of the diseases to which urinary infection was secondary

DISEASE	Total No. of Cases under Treatment	No. of Cases developing Pyuria.	Percentage
Gastroenteritis	30	8	26.6
Upper Respiratory Tract Infections	70	4	5.7
Skin Diseases	66	4	6.0
Rheumatic Conditions	13	3	23.0
Genito-Urinary Conditions	16	3	18.9

Table 8 shows that among a total of 30 cases of gastroenteritis under treatment in hospital, pus and organisms were present in the urine of 26.6%. With one exception the cases of enteritis complicated by pyuria were of the infectious type, the organisms obtained from the stools being B.Morgan, B.Proteus, B.Pyocyaneus and B.Dysenteriae (~~some~~ ^{some}). This excludes the possibility of diarrhoea being merely a symptom of primary pyelonephritis.

Table 9

Occurrence of Secondary Pyuria in Gastroenteritis

	Cases of Gastroenteritis	No. of Cases of Pyuria.	Per-Centage
Total	30	8	26.6
Boys	17	2	11.3
Girls	13	6	46.0

In Table 9 are shown the total number of cases of gastroenteritis under treatment and a comparison is given between the number of cases of pyuria occurring in boys and girls who were admitted with this condition. A study of these figures shows that urinary infection as a complication of gastroenteritis was four times more frequent in the girls than the boys and that 46.0% of the girls who were admitted to hospital with this condition developed pyuria.

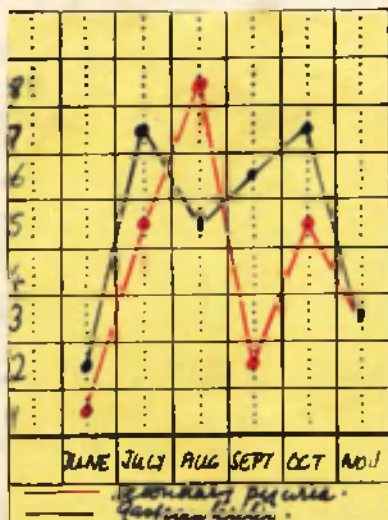
Table 10Comparison between cases of Gastroenteritis and secondary urinary infection

Table 10 gives a comparison between the number of cases of enteritis under treatment each month and the cases of secondary pyuria. It will be seen that with the exception of the months of August and September the two diseases tended to run a parallel course, there being an increase in the number of children developing urinary infection when the rate of gastrointestinal upsets was highest.

The diseases of the upper respiratory tract under observation include cases of tonsillitis, rhinitis, otitis media and laryngitis. The total number of these cases under treatment was 70, out of which number four children (5.7%) developed urinary infection, a very much lower figure than for the gastrointestinal conditions.

The skin lesions under treatment consisted of impetigo, scabies, urticaria and infantile eczema. Burns and scalds have been included in this section. Among a total of 66 of these cases only four (6.0%) developed pyuria.

The incidence of infection in the rheumatic diseases (chorea, acute and subacute rheumatism) was higher than in the last two groups since among 13 cases there were three cases of secondary infection (23.0%). The number of children in this group was too small for any definite conclusions as to the frequency of this complication to be reached.

Sixteen children suffering from genito-urinary conditions other than acute pyelonephritis were under treatment. These comprised three cases of acute focal nephritis, and thirteen local conditions of the external genitals such as balanitis and vaginitis which ~~were~~^{will} be considered separately. Among these sixteen cases there were three cases of secondary infection of the urine (18.8%), but here again the number of children in the group is too small for any definite conclusions to be drawn.

These results are consistent with those of Schwartz and others and indicate that urinary infection is a frequent complication of gastroenteritis especially in girls.

8. Local conditions

The local conditions which are considered as possible precursors of urinary infection are balanitis, phimosis, vulvovaginitis and any septic condition of the external genitals.

Osler (1894) described a case of chronic pyuria associated with phimosis, which only improved after circumcision had been performed. Morse (1909) reported two cases following circumcision, and Thomson (1910) considered that phimosis was the predisposing cause in one of his cases, and noted that another case followed circumcision. Paterson (1931) reported two cases in the neonatal period which occurred after circumcision. In one of these cases the child had not gained weight well since birth, and the day after circumcision was feverish and had pus and coliform bacilli in the urine. It is quite possible here that infection of the urine of a mild type had been present prior to operation and had been the cause of the failure to gain weight.

Vulvo-vaginitis is usually considered to be a cause of urinary infection, though Baginsky (1897) stated that it did not often give rise to the condition. It is possible that in many cases of so-called pyelonephritis the pus cells have come from the vagina.

Seventeen children under observation in hospital had some local condition of the external genitals. These included seven cases of phimosis, of which six were circumcised while in hospital, one case of balanitis following circumcision a week previously, four mild cases of vaginitis and an infant aged eight days which had a ritual circumcision performed. There was no case of urinary infection among the children admitted with phimosis, either before or after circumcision. Scanty pus cells were found in the urine of the child suffering from balanitis, but the cultures were sterile and he had no constitutional symptoms suggestive of urinary infection. Among the four cases of vaginitis which came under treatment two were admitted with typical symptoms of pyelonephritis - headache, vomiting and pyrexia - and with frequency of micturition and dysuria in one case. These two children were sisters and came into hospital within a day or two of each other. A vaginal discharge was present in both cases and pus and coliform bacilli were obtained from the urine. The symptoms subsided rapidly with alkaline treatment. The organism grown from the vagina was a staphylococcus in one case and a non-haemolytic streptococcus in the other. The only other case of urinary infection following a local condition was that of the infant which had a ritual circumcision

performed. This was followed by rapid development of toxic symptoms and ended fatally six days after operation - death being due to ascending purulent pyelonephritis and pyaemia. Observation of a large number of infants upon whom ritual circumcision was performed failed to reveal evidence of infection of the urine in any other case.

Although local genital infection must be considered as a possible precursor to urinary infection, it does not appear to be a frequent cause. It is possible that a mild cystitis sometimes results, but that the symptoms clear up rapidly without the child being admitted to hospital. Exceptionally pyelonephritis appears to result from one of these conditions.

9. Abnormalities of the Genitourinary tract

Where any large series of cases of urinary infection have been investigated, a certain number of the chronic ones have been found to possess anatomical abnormalities of the urinary tract. Mixer (1923) in a study of 185 cases of pyuria under observation in the Children's Hospital, Boston, found lesions of the urinary tract in 25%, of which 80% were amenable to surgical treatment. Bugbee (1924) in a series of 4,000 autopsies on children, found congenital hydronephrosis in 53 (1.3%). Hyman (1930) has found the incidence of

anatomical malformations to be as high as 2.3% of children examined post-mortem.

Except for those cases which came to operation or autopsy however, little was known of the anatomical abnormalities until cystoscopy and pyelography came into practice, and it is only in the past few years that sufficiently small instruments have been available to make this method of treatment possible in young children.

Investigations by Kretschmer (1927), Neale (1931), and White (1933) show that the commonest congenital abnormality in the urinary tract is hydronephrosis and hydroureter, which is apparently due in some cases to stricture of the ureter. Hurst (1930) suggests that others are due to achalasia of the ureterovesical valve, and White considers that the condition may be allied to Hirschsprung's disease. Kretschmer found stricture of the ureter, with dilatation above in ten cases of chronic pyuria, investigated by cystoscopy and intravenous pyelography. Neale found unilateral congenital hydronephrosis in three cases, and a bilateral condition in two others.

Other abnormalities occasionally found are aberrant renal artery, horse-shoe kidney, congenital cystic kidneys, sarcoma of infants, kinked or double ureters, congenital valves in the urethra, vesicovaginal or rectal fistula and hypospadias.

White found one case of aberrant renal artery, producing hydronephrosis and chronic pyuria in a child, which was amenable to surgical treatment. Craig (1935) reported a fatal case of pyelonephritis in a boy of a few days old in which a horse-shoe kidney was present.

B. ACQUIRED ABNORMALITIES

The acquired abnormalities which give rise to chronic pyuria may also be investigated by cystoscopy and pyelography. The most frequent cause is a calculus in some part of the urinary tract. Kretschmer found a ~~small~~^{renal} calculus once, stone in the ureter twice and vesical calculus once in an investigation of children with urinary infection. White found renal calculus present on three occasions, and a stone in the ureter twice and in the bladder once.

Tuberculosis of the kidney in children appears to be more frequent than has been supposed, and was found seven times by White in an investigation of 50 cases. Kretschmer found the condition present in five out of 52 cases. Sarcoma occasionally occurs and was found three times in each of the above investigations.

Phimosis has already been referred to as a cause of chronic pyuria and circumcision is then indicated.

Abnormalities of the genito-urinary tract, whether congenital or acquired may lead to urinary infection. If the condition fails to respond to the usual methods of treatment or recurrent attacks occur, some abnormality of the tract should be suspected, and investigations by means of X-rays, cystoscopy and pyelography should be employed.

10. Dehydration

It has already been shewn that urinary infection frequently follows gastroenteritis. Several factors are probably concerned in its production. Damage to the intestinal mucous membrane may render possible the escape of organisms from the bowel to the blood stream. It is well known that organisms, normally harmless in the intestinal tract, may become pathogenic in other situations of the body. Absorption of toxic substances from the intestine may be a further cause of renal damage.

Dehydration is a condition which occurs as a result of gastroenteritis, and was absent in all the other conditions to which urinary infection was secondary. It, therefore, seems probable that it may be a factor in the production of infection of the urinary tract. Helmholtz (1926. 1929) and others have shewn that organisms present in the blood do not damage the

kidneys unless urinary outflow is interfered with or the organism is very virulent. When diarrhoea and vomiting are severe, anuria, partial or complete, occurs, owing to loss of body fluid, and if organisms are present in the blood stream the kidney fails to excrete them and pyelonephritis may occur.

Urinary infection in the neonatal period is another condition which may be dependent upon dehydration. Observation of a large series of young infants by Graham (1925), Conrad (1926) and Craig (1935) show that symptoms of urinary infection most frequently make their appearance between the second and fourth days of life. A study of the new-born child shows that normally loss of weight takes place for two days, the lowest weight being reached about the third day of life. Where a practice is made of recording the morning and evening temperature of the infant, it is not uncommon to find that slight pyrexia develops about this time. Examination rarely reveals any physical signs to account for this except perhaps that the child smells of acetone and the usual diagnosis is "dehydration fever". If a routine examination of the urine is made in all these cases, pus and organisms will be found in a certain number. The type of organism varies, coliform bacillus,

streptococcus or staphylococcus being the usual invaders. It seems probable that as the pyrexia almost always occurs when the weight of the child is lowest, the two conditions are associated. During the first two or three days of life the fluid intake is small, while fluid is lost from the bowel and skin, and if this loss is not made up there is an interference with the urinary output. It is possible in a few cases that organisms have gained access to the blood stream through abrasions in the skin, the cut end of the cord, or even before birth through the placenta. If the infant in question is allowed to become dehydrated and stasis of kidney function results, renal infection may occur, with resultant pyelonephritis.

Investigation of twelve infants developing pyrexia in the neonatal period showed that the urine of five contained pus and organisms. In four cases pyrexia developed on the second, third, fourth and fifth day of life respectively, in each case when the weight was lowest. The fifth child did not develop symptoms till the seventh day, except that she had continued to lose weight until this time. The first four cases responded at once to adequate amounts of fluid and a small quantity of alkali, and with the rise in weight the temperature fell and the urine became clear. (Chart 6)

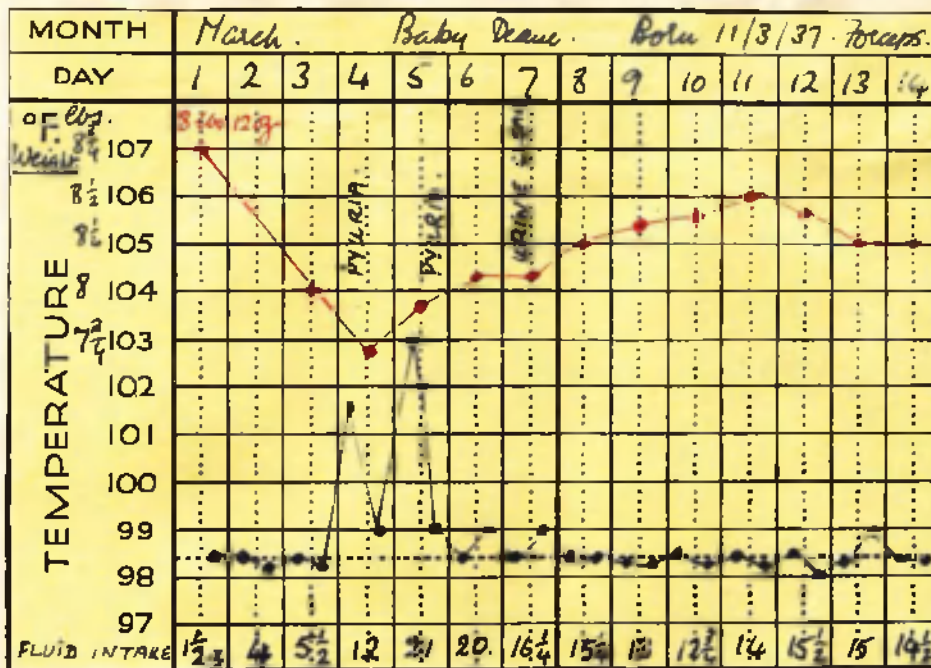


Chart 6. Pyrexia on fourth day of life due to pyuria. Staphylococcus aureus was grown from the urine.

The fifth case, the only girl in the series, was more severe and ended fatally.

Although a state of dehydration does not account for every case of urinary infection, it appears to be a factor of some importance in its development, and affords a possible explanation of the high incidence of cases following gastroenteritis, and of those cases which occur during the first few days of life.

11. Other factors

A few other factors which may be concerned in the development of urinary infection remain to be considered.

The social position of the child does not appear to have much influence and Thomson (1910) considers that the condition is equally common among well-to-do children and those of poorer classes, but it is difficult to obtain figures to prove this. It is probable, however, that secondary infection is more common among the hospital classes, as these children are more likely to contract gastroenteritis, respiratory and skin infections. There does not appear to be much tendency for more than one member of a family to develop the condition, although two of the children of this series were sisters, but here vaginitis had been the predisposing cause.

The diet of the child is of importance. Pyelonephritis is rare in breast-fed infants, occurring almost exclusively in those who are artificially fed. A history of recent change of diet or weaning is often obtained. Among eight infants in this series, below the age of nine months, who developed urinary infection all but one were artificially fed, and in one case the milk had been changed from "Cow and Gate" to Nestlé's a week before the illness developed.

Enuresis is sometimes considered to be a predisposing cause of infection, but it seems possible that the condition

itself may be a symptom of mild chronic pyuria. A history of enuresis was obtained in two of the primary and one of the secondary cases. These children were aged seven, eight and four years respectively and were of average intelligence in every other way.

The influence of movements of the body has already been referred to and it does not seem that exercise or the lack of it plays any part in the production. It has been suggested that pyelonephritis is more likely to develop in children who have not yet learned to walk, for this reason, but there is little evidence to support this view.

CLINICAL FEATURES

Pyelonephritis in children may be divided into two main groups, according to the age of the child.

The first group includes mainly those cases occurring in infants below the age of one year, to which Thomson (1902) drew attention. The child, most often a girl, while apparently in good health, is suddenly seen to shiver or have a definite rigor, and a few moments later is found to be rather blue and cold. The temperature is raised and thereafter runs a high, irregular, remittent course. While the fever is at its height

the child is pale and irritable, resents being handled and sometimes screams out as though in pain. Periods of drowsiness and irritability alternate with each other. At intervals the infant is quite bright, but soon passes again into that state which has been described as one of "wakeful misery". The urinary output is diminished and anuria may be present for long periods. Vomiting is a characteristic symptom, thirst is marked, and green stools are usually present. The attacks of blueness and collapse tend to recur at intervals.

If the previous health is inquired into it will be found that in most cases there has been some recent mild intestinal derangement such as constipation or a green stool. The majority of these infants are artificially fed and it is often found that the type of milk has been changed recently or the child has been weaned.

The majority of cases under treatment recover, the duration of the illness varying from a few days to several weeks.

Chart 7 shows the course of the disease in a baby girl aged seven and a half months who was admitted to hospital on the third day of illness and whose symptoms and progress were so characteristic of the condition as to be worthy of recording in detail.

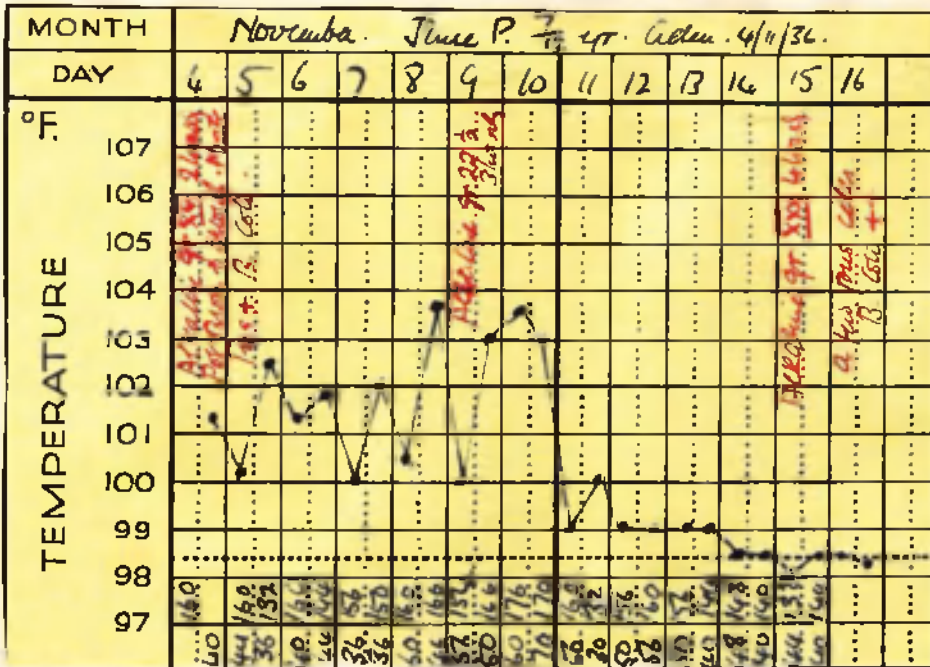


Chart 7. Acute Pylonephritis in a girl aged 7 $\frac{1}{2}$ months.

History. The child was in good health until 2.11.36 when she suddenly became shivery and vomited. The mother volunteered the information that she was "well one moment and ill the next". During the day she became feverish and very irritable, though for short periods she seemed quite normal again. The following day she had attacks of blueness and shivering and a doctor called in in the evening found the temperature to be 104°. She was admitted to hospital 4.11.36.

Past History. The child had always been healthy. She had been breast fed until she was six weeks old and this had then

been changed to Nestlé's milk. A week before the onset of symptoms this had again been changed to "Cow and Gate". There was no history of intestinal derangement.

On admission to hospital the child was seen to be well nourished, but very pale and cross, screaming every time she was touched. She had a slight cough. The temperature was 101.4, pulse 160 and respirations 40. A thorough examination failed to reveal any physical signs of disease. A catheter specimen of urine was found to contain pus cells and coliform bacilli.

Progress. The day after admission the infant was very irritable and although she took her feeds well there was a tendency to vomit them. Stools were normal. During the next few days she remained very fretful, with occasional intervals when she was quite bright. A little vomiting occurred. On the sixth and seventh days after admission she became dull and drowsy, refused feeds and had several relaxed stools. Towards the evening of the seventh day she became much brighter, sat up in her cot and began to take an interest in things. Thereafter recovery was uneventful.

The disease as it occurs in older children does not present the same characteristics as in infancy. The onset is usually less abrupt, the symptoms often coming on so insidiously

that the mother is unable to say when the child first became ill. The pallor, listlessness, loss of appetite and slight pyrexia which occur sometimes suggest typhoid fever. There may be nausea and vomiting early in the disease and headache is often one of its first symptoms. Many of the children complain of pain in the abdomen or loin, and generalised aching pains in the back and limbs may occur. Frequency of micturition and dysuria are sometimes marked symptoms. The extreme irritability and restlessness so common in infants is not often found in older children. A few cases come on acutely with headache, vomiting, abdominal pain and frequency of micturition, but the rigors and attacks of cyanosis and collapse which are so characteristic of the disease in infancy do not occur. Pallor and puffiness of the face is sometimes the first symptom.

On inquiring into the past history it is not uncommon to find that an otherwise normal child of six or seven years has suffered from nocturnal enuresis all its life, and a history of previous "kidney trouble" is sometimes obtained.

On examination the child looks pale and ill. There may be only slight pyrexia or the temperature may be high. As a rule a corresponding increase in pulse rate is found, but sometimes in spite of pyrexia the pulse rate remains about

80 per minute. Little is found in the way of physical signs but there may be tenderness in one or both loins or in the abdomen.

The progress is variable. The symptoms in a mild case tend to subside as soon as treatment is started, but the more severe case continues for a varying number of weeks. Relapses are common, but the ultimate prognosis is excellent.

Consideration must be given to that group of cases which occur during the course of another disease. A severe type of infection complicates gastroenteritis in infants, but the condition appears to be mild after other illnesses, though characteristic symptoms may occur. Where pyrexia is already present it may be difficult to say when the urinary infection began. In other cases the symptoms are so mild that beyond a little malaise nothing is noticed to be wrong with the child, but pyuria is discovered on routine examination of the urine.

Chart 12 shows the course of a typical secondary case. This child, a girl aged seven years, was recovering from subacute rheumatism and suddenly developed headache, vomiting and pyrexia. The following day pus and coliform bacilli were present in the urine. The condition rapidly subsided, the

child feeling quite well in three days, though the urine was not free from pus for two weeks.

Table 11 gives a comparison between the chief symptoms in the two groups of cases, and includes twenty three children over one year old and nine below one year. A study of this shows that the symptoms were quite different in the two groups, with the exception of vomiting and pallor, which occurred in a high percentage of cases in each group.

Table 11.

Comparison of symptoms in the two age groups

Group I. 23 cases over one year

Group II. 9 cases below one year

SYMPTOM	Group I.	Percent.	Group II.	Percent.
Vomiting	17	74	8	88
Diarrhoea	6	26	9	100
Constipation	7	30	0	0
Abdominal pain	11	48	?	?
Headache	5	21	?	?
Frequency of micturition	9	39	0	0
Dysuria	6	26	0	0
Diminished urinary output	1	4	2	22
Irritability	3	13	4	44
Pallor	10	42	5	55
Attacks of Cyanosis	0	0	2	22
Shivering	0	0	1	11
Meningismus	1	4	1	11
Oedema	2	8	1	11

Pyrexia

A study of the pyrexia associated with urinary infection in childhood shows nothing constant, but certain of its features are so characteristic as to be worth noting. In a typical case the temperature runs a high irregular remittent course, often reaching 105° or more, the highest point usually being in the evenings and the lowest point early in the morning. It frequently shows signs of becoming normal, only to rise again in a few hours to as high or higher levels. In a favourable case the fever subsides by lysis, while in others it only reaches normal after a long series of irregular rises and falls. In many cases a slight evening temperature persists for days or weeks after the acute symptoms have subsided. Relapses, with a return of all symptoms and high fever are common, and long after the child is convalescent there may be sudden elevations of temperature to a high level for a few hours. (Chart 5)

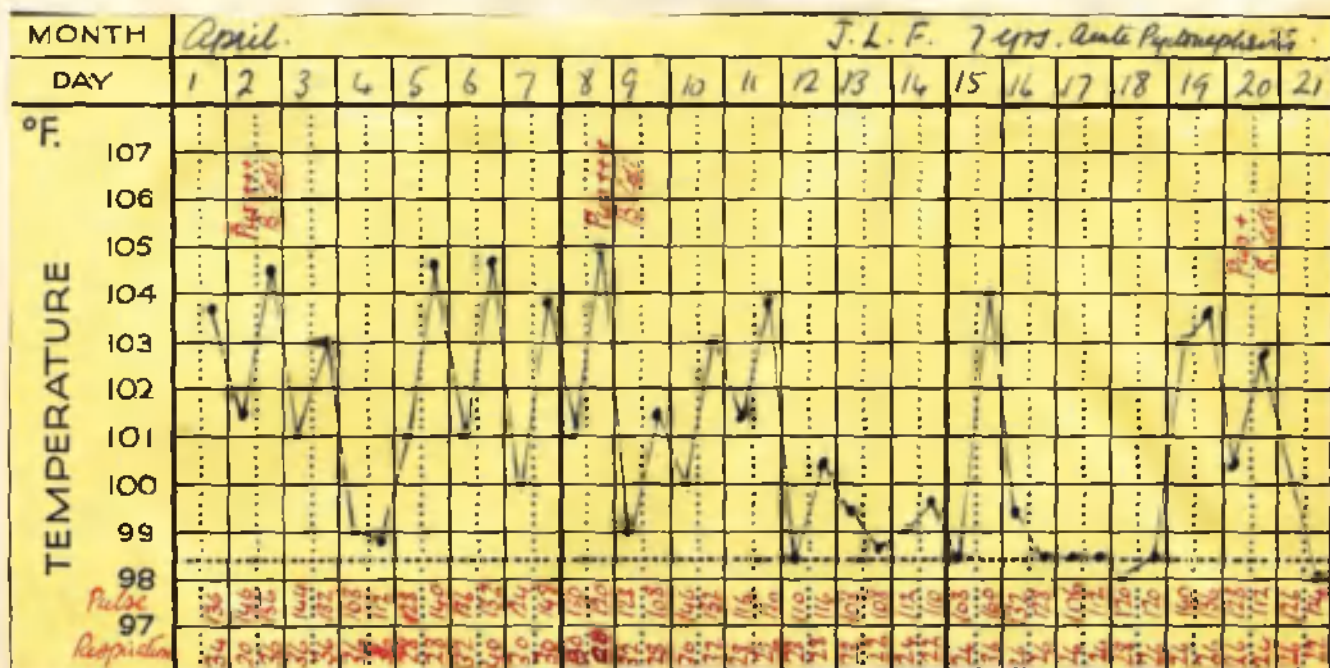


Chart 8. Pyelonephritis. Girl, aged 7 years

There is perhaps no disease in which the pyrexia is more variable in character, and all extremes are met with from the mild case where the temperature settles immediately with treatment to the rapidly fatal one which ends with hyperpyrexia (Charts 8, 9 and 10).

The duration of the initial pyrexia varies considerably. In a series of children the average number of days was nine, the shortest time being two and the longest twenty-one.

Where pyuria develops as a complication of another disease it is sometimes impossible to say definitely when the pyuria started, if the temperature is already elevated. In a typical attack complicating some mild disease there is sudden elevation of temperature with symptoms suggestive of urinary infection. (Chart 12). In many mild cases little or no pyrexia occurs. In the cases secondary to gastroenteritis the infection tends to be severe and the fever high.

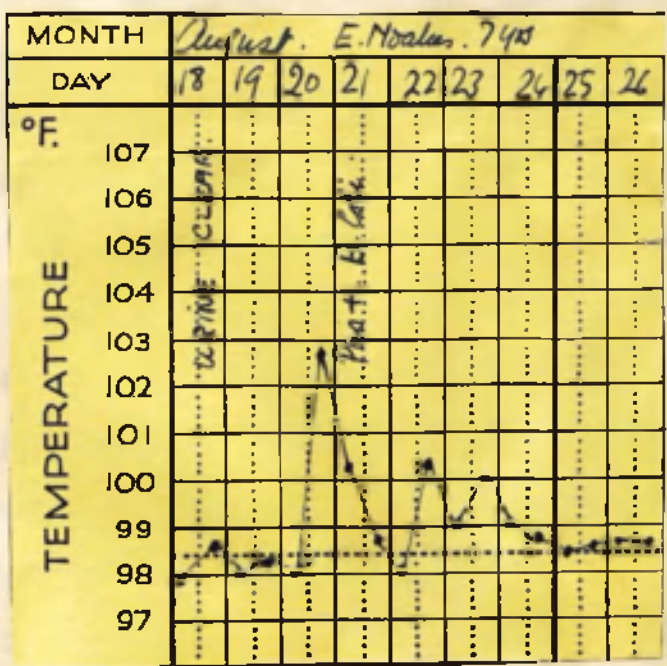


Chart 12. Pyrexia due to urinary infection complicating subacute rheumatism. Girl, 7 years.

Extreme hyperpyrexia is of grave significance, especially where the temperature gradually rises, in spite of treatment and in two fatal cases it reached 108° before death. (Chart 10).

Sudden elevations of temperature in a child who is convalescent from pyelonephritis are often associated with constipation and rapidly subside upon administration of appropriate treatment. (Chart 5)

In the majority of cases the pulse rate is increased and corresponds to the degree of pyrexia. Occasionally in older children the pulse rate is slow, giving the condition the characteristics of typhoid fever.

Duration of illness

The duration of an attack of acute pyelonephritis shows considerable variation. Poulsen (1923) stated that in a series of 43 children the average duration of this condition was eight weeks. Neale (1931) in an investigation of 117 cases found that the length of the illness varied from two to four weeks. Craig (1935) in a study of 63 neonatal cases found that severe symptoms sometimes persisted for six weeks from the time of onset.

In a series of 33 non-fatal cases of urinary infection in children, the duration of the illness from the onset of

the first symptom until the child was considered fit for discharge from hospital, varied from ten to eighty days, the average time being twenty-four. Considerable difference was found to exist between the length of a primary attack and one complicating another disease. The average duration of the primary condition was thirty-three days, and that of a secondary attack fourteen. The length of illness also varied according to the age of the child, being longer in the cases above the age of three years. In the younger child it was found that the illness was either rapidly fatal, or responded quickly to treatment. Among eight such cases the average length of the illness was nineteen days, while in the group of 25 children over three years it was twenty-seven days.

Blood Changes

The blood picture of a child suffering from urinary infection shows nothing characteristic.

Carpenter (1907) described a case of severe anaemia secondary to chronic pyelonephritis in an infant of eleven months in which the blood changes were those of a megalocytic anaemia. I have been unable to find any other account to compare with this one.

Observations of a series of children shows that a mild secondary anaemia is the usual blood picture in pyelo-

nephritis. In a group of sixteen cases the average red cell count was 3,500,000 per cubic millimetre and the haemoglobin 55%. A moderate leucocytosis was generally present, the highest count being 17,500 per cu.mm. In some cases there was no increase of white cells. Leucocytosis when present is due to an increase of granular cells, especially the polynuclear neutrophils. In the series of cases under observation the highest number of polynuclear neutrophils was 72% and the average 56%. This, in young children who normally have a high percentage of lymphocytes is above the normal number. A marked increase in the number of eosinophils sometimes occurs. In this series of children the average number was 2%, but in one case it was as high as 8.5% and in another 7%. As recovery takes place there is a diminution in the number of granular cells with a relative increase of lymphocytes. This is shown in the following record of a child of three years, the first count being done while the illness was at its height, and the second a month later, when she was convalescent.

	<u>First Count</u>	<u>Second Count</u>
<u>WBC</u>	13,250 per cu.mm.	11,500 per cu.mm.
<u>Polymorphs</u>	68%	31%
<u>Eosinophils</u>	1%	0
<u>Lymphocytes</u>	29%	67%
<u>Monocytes</u>	2%	2%

Focus of Infection

A focus of infection has frequently been held responsible for the development and persistence of pyelonephritis. Hodge (1925) stresses the importance of recognising tonsillitis as a cause of staphylococcal pyelitis and pyelonephritis, advocating tonsillectomy in treatment. King (1931) considers that 90% of the cases of urinary infection in children are due to upper respiratory tract lesions.

As the majority of cases of pyelonephritis are due to the coliform bacillus the possibility of direct infection from the upper respiratory passages can be excluded, since this organism is practically never found in this situation. It is well known however that a septic focus in some part of the body may set up a focal nephritis and it seems possible that this may be the starting point in some of the cases of urinary infection.

In order to determine whether any particular organism was constantly present cultures were made from the throat in a group of children under treatment for pyelonephritis. If there was any obvious focus of infection cultures were also made from this.

The results are shown in Table 12.

Table 12.

ORGANISM	Throat	Nose	Ear	Eye	Total	Percent.
Haemolytic Streptococcus	11	1	-	-	12	80
Pneumococcus	6	-	-	-	6	40
Staphylococcus Aureus	-	2	1	1	4	20

In a group of fifteen children under treatment for pyelonephritis haemolytic streptococci were isolated from the throat eleven times and from the nose once. Pneumococci were isolated from the throat in six instances, in three of which haemolytic streptococci were also found. Staphylococcus aureus was obtained from the nose twice and from the ear and eye once.

It will be seen that a high percentage of children under treatment for urinary infection were carriers of haemolytic streptococci. One of these children was admitted to hospital with acute nasopharyngitis and another with tonsillitis, but there was no acute local condition to account for the presence of the organism in the other cases, though several children had enlarged tonsils.

It is possible in some of these cases that a mild focal nephritis was the primary condition, though there was no evidence of such a condition being present.

Pyelonephritis of the Newborn

Until 1931 about thirty cases of urinary infection occurring during the neonatal period had been put on record. In the past few years a larger number have been recognised and reported.

The first account of the condition was given by Kovalesky and Moro (1901) who recorded two cases of B.Coli septicaemia associated with pus in the urine, in newborn male infants. Goeppart (1908) noted that the condition was more frequent in boys at this age. Sauer (1918) showed that non-thriving in infancy was often due to unsuspected urinary infection, and found that the condition was present in fourteen out of fifteen infants who had failed to gain weight after birth. Graham (1925) gave an account of six cases in the neonatal period, three of which were boys and three girls. The infecting organisms were found to be B.Coli in two cases, staphylococcus aureus in two cases and non-haemolytic streptococcus in two cases. Conrad (1926) discussed "congenitally acquired pyelitis" with reference to three female infants, in whom symptoms came on so rapidly after birth as to suggest that infection had occurred through the placenta, particularly as the mothers of two of these infants had suffered from pyelitis during pregnancy. Paterson (1931)

reported two cases following circumcision and drew attention to the preponderance of cases occurring in boys at this age. Sixty one cases occurring during the first two weeks of life were described by Craig (1935), forty of which were boys.

There are a few points of difference between the neonatal case and that of the older child. Boys appear to be affected rather more frequently than girls, the proportion of cases being about two to one. The infecting organism may be a staphylococcus or a streptococcus, whereas in the older infant it is almost always the coliform bacillus. These variations can be understood if it is remembered that the newborn child is subjected to risks of infection through several paths which do not have to be considered after the first two weeks of life. It is possible that infection may occasionally occur before birth, through the placenta. During the delivery infected material from the birth canal may be swallowed, organisms later passing to the kidneys from the intestine. After birth organisms may gain access to the blood stream through the cut end of the umbilical cord.

The symptoms come on about the third day of life, sometimes earlier, and are most often noted when the child's weight is lowest. (Chart 6). There may be little or no pyrexia, but a rise of temperature to 100° - 103° is often

the first sign. The child looks dehydrated, its breath smells of acetone, thirst is marked, and attacks of blueness or greyish pallor may occur from time to time. Vomiting is a frequent symptom, and the stools are often green. In other cases the predominating symptoms are progressive loss of weight, vomiting and relaxed stools, with or without pyrexia. These are the dangerous cases, in that as all the symptoms are referable to the gastrointestinal tract the correct diagnosis may be missed.

Twenty infants, sixteen boys and four girls, who developed pyrexia during the neonatal period were investigated and seven were found to have pyuria. Five of these were boys and two girls. Two of them were fatal and have already been referred to. One infant was seriously ill but recovered after treatment. The remaining four cases were mild and little treatment was required. The infecting organism was found to be B.Coli in three cases and staphylococcus aureus in three cases. No cultures were made in the seventh case.

The treatment is the same as for older children. Mild cases improve immediately the fluid intake is increased. Feeds should be diluted and given every two hours, and extra fluid in the form of weak saline solution should be given between feeds. Alkalies must be given to all but the mildest

cases and the dose must be sufficient to render the urine alkaline. As much as gr.75 in the twenty four hours may be required at first.

In all cases where pyrexia develops in the neonatal period, or the child fails to thrive, the possibility of urinary infection must be borne in mind, since prompt treatment may be the only chance of saving the child's life.

Severity of infection

Among the children who were admitted to hospital with pyelonephritis, or developed the condition during the course of another disease the illness varied in severity, from the mild almost symptomless case to the rapidly fatal one. The mortality rate from this condition is shown in Table 13.

TABLE 13

Mortality Rate in Pyelonephritis

	Cases under treatment	Deaths	Per-cent-age	Per-cent-age for sex	Prim-ary Cases	Deaths	Per-cent-age	Per-cent-age for sex	Second-ary Cases	Deaths	Per-cent-age	Per-cent-age for sex
Total	43	7	16.2		20	2	10		23	5	21.7	
Boys	8	2	4.6	25	2	0	0	0	6	2	8.7	33.3
Girls	35	5	11.6	14.2	18	2	10	11.0	17	3	13.0	17.6

Among the forty-three cases of urinary infection under observation, the total number of deaths was seven (16.2%). This is not so high a figure as it appears, since the largest number of deaths occurred among those children who were already debilitated by some other disease. The table shows that the mortality rate was twice as high in the secondary group of cases as in the primary group, being 21.7% and 10% in these two groups respectively. Neale (1931) in a study of one hundred and seventeen cases found the mortality rate to be 7%, and Craig (1935) found it to be 14.7% among his group of sixty-one neonatal cases.

Where pyelonephritis occurs as the primary disease it usually runs a more severe course than the secondary case, with the exception of those cases following gastroenteritis in young infants.

As a rule the younger the child the more severe is the condition and six out of seven fatal cases occurred below the age of a year. The only other death was a boy of two and a half years, whose resistance to infection was already lowered by measles, pneumonia and enteritis, before the onset of a terminal pyelonephritis. Although there were several severe cases among the older children the response to treatment was better, and there were no deaths among them.

Table 13 shows that more deaths occurred among the girls than the boys of the series. If the number of children of each sex under observation is considered it is found that the actual percentage of deaths was higher in the boys in the total and secondary groups. The number of boys under observation is however too small for any conclusions to be drawn as to the severity of infection in this sex.

The high mortality rate in the secondary group is due to the severity of the illness when it followed gastroenteritis, four out of eight such cases being fatal. If this type of case is excluded the mortality rate of this group is lower than the primary group.

The number of pus cells in the urine is not necessarily an indication of the severity of the disease. Chart 11 shows that while the illness is at its height there may be no pus in the urine, and that as soon as improvement sets in a large amount of pus is found. Monti (1893) noted this and stated that "clear urine is a harbinger of evil, cloudy the promise of a successful ending". It was noted however that in the severe cases under observation a larger number of pus cells were found at some stage of the disease than were ever present in the mild cases.

Epithelial and granular casts were more often found in

the severe cases and where numerous usually indicated that infection was severe. Repeated examinations of the urine of the forty-three children with urinary infection, revealed the presence of casts in seven. Five of these were severe and three died. The remaining two cases were mild and only a few casts were seen.

In all the acute cases albumen was present, but a large amount, especially if associated with the presence of casts in the urine appeared to indicate that severe renal damage had occurred.

Table 14 shows the urinary findings in six fatal cases.

TABLE 14

Urinary findings in six fatal cases

Case	Age	Sex	Initial Disease	Albu- men	Pus	Casts	Organisms
R. B.	6/12	F	Pyelonephritis	+	**	-	***
P. W.	10/365	F	Pyelonephritis	+	**	**	***
G. P.	2 $\frac{1}{2}$	M	Measles and Enteritis	**	**	**	**
H. D.	9/12	F	Gastroenteritis	+	+	+	**
E. B.	6/12	F	Gastroenteritis	**	+	-	**
S. H.	3/12	F	Gastroenteritis	+	+	-	+

In the group of children below the age of a year the symptoms indicative of severe infection were persistent diarrhoea and vomiting, cyanosis, extreme pallor, meningismus, drowsiness and diminished urinary output. In the older children the severity of the disease was evidenced by pallor, puffiness of the face and attacks of one-sided pain, with temporary absence of pus in the urine. In both groups hyperpyrexia occurred in the severe cases and was a particularly grave symptom in the younger child.

Diagnosis

In many cases, where the symptoms are characteristic and an accurate history is obtainable the diagnosis of acute pyelonephritis can be confidently made, before a specimen of urine has been examined to confirm it.

In infants the attacks of blueness and collapse and the occurrence of shivering or rigors are practically diagnostic. In older children an indefinite illness with abdominal pain and frequency of micturition is suggestive of this condition.

On examination few physical signs are found except pyrexia. The infant is very irritable, resents being handled and may seem to be tender all over the body. The older child is usually pale and looks ill and tenderness in the abdomen or

loin may be found. Examination of the urine will usually confirm the diagnosis except in the cases where the affected kidney has temporarily ceased to drain. In these cases there is frequently tenderness in one loin and a tumour corresponding to the enlarged kidney is sometimes felt.

In infants the differential diagnosis will rest between gastroenteritis, pneumonia, meningitis and otitis media. As diarrhoea and vomiting are frequently present many of these children are at first thought to be suffering from gastroenteritis and the two conditions can only be distinguished by the examination of the urine and the response to alkaline treatment. The rapid respirations, high fever and attacks of blueness often lead to an initial diagnosis of broncho-pneumonia particularly when a slight cough is present. There is however a complete absence of signs in the chest. Where drowsiness, vomiting and head retraction are the predominating symptoms it may be impossible to exclude meningitis without a lumbar puncture. Where the child is irritable and appears to have pain, otitis media may be suspected, but can be excluded by an inspection of the ear drums.

In older children the conditions most likely to give rise to difficulty in diagnosis are appendicitis, typhoid fever, pneumonia and military tuberculosis. An inflamed pelvic

appendix frequently gives rise to dysuria and frequency of micturition. An examination of the urine will usually solve the problem and a rectal examination may also be helpful by revealing pelvic tenderness in appendicitis. The pulse is likely to be more rapid, and the temperature lower in appendicitis. In doubtful cases a leucocyte count may be of use, as the white count will be higher in acute appendicitis. Where the onset is insidious and pallor, lassitude, abdominal pain and diarrhoea are predominating symptoms typhoid fever may be suspected. There is however an absence of rose coloured spots, The spleen is not often palpable and the widal reaction will be negative. As in the younger child the short dry cough, pain in the chest and increased respiratory rate which are sometimes present may lead to an early diagnosis of pneumonia or basal pleurisy. These conditions can be excluded by the absence of signs in the chest and if necessary X-ray examination. Leucocytosis will be more marked in pneumonia than in pyelonephritis. Occasionally acute miliary tuberculosis is suspected, especially where increasing pallor and lassitude and irregular pyrexia are marked symptoms. The examination of the urine, the response to treatment and if necessary a Mantoux test should exclude this.

Prognosis

The prognosis in pyelonephritis in children must be given guardedly, since relapses and recurrent attacks tend to occur, especially if some unsuspected abnormality of the urinary tract is present. Generally speaking however, the older the child the better is the prospect of recovery, and in a child above the age of two years the ultimate prognosis is excellent. The majority of fatal cases occur below the age of a year. Pyelonephritis is especially serious when it occurs as a complication of gastroenteritis in a young infant and is frequently fatal. The more dehydrated the child, the worse is the prognosis.

The condition must be considered grave when a gradual rise of temperature to a high level occurs, in spite of full alkalinisation of the urine (Chart 13). Long periods of anuria, much restlessness, drowsiness or meningismus are serious symptoms. The significance of casts and much albumen in the urine has already been referred to.

The sooner treatment is commenced the better are the prospects of recovery and alkalies should therefore be administered immediately the condition is suspected and before examination of the urine has confirmed the diagnosis.

Chart 10 is from a fatal case of primary pyelonephritis in a child of six months in which the response to alkaline therapy was only temporary. Chart 13 is from another fatal case, in a child of three months, in which the condition occurred as a complication of infective diarrhoea. In this case there was a complete absence of response to alkalinisation of the urine and a steady rise of temperature occurred, death ensuing on the fourth day.

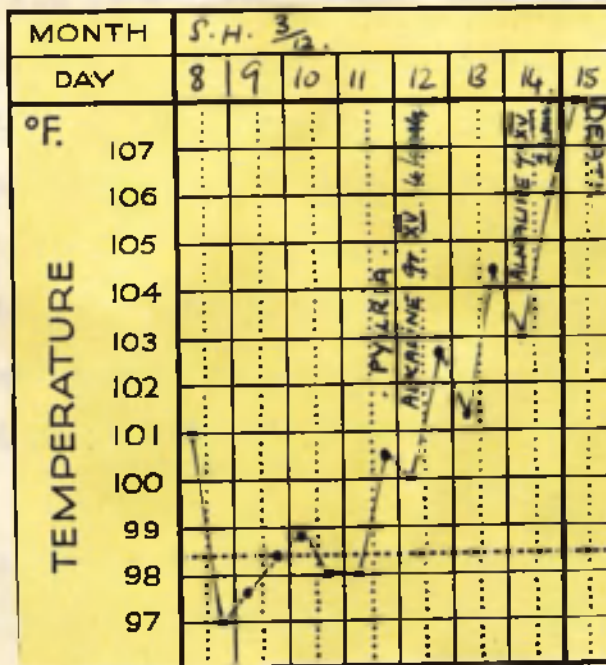


Chart 13. Fatal case of pyelonephritis following infective enteritis in which there was complete absence of response to treatment. Girl aged three months.

Prophylaxis

If the factors which tend to precipitate pyelonephritis are born in mind, it should be possible in many cases to prevent its occurrence or to modify the severity of the attack.

As urinary infection develops so frequently after gastrointestinal disorders, their prevention is of primary importance, and every attack of diarrhoea and vomiting should be regarded as a possible precursor of the condition, especially in children below the age of a year. Fewer cases would be overlooked if it were remembered that green stools are frequently a symptom of urinary infection and not always due to enteritis. Any tendency to constipation must be guarded against, but it is essential that violent purgation should be avoided since it may precipitate an attack of pyuria. As a sudden change in diet is sometimes a factor, this should as far as possible be avoided during hot weather or if the health of the child has been poor recently.

Local conditions such as phimosis require attention if there has been any tendency towards urinary symptoms. Children suffering from enuresis must be carefully observed, since it may happen that this is the only symptom of a mild urinary infection, which at any time may become more acute.

Where recurrent attacks of pyelonephritis occur a full investigation is called for in order to determine whether any abnormality of the urinary tract, either congenital or acquired, exists. The possibility of renal tuberculosis must be

remembered, especially in older children.

Finally, in all illnesses, especially those involving the gastrointestinal tract or giving rise to prolonged pyrexia, wasting or dehydration, the urine should be examined for pus at frequent intervals, and if urinary infection is suspected, alkaline therapy should be started immediately, without waiting for a specimen of urine to confirm the diagnosis.

Treatment.

The successful treatment of acute pyelonephritis in children is dependent upon three main principals - alkalies should be administered early and in large doses, an abundant supply of fluid should be given and the general health of the child should be maintained.

Various methods of treatment have been advocated, from Monti's "milk diet, luke-warm baths, every second day a good rubbing", to a variety of drugs. The character of the pyrexia has led to the use of quinine and salicylates in its treatment, neither of which have been found to be of value. Tannin, lead acetate, salol and guaiacol have been recommended, and Spa treatment has been advocated in resistant cases.

Urotropine has enjoyed a reputation in the treatment of urinary infection for many years, though it was not till 1906 that it was recognised by Boorse that it acted better in acid medium. This drug is still used in a certain type of case,

but in acute cases it has largely been superseded by the use of alkalies. It is easy to see how the alkalies attained the reputation they now possess. They were first used in the treatment of dysuria caused by the passage of oxalates or uric acid. In time it was noted that these drugs were also of use in the treatment of acute infective conditions of the urinary tract. Holt (1893) was the first to use potassium citrate in children suffering from pyelonephritis. The dose which he recommended was the smallest amount which would neutralise the urine and keep it so, and varied between grs. 24-48 in the day. It was employed by Thomson (1902) and Kastner (1905) in the same small doses, but as late as 1907 many clinicians had either not heard of it, or had failed to give it a trial.

This method of treatment is now widely used and is indeed almost specific in acute cases. It must be given in large enough doses to render the urine alkaline and keep it so throughout the day and night. For this reason it should be given at short intervals through the day and only slightly longer ones at night, the child being wakened to receive the dose. The drugs found to give the most satisfactory results are potassium citrate and sodium bicarbonate, and in hospital it is found that good results are obtained if a mixture containing these two drugs is administered at three hourly intervals during the day and four hourly at night. In very acute cases it may be necessary to give the medicine even more frequently, before the urine can be made alkaline. Once

this reaction is attained the dose can usually be decreased. The amount of alkaline varies from grs. 60-70 a day for an infant in the neonatal period, to grs. 200-300 a day for an older child. In the majority of cases an immediate improvement takes place and the acute symptoms begin to subside (Chart 14).

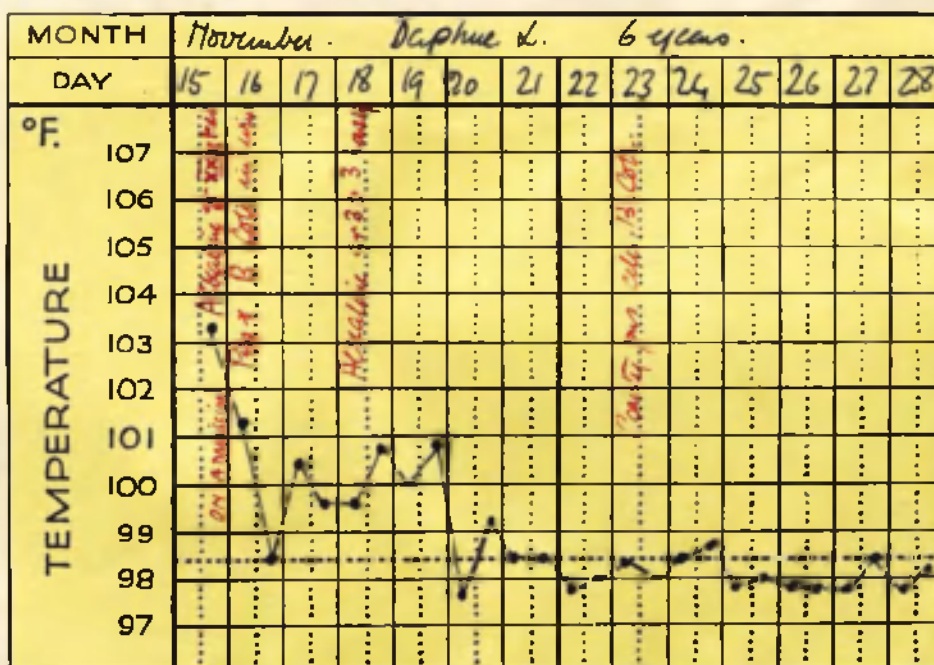


Chart 14. Acute pyelonephritis. Girl, 6 years.
Immediate response to alkaline therapy.

Although the acute symptoms are improved by alkaline therapy it is often found that the infection of the urine persists and other methods of treatment may have to be resorted to before it becomes sterile. Urtropine, used alternately with alkalies, may sometimes have this effect.

Better results have been obtained by the use of a Ketogenic diet, introduced by Helmholtz and Clark in 1931, as a result of observations upon children treated for epilepsy by this method. It is, however, a difficult method of treatment for a patient to employ at home and it has been largely superseded by the use of mandelic acid, which was found by Rosenheim (1935) to have a good effect in treatment of urinary infections of adults, and has now been modified for use in children. These two methods of treatment are especially useful in those cases which fail to clear up entirely with alkalies. In the past few months "Prontosil" (p - amino - phenyl - sulphonamide) has been advocated in the treatment of B.coli pyelitis during pregnancy, but I have had no experience of this method in children.

During the acute stage an abundance of fluid is an essential part of the treatment. Older children will take fruit drinks, barley water and milk. Infants should be given their feeds at more frequent intervals, diluted if vomiting is troublesome, and extra fluid in the form of boiled water or weak saline between feeds. Small quantities of weak tea are sometimes useful, as it not only quenches thirst, but also acts as a stimulant and diuretic, as well as having an astringent effect upon the bowel which is helpful if the stools are loose. Where vomiting is severe, a dehydration marked fluid must be given by other routes. A continuous drip of saline per

rectum can be given but as this is not often retained for long periods better results may be obtained by subcutaneous or intravenous saline administration. Blood transfusion has been recommended in the treatment of severe cases, (Bayma, 1928). Colon lavage has been advocated by Sack (1923) and Albee (1927) in the treatment of urinary infection in adults but the results in children are disappointing, though it is a useful method of treating diarrhoea when present.

The sudden attacks of cyanosis and collapse are best dealt with by the application of warmth, and the administration of small quantities of a stimulant such as brandy and coramine. Spirit of nitrous ~~oxide~~^{ether} in doses of M. 5-10 is sometimes useful in the treatment of recurrent collapses.

For the anaemia which follows or accompanies the condition some form of iron should be given. Children will take iron and ammonium citrate, flavoured with syrup, or Parrish's food.

In all cases the general health must be improved and the Vitamin content of the food should be high. Infants should be given orange juice daily and some form of cod-liver oil. Older children should have a good mixed diet, with plenty of milk, eggs and fresh fruit. Cod-liver oil should be given, especially in winter, and a course of sunlight treatment will sometimes be found to be beneficial. If possible the child should be sent to the country or seaside when well enough.

Summary

An investigation was made of 310 children admitted to hospital for treatment of a variety of conditions and the following facts were noted :-

1. The total incidence of urinary infection among these children was found to be 13.8%.
2. Urinary infection was found to occur four times more frequently in girls than boys, and the incidence was highest below the age of a year.
3. The condition frequently follows gastroenteritis, especially in infants. It is not a common complication of other diseases, and when it occurs, tends to run a mild course.
4. Normal urine, collected under aseptic conditions, contains not more than one leucocyte per high power field. During infection of the urinary tract this count is increased, but is not necessarily high.
5. The coliform bacillus is the infecting organism in the majority of cases.
6. Pyelitis is rare in children. The lesion most frequently present is bilateral suppurative interstitial pyelonephritis.
7. The pH of the urine shows no constant changes, either before the onset of urinary infection or during its course.
8. The symptoms of pyelonephritis vary according to the age of the child.

9. Important factors in the production of urinary infection are constipation, diarrhoea, purgation and a state of dehydration.
10. Chronic and recurrent cases may be due to congenital or acquired abnormalities of the urinary tract.
11. A moderate leucocytosis, due to an increase of the polynuclear neutrophils, was found to occur during the acute stage of the disease.
12. Haemolytic streptococci were isolated from the throat in a large number of cases of acute pyelonephritis.
13. The mortality rate from urinary infection was 16.2%. Where pyelonephritis was the primary condition the mortality was 10%. The largest number of deaths occurred in infants below the age of one year, and where the condition occurred as a complication of gastroenteritis.
14. The methods of prophylaxis and treatment are discussed.

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