PYOGENIC INFECTION OF THE URINARY TRACT IN CHILDREN.

THESIS PRESENTED FOR THE DEGREE OF DOCTOR OF MEDICINE, GLASGOW UNIVERSITY.

By Ethel Crawford, M.B., Ch. B.

April 1921.

PYOGENIC INFECTION OF THE URINARY TRACT IN CHILDREN.

Pyogenic infection of the urinary tract is a comparatively common disease in infancy and should always be borne in mind as one of the common causes of so-called "obscure fever".

It frequently gives rise to prolonged fever with profound constitutional disturbance and few or no local symptoms and this consequently leads to errors in diagnosis. When nervous symptoms predominate the condition may at first be mistaken for meningitis or otitis media. Owing to the prolonged fever a diagnosis of typhoid fever may be made, while the marked pallor and the wasting may suggest anaemia or merely marasmus.

ETIOLOGY

Although there are many predisposing causes the exciting factor is one of the pyogenic organisms and of these the bacillus coli is by far the most common. In many cases this organism is found in the urine in pure culture, but in some instances there is a mixed infection, usually with staphylococci or streptococci.

Among 70 cases admitted to Dr. Findlay's wards in the Royal Hospital/

Hospital for Sick Children, Glasgow from 1914 to 1920 the bacillus coli was present in 67 or 95.7%.

The following table gives an idea of the relative frequency with which different organisms occurred in the urine of these children.

TABLE 1.

B. Coli alone.	B. Coli with staphylococci or streptococci.	B. Coli with other organisms.	B. Proteus..	Strepto-cocci alone.	Total.
53	9	5	2	1	70

The infection may give rise to a simple bacilluria, to cystitis, to pyelitis or to suppurative pyelonephritis.

As the bacillus coli is thus almost invariably found to be the infecting organism the question of how it passes from the intestine to the urinary tract is of considerable importance and interest.

There are several different paths by which the bacilli may reach the kidney or bladder. They may ascend from without by way of the urethra: they may pass from the bowel by direct extension into the bladder or kidney where these viscera come into contact with the intestine, or they may be carried by the lymphatics and the blood stream.

An ascending infection by the lumen of the urethra has been thought to be the most probable mode of infection.(1) This hypothesis is based on the fact that females are more frequently affected than males/

males, that the female urethra is shorter than the male, that itis in close proximity to the anus and that the disease occurs in many cases after diarrhoea and at an age when there is the most frequent soiling of the parts by faeces. But a considerable number of boys are also affected by the disease in infancy and in these there is the same tendancy to diarrhoea as in girls, yet it is improbable that in boys the bacilli ascend per urethram.

Experiments carried out by Thiele and Embleton (2) to elucidate this have shown that it is difficult to produce an infection in this way. These authors found that when they placed organisms within the urethra they did not ascend the lumen, but were rapidly absorbed into the lymphatics in its wall and so passed along the wall of the bladder and the ureters and collected beneath the capsule of the kidney. From there they did not infect the kidney or enter the urine stream but passed quickly through the lumbar glands into the thoracic duct and so into the blood-stream. When they placed small doses of bacteria in the alimentary canal they were not absorbed at all but if the dose were large /and/ virulent the bacteria could pass through the uninjured mucous membrane of the intestine, enter the thoracic duct and so reach the blood-stream. They found that after intra-peritoneal inoculation the bacteria appeared in the urine in from ten minutes to half-an-hour, but if the thoracic duct were cut they did not reach the kidney or the urine at all, this affording proof that they had reached the kidney by the blood-stream.

Dr. Findlay (3) found, when experimenting on animals with the tubercle bacillus that although the bacilli could pass through the/

the uninjured mucous membrane of the intestine this did not often happen but when a catarrhal condition of the mucous membrane had been artificially produced the dissemination of the infection through the wall of the intestine was greatly facilitated.

In children a catarrhal condition of the intestinal mucous membrane is very common and may accompany diarrhoea, ileo colitis, or chronic constipation and thus allow the bacillus coli to migrate through the wall of the intestine and reach the kidney by the lymphatics and the blood-stream.

The pelvis of the kidney is especially susceptible to a bacillus coli infection and there the organism may settle down and multiply, producing pyelitis, and, if the substance of the kidney becomes involved, pyelonephritis.

The toxic appearance of the infants, the acute general disturbance, the fever, the nervous symptoms, and the occurrence of purpuric and septic eruptions all point to a blood infection. Although it is not easy to isolate the bacillus coli from the blood it has /been/ found on several occasions.

In cases of acute pyelitis in adults Kidd and Panton (4) found that the best time to obtain blood for cultures was during or immediately after a rigor. Rigors, however, are extremely rare in children and in this series of cases none was observed. On admission to hospital the infants are usually so acutely ill that one is loth to withdraw blood for culture, though undoubtedly the best time to find the bacillus would be during the acute febrile stage.

In 5 cases of acute pyelonephritis in this series blood cultures were made. In 4 of these cases blood was taken during the febrile /

febrile period within a week after the onset of the acute symptoms, while in the fifth case the temperature had fallen to normal on the day on which the blood culture was made, although it rose again on the following day. In the 2 cases in which the cultures were positive there was /a/ mixed infection; in the one bacillus coli and streptococci, in the other bacillus coli, streptococci and staphylococci. In the other 3 cases the cultures were negative.

Among the 70 cases in this series there was one case of a pure streptococcal infection of the kidneys.(See following example)

Case 1. The child was moribund on admission to hospital and died within a few hours. There were large subcutaneous haemorrhages over the body and many small purpuric spots. On post mortem examination numerous small abscesses were found in both kidneys. No other lesions could be found; the tonsils appeared normal. Films of pus from the kidney abscesses and of blood from asubcutaneous haemorrhage showed streptococci alone.

PREDISPOSING CAUSES.

Although the bacillus coli is the actual exciting cause of this condition there are, as previously mentioned, many factors which predispose to the infection. Any severe illness which lowers the resisting power of the patient may be a predisposing cause, but by far the commonest one is some disturbance of the intestinal tract such as gastro-enteritis, ileo-colitis or chronic constipation, while scurvy, where there has been haemorrhage from the mucous membrane of the bowel and from the pelvis of the kidney, would also seem to predispose.

It may be due to a calculus in the bladder or the kidney, although in one case in this series the calculus developed after years of/

of a chronic pyelitis.

Any condition which retards the downward passage of the urine may be a predisposing cause and cases of congenital stricture of the urethra, hydronephrosis and cystic kidney almost invariably, sooner or later, become infected in this way. In this series there were two cases of congenital hydronephrosis and one of cystic kidney. The following two cases illustrate the association of these conditions with pyelitis.

Case 2. Congenital Hydronephrosis. S.K. a girl aged 7 months. History of persistent vomiting and diarrhoea for a week with irritability and fever. On examination on admission to hospital nothing abnormal was found in heart, lungs or abdomen. The urine contained abundant pus and coliform bacilli. The day after admission the child was very ill and collapsed and saline solution was injected into the longitudinal sinus. The temperature varied between 103 and 104.6 degrees. Two days later the abdomen was somewhat distended and a mass was felt in the right iliac fossa. The urine still contained abundant pus. The child died on the fourth day after admission.

On examination post mortem the right kidney was found much enlarged, weighing $2\frac{3}{4}$ ounces and measuring $3\frac{1}{4}$ inches in length, with a cortical thickness of $\frac{1}{4}$ inch. The right ureter was much thickened and dilated, being at least as thick as a lead pencil, and a probe could be passed into the bladder through the ureter. The left kidney showed foetal lobulation, and weighed 5/8 ounces and was $2\frac{1}{8}$ inches long. It was distinctly hydronephrotic. The whole thickness of the organ from capsule to pelvis being 3/16 inches. The ureter was no thicker than string 1/16 inch, and, while patent towards the bladder, it was completely occluded at the junction of the ureter with the pelvis of the kidney. The bladder was contracted and the mucous membrane congested.

Case 3. Congenital cystic kidney. N.C. a boy aged 1 year. History of vomiting for a week and diarrhoea for three weeks. On admission the child was very ill, the eyes were sunken and he was much emaciated. The temperature was 100 degrees. pulse rate was 160 and respirations were 52 per minute. There was frequent cough, the/contained abundant pus and/urine/ coliform bacilli, and the motions were loose. Alkalies were given and the temperature fell to normal but the reaction of the urine remained acid and the pus increased in/

in amount. There was no improvement in the general condition of the child. At mid-night five days after admission the temperature suddenly rose to 107 degrees, the child became semi-comatose, and had fine tremor of the hands. He died the next morning.

Post mortem examination showed the left kidney slightly enlarged with multiple congenital cysts. The left ureter was greatly distended and full of purulent matter. The right kidney was normal. Both lungs showed recent broncho-pneumonia at the bases.

AGE.

The disease is much commoner in children under 2 years than in children over that age and the younger the child the more acute the disease.

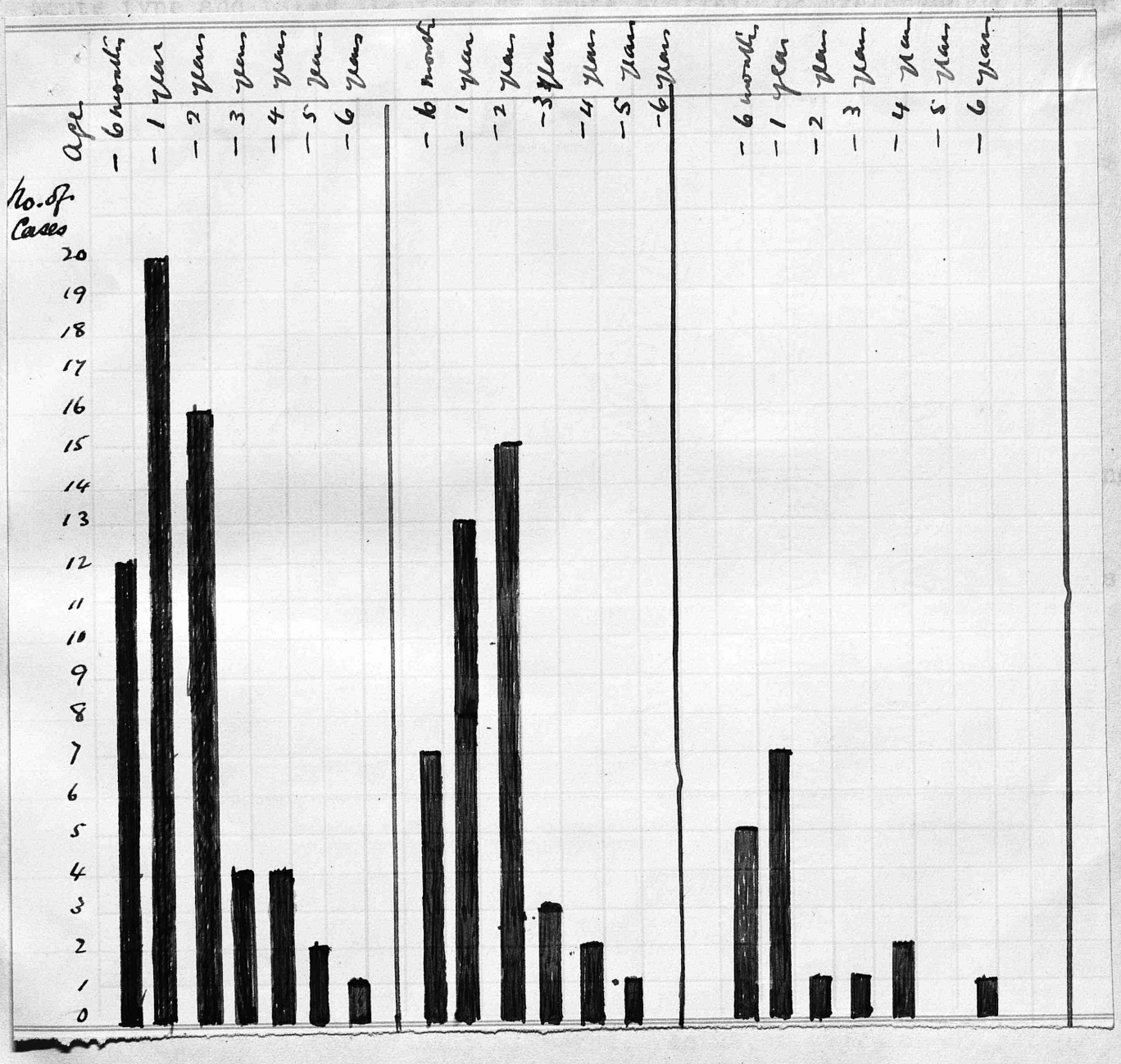
Among the 70 cases in this series 48 were under 2 years of age (68.5%). The following table illustrates the frequency with which the infection occurs in children under 2 and the comparatively small number of cases over 2 years of age.

TABLE 2.

Age of children.	Number of cases.
Under 6 months	12
Between 6 months and 1 year	20
Between 1 year and 2 years	16
Between 2 years and 3 years	4
Between 3 years and 4 years	4
Between 4 years and 5 years	2
Between 5 years and 6 years	1

Between 6 and 12 years there were 11 cases but as many of these gave an indefinite history, and were either chronic or recurring cases, it was difficult to ascertain at what age the disease had begun and, therefore they have been omitted from the above table.

CHART 1.



Number of cases and age of children up to 6 years.

Girls.

Boys.

In children under 2 years the disease is generally of an acute type and takes the form of acute pyelitis or pyelonephritis. In children over 2 the infection is of a subacute or chronic type and cystitis is more common than pyelitis. The prevalence of intestinal disorders in infants renders them especially susceptible to a bacillus coli infection.

Among 70 cases there was a history of diarrhoea immediately preceding the attack in 27 cases and of ileo-colitis in 1 case: 26 of these were under 2 years and 20 were under 1 year.

Children under 2 years of age undoubtedly show a marked susceptibility to many infections, as for example, measles and whooping-cough. As mentioned when tracing the course of the bacillus coli infection from the intestine I have taken it for granted that the pelvis of the kidney in the infant is especially susceptible to the bacillus coli as it is the site which usually first becomes infected, and in support of this may be mentioned other well known instances of susceptibility of special tissues in infants to specific micro-organisms. These are the eye and the female vagina to the gonococcus and the meninges to the meningococcus.

In later life these infections are comparatively rare.

SEX INCIDENCE.

The number of girls affected is much larger than that of boys.

Among 70 cases there were 52 girls (74.3%) and 18 boys (25.7%)

TABLE 3.

Age of children.	No. of girls.	No. of boys.
Under 6 months.	7 (58.3%)	5 (41.7%)
Between 6 months and 1 year.	13 (65%)	7 (35%)
Between 1 year and 2 years.	15 (93.7%)	1 (6.3%)
Between 2 years and 3 years.	3	1
Between 3 years and 4 years.	2	2
Between 4 years and 5 years.	2 (78%)	0 (22%)
Between 5 years and 6 years.	0	1
Between 6 years and 12 years.	10	1

Table 3 shows that under 6 months almost as many boys as girls are affected but that over 6 months girls are undoubtedly much more susceptible to the infection. It is possible that in infants under 6 months the portal of entry is by the bowel for at that age the bowel is extremely liable to injury. This would account for the greater prevalence of the disease at this age and the fact that boys and girls are almost equally affected. In later years when gastro-intestinal disturbances are less common it is possible that in many of the cases entry of the organism is effected through the urethral mucous membrane.

SYMPTOMS.

A. In infancy.

In infants the constitutional symptoms are marked and there may be no local manifestations pointing to an infection of the urinary tract. In some cases the disease seems to begin abruptly during good health, in other cases it developes during the course of some other illness, such as gastro-enteritis or pneumonia.

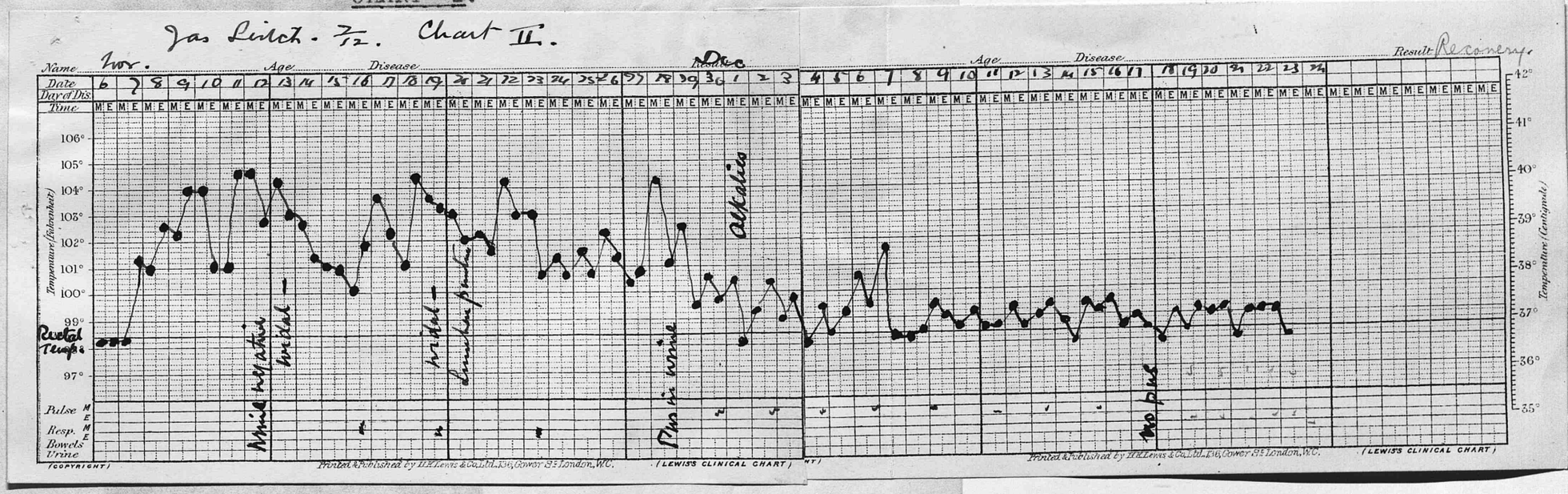
When the child comes under observation it is generally acutely ill and the symptoms may suggest meningitis, otitis media, typhoid fever, gastro-enteritis or nephritis. There is marked pallor, extreme general misery , restlessness, irritability, general tenderness, anorexia and sometimes oedema. The temperature is high, 104 degrees or more, and the pulse and respirations are rapid. There is sometimes retraction of the head, twitching of the limbs or even convulsions, but on examination of the cerebro-spinal fluid, a proceeding which was carried out in the cases which were in the first instance diagnosed as possibly meningitis, nothing abnormal was found.

It is only when the urine is examined microscopically and is found to contain pus and organisms that the diagnosis is clear. In some cases no pus or organisms may be detected at first, and the disease may run a course simulating typhoid fever, and pus and organism only be discerned later. The following is an example of this type of case.

Case 4. Chart 2. J.L. a boy aged 7 months was admitted to the surgical ward for an operation for inguinal hernia. The day after admission fever developed and as wheezing was noted in the chest he was transfered to a medical ward. On further examination nothing more was detected. The temperature/

temperature remained high, varying between 101 and 104.6 (rectal). On the 5th and the 12th days after admission blood was taken for the Widal test, which was negative on both occasions. Except for a trace of albumin nothing abnormal was found in the urine. Fever continued and lumbar puncture was performed but the cerebro-spinal fluid showed nothing abnormal. The motions now became loose and the child vomited frequently. During the fourth week of the illness pus and coliform bacilli were found in the urine. Alkalies were administered and the temperature gradually fell. In two and a half weeks the urine was free from pus and a week later the child was dismissed well.

CHART 2.



Tenderness of the kidney is frequently mentioned by writers as a symptom which is sometimes present, but owing to the general tenderness and the irritability of the infants I found it difficult to ascertain when there was definite pain of tenderness in the kidney regions, although sometimes an enlarged kidney was palpable. In infants a convulsion at the onset of the disease is not uncommon. In no cases in this series was a true rigor observed either in infants or in older children.

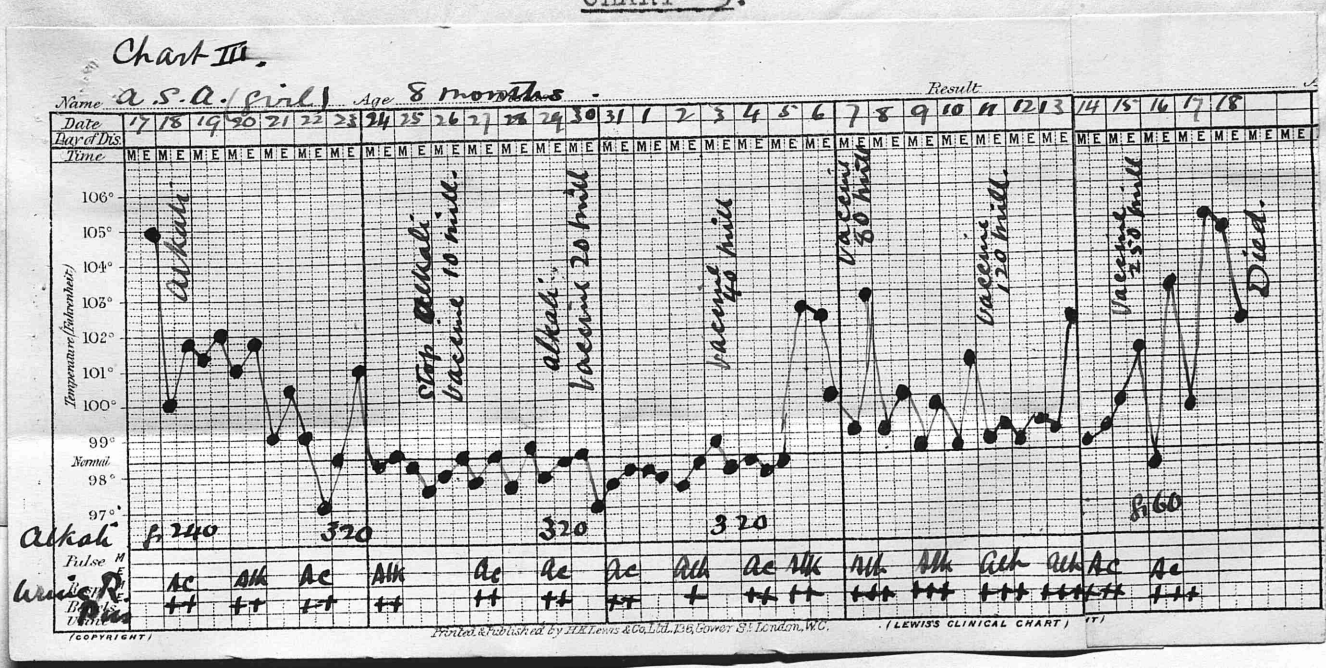
The following is a typical case of acute uncomplicated pyelonephritis/

pyelonephritis in an infant, with fatal result.

Case 5. Chart 3A.S.A. a girl aged 8 months, had always been a healthy child till 3 days before admission to hospital when she became fevered and seemed out of sorts. Two days before admission severe vomiting had begun and had continued, occurring after every feed. The day before admission there was diarrhoea and immediately before admission the child was said to have had a convulsion. On admission the child was very irritable, the temperature was 105, pulse 148, and respirations 50 per minute. She was a well nourished healthy looking child. The tongue was furred and dry, the throat somewhat congested. The heart, lungs, and abdomen were normal. The urine was acid in reaction, turbid in appearance and on boiling there was a haze of albumin. Microscopically there were abundant pus cells and coliform bacilli.

Alkalies were given, 240 grains daily and in two days the urine became alkaline. Two days later it again became acid and the alkali was increased to 320 grains. The urine again became alkaline and the temperature fell to normal, but the child became very drowsy, with a weak pulse and cold extremities. There was severe vomiting. The alkali was stopped and an antogenous vaccine was begun. The child improved although the vomiting continued. Smaller and more frequent feeds were given and the vomiting diminished. As the urine had again become acid the alkali was recommenced. The vaccine was given in increasing doses every fourth day. After twelve days of apyrexia the fever returned and the child became very irritable and restless. The amount of pus in the urine increased in spite of treatment with alkali and vaccine and the temperature was remittent in type. The left kidney was palpable but not tender. The child looked extremely ill, with sunken eyes and pulse almost imperceptible. The temperature rose to 105. The child died 5 weeks after the onset of the illness. Post mortem examination showed both kidneys slightly enlarged and congested. There were small haemorrhages into the substance and pus in minute amounts could be expressed from the pyramids. All the other organs were normal.

CHART 3.



B. In Older Children.

Among older children there are almost always symptoms which point to an infection of the urinary tract such as frequent and painful micturition and tenderness over the bladder or in the kidney region. There is often a considerable quantity of blood in the urine in these cases and they may at first be mistaken for nephritis.

Cystitis and subacute or chronic pyelitis are the forms the infection takes in older children and acute pyelonephritis is rarely found. Fever is not usual, the temperature generally remaining/normal/throughout the course of the disease. These cases often prove very intractable to treatment and the condition is liable to become chronic or to recur.

It occasionally happens that a child, who has had a mild chronic or recurring infection, suddenly developes acute symptoms. Recently a case of this kind was admitted to the ward.

Case 6. D.S. 2,5/12. female. History of having had an acute attack of pyelitis 2 years ago. The urine had not become entirely free from pus when, after 3 months treatment, the child was dismissed to a fever hospital as she had developed measles. After recovering from measles she had been seen occasionally in the outpatient department and had been treated with a vaccine. She had kept fairly well, but was said to have occasional "feverish turns" which only lasted for a day or two.

Fourteen days before admission she had become very irritable and vomited occasionally. On admission the child was highly fevered and the urine contained abundant pus cells. The temperature remained high, 105 and 106. On the third day a definite rounded mass, which was tender on palpation was felt in the left kidney region. The child was examined by a surgeon and removal of the kidney was advised. This was done, and the child is now apparently making a good recovery. The pathological report on the kidney stated that sections showed interstitial inflammation of a septic type. Small abscesses were found in the interstitial/

interstitial tissue of the kidney, and there was some catarrh in the tubules.

URINE.

As the diagnosis of this disease ultimately depends on the detection of pus and organisms in the urine it's examination is a matter of importance.

For examination a sterile specimen must be obtained. In order to make a diagnosis it is not absolutely necessary to pass a catheter if there is careful cleansing of the parts and absolute sterility of the receptacle. If, however, exact bacteriological diagnosis is desired it is essential to obtain a catheter specimen..

In appearance the urine is opalescent or turbid and the reaction is usually acid. The amount of albumin is generally small, and blood is rarely found in cases of pyelonephritis, but frequently in cases of cystitis.

For microscopical examination I find that the best method is to examine the freshly passed specimen immediately. If a deposit has had time to settle it should be shaken up, and, with a pipette a few drops obtained from the middle of the glass. When this is examined /under the microscope/ it reveals numerous pus cells and organisms. The number of pus cells to a field varies greatly in different cases and in the same case at different times. There may be only 5 or 6 or as many as 100 or 200 cells, this depending on the severity of the infection. In some cases the pus disappears altogether from the urine for a few days and one supposes that in these cases the pus is coming from one ureter only and that this/

This becomes blocked from time to time. When a few pus cells and organisms are found in the sediment of a centrifugalized specimen this is not necessarily to be considered as evidence of an infection of the urinary tract if no other symptoms are present, as in almost any urine a few leucocytes may be found and organisms cultivated from the sediment. On correlating the results of many clinical and pathological examinations of cases of pyelitis and of control cases, one comes to the conclusion that the most reliable test is the cultivation of organisms from a fresh drop of urine and not from a centrifugalized sediment.

Stained films show different forms of bacillus coli, the most usual being a short thick rod, others are long, chained and filamentous.

RENAL EFFICIENCY IN PYOGENIC INFECTION OF THE URINARY TRACT.

In several cases of pyelitis I tested the renal efficiency by the method described by Rowntree and Geraghty (6), who investigated the excretion of phenolsulphonephthalein by the kidney and introduced it as a test of the renal function.

The following technique was employed. 300 or 400 cc. of water was given half an hour prior to the test. The bladder was emptied with a catheter and 6 mgs. of phenolsulphonephthalein, neutralized with sod. hydrate in 1 cc. of water, was injected intramuscularly into the buttock. The urine was allowed to drain through a catheter into a test tube containing a drop of 25% sodium hydrate solution and the time of the appearance of the first pink tinge was noted. The catheter was removed and the amount of the pigment excreted was determined/

determined colorimetrically. Normally the pigment appears in the urine in from 5 to 11 minutes, and from 38 to 60% is excreted in the first hour, and from 22 to 25% in the second hour.

The delayed appearance and especially the diminished excretion are indications of functional derangement.

In all the cases of pyelitis examined the excretion of phenolsulphone-phthalein in the urine in 2 hours was much below the normal, although the time of the appearence of the pigment was within normal limits. (See Table 4)

TABLE 4.

No.	Name.	Sex.	Age.	Time of appearance of pigment in the urine.	Amount excreted in 2 hours.
1	M.N.	F.	2,4/12	7 minutes.	36%.
2	K.M'D.	F.	2,4/12	6 minutes.	18%.
3	C.N.	F.	6/12	10 minutes.	37%.
4	P.D.	M.	8/12	7 minutes.	51%.

DIAGNOSIS.

The diagnosis ultimately depends on the detection of pus and organisms in the urine, but it must be borne in mind that general symptoms such as fever, vomiting, convulsions, etc., may raise a suspicion of the disease before the urinary changes become manifest (See Chart 2) page 12).

The occasional appearance of a few pus cells and organisms in urine is not to be ascribed to an infection of the urinary tract in the/

the absence of general or local symptoms pointing to infection of the kidneys or bladder. As previously mentioned it is very common to find, especially on centrifugalizing, a few lencocytes and organisms in urine from cases in which there are no signs of any urinary infection. No doubt in normal individuals organisms are frequently entering the tissues and being excreted in the urine, but they produce no symptoms, are of no clinical significance, and are merely washed out by the urine.

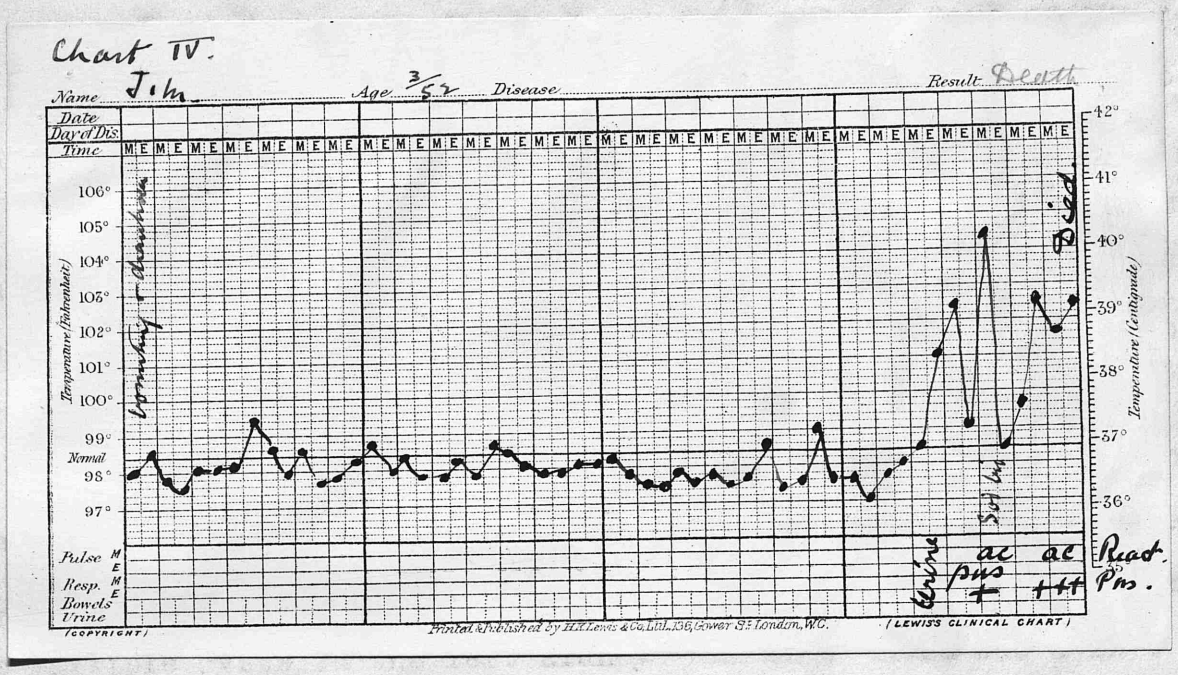
When the infection occurs during the course of some other disease it may run for a time unsuspected, but any unaccountable rise of temperature, especially during or after some disturbance of the intestinal canal, such as gastro- enteritis, should make one suspect a bacillus coli infection of the urinary tract, and demands an examination of the urine.

The following case illustrates this.

Case 7. Chart 4. J.M., a girl aged 3 weeks, was admitted to hospital with a history of vomiting, diarrhoea and wasting since she was one week old. On admission the child was much emaciated, the tongue was furred and there were patches of thrush on the buccal mucous membrane. The heart, lungs and abdomen were normal. The urine contained nothing abnormal. A few days after admission the diarrhoea and vomiting ceased and the child began to gain in weight. For the next three and a half weeks the child steadily improved and the gain in weight was 13 ozs. Then vomiting began again and the motions became loose. The temperature rose to 101. Two days later the urine contained a large quantity of pus. Sod. bicarb., 80 grains daily, was given, but the fever continued, the urine remained acid and the pus increased in amount. The child died 4 days after the onset of the fever.

Post mortem examination revealed multiple small abscess in both kidneys. There was a moderate degree of gastro-enteritis. The heart, lungs, liver and spleen were normal.

CHART 4.



In cases in which severe nervous symptoms are present acute pyelonephritis may at first be mistaken for meningitis . Other cases which may not be diagnosed at the beginning are those which run a course simulating typhoid fever, and in which no pus is found in the urine during the first two or three weeks. (See Chart 2) page 12).

PROGNOSIS.

In older children the prognosis is usually favourable as to life, but some cases prove very intractable to treatment and even after the urine has become apparently sterile the disease is liable to recur after longer or shorter intervals. This may be due to a new infection or a few bacilli may be retained in some pocket in the urinary tract where they remain inactive for a time until some upset, such as a chill or/

chill or one of the common infectious fevers, renders them infective again. (See Case 6.) page 14).

In infants the prognosis must be guarded. Some of the acute cases do not respond to treatment and death occurs in a few days or in a week or two after the onset of the disease.

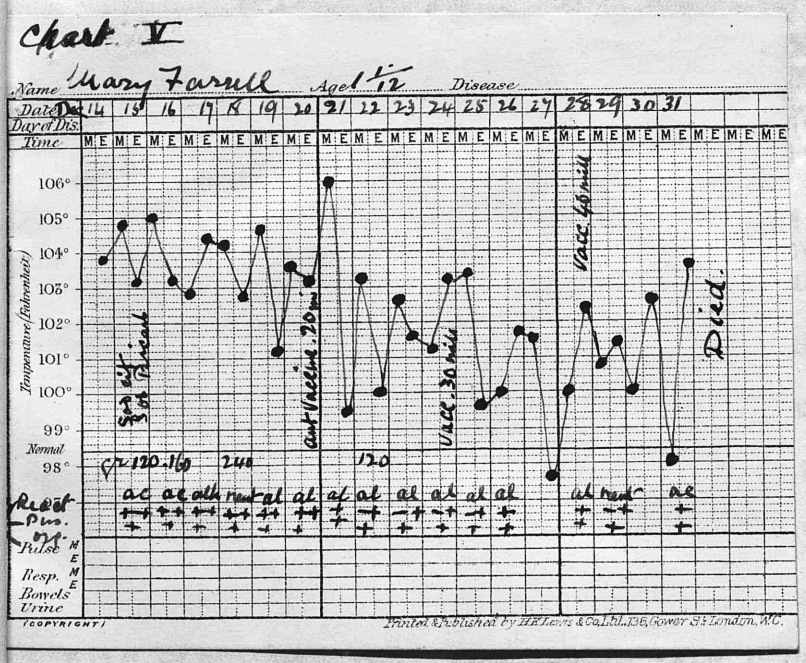
Among 18 cases in this series which were examined post mortem both kidneys were involved in 11 cases. In 8 there were multiple abscesses in both kidneys and in 2 there was early congestion of both. There was congestion of the pelves of both kidneys with abscesses in the right kidney in 1 case. In 1 there were abscesses in the right kidney only and in 1 in the left kidney only. In another there were abscesses in one kidney, (but in which was not stated.) In one there were multiple cysts in the left kidney and in 1 there was a left pyelitis. In one /of these/ cases there was a small patch of congestion in the bladder mucous membrane. In the 2 remaining cases the kidneys appeared normal to the naked eye, but in the one case there was congestion of the gastric and intestinal mucous membrane and hypostatic pneumonia: and in the other an early broncho-pneumonia and many enlarged glands in the mesentery.

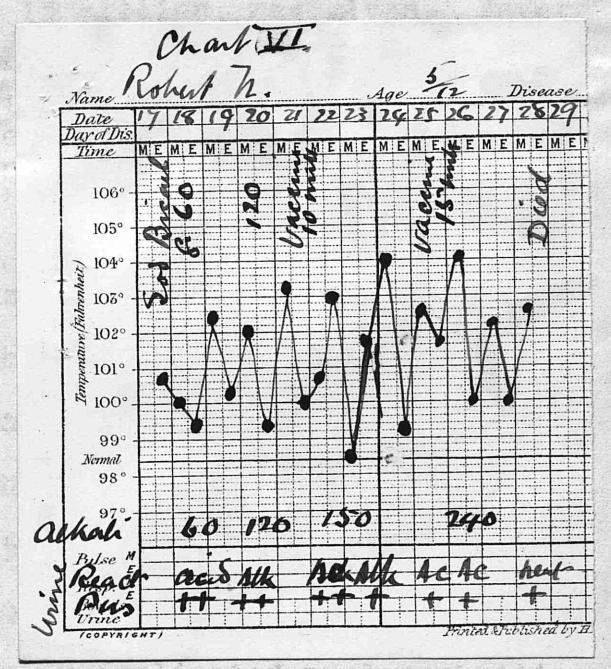
The following is an example of an acute fatal case with multiple kidney abscesses.

Case 8. Chart 5. Mary F. aged 1,1/12 years, was admitted to hospital with a history of fever, vomiting and cough for five days. The bowels were constipated. The child was small and spare with evidences of rickets. She was pale and miserable looking and was highly fevered. There was dulness at the extreme base of the left lung with deficient R.M. and moist rales, and/

and there was wheezing all over the chest. The left kidney was palpable. The urine was acid in reaction and contained abundant pus and coliform bacilli. Alkalies were given, but, in spite of the urine being rendered alkaline the temperature remained high varying between 102 and 105 and large quantities of pus persisted in the urine. After a week an autogenous vaccine was given. The next day the temperature rose to 106, the pus diminished slightly, but the child was very ill. Septic foci began to appear on the head and feet, and there was great tenderness in the renal regions. There was dulness over the interscapular region of the left lung, and moist rales were heard over the right back. The child became worse and died seventeen days after admission. At post mortem examination both kidneys showed multiple small abscesses situated especially in the cortex. The pelves contained some purulent matter. The bladder wall was hypertrophied. There was congestion at the base of both lungs.

CHARTS 5 AND 6.





In some cases when death occurs it is not due to the pyelonephritis alone, but to an intercurrent broncho-pneumonia, as, owing to the enfeebled condition of the child, this or some other complication is apt to arise.

The following is a case of acute pyelonephritis complicated by/

by broncho pneumonia.

Case 9. Chart 6. Robert N. aged 5 months. History of vomiting and diarrhoea for 2 days ten days before admission, with oedema of sacrum and scrotum for one week. The child was pale and seemed in pain. The tongue was furred and there was a slight cough. The abdomen was full and the right kidney was palpable and tender. The urine was acid and numerous pus cells and coliform bacilli were present. The temperature was 100.6, pulse 148 and respirations 56 per minute. Sod. bicarb., 60 grains daily, was given and the urine became alkaline two days later, but the temperature remained high and pus continued abundant. The alkali was increased to 120 grains daily. Three days after admission the breathing became rapid and there was impairment ofpercussion note in the lateral region of the right lung and moist rales at the base. Two days later as pus in the urine had not diminished an antogenous vaccine, 10 million bacilli, was given. The fever continued and the pus diminished slightly. Four days later the 2nd dose of vaccine, 15 million, was given. Fever still continued, the pulse rate rose to 164 per minute, the child became weaker and died on the 10th day after admission. to hospital. Post mortem examination:- There were multiple abscesses in both kidneys. The right one showed foetal lobulation with pale patches in the cortex and necrotic areas. The left was pale and the upper part was markedly necrosed and black. There was congestion at the apex of the right lung, and there were patches of broncho-pneumonia at the base. All the other organs were normal.

Out of the 70 cases 10 were lost sight of before any results were obtained as they had developed measles or some other infectious fever necessitating their removal from hospital.

Among 60 cases, 26 recovered 5 improved and 29 died. This gives a mortality of 48%, but this includes cases of pyelonephritis with complications. The death rate from uncomplicated pyelonephritis was 23%.

In 15 fatal cases broncho-pneumonia was present in 4, gastro-enteritis in 4, meningitis in 2, tetany in 2, congenital hydrnephrosis in 2 and cystic kidney in 1 case.

Of children over 2 years none died. Under 2 years there were 48 cases with a mortality of 60%. In /un-/complicated cases the death rate/

rate was 29%. In children under 1 year the mortality was 62.5%. In uncomplicated cases it was 31%.

TREATMENT.

1. Alkalinization of the urine.
2. The administration of antiseptics,
   Urotropin and helmitol.
   Flavine or proflavine.
3. The use of antogenous vaccines.
4. Combinations of these methods.

The aim of any form of treatment is to inhibit the growth of the infecting organism and to strengthen the tissues to resist the infection.

The bacillus coli undoubtedly flourishes best in an acid medium, as the reaction of the urine in which it is found is almost invariably acid.

Houston's experiments on the influence of reaction showed that although the bacilli grew equally well in urine whether it was faintly acid or faintly alkaline. strong degrees of acidity or alkalinity inhibited its growth. Martin carried out tests on the acidity of urine and found that it was impossible to raise the acidity of the urine to that degree which inhibits the growth of the bacillus coli. Fortunately the urine can be rendered sufficiently alkaline to modify its effects.

Alkalinization of the urine is, therefore, the method usually employed. This is the mode of treatment advocated by Thomson (5) and used by him with much success.

It is found that, when the urine has been rendered alkaline and has remained so for some days, the temperature usually falls and the acute symptoms subside. In the cases in the series which I followed/

followed while they were under treatment in the ward it was usual to begin with a dose of 60 or 90 grains of potassium citrate or sodium bicarbonate daily. In many cases the urine became alkaline in a few days, but in some cases large doses of the alkali were required, 240 or 340 grains, to keep the urine alkaline, as even after it had become so it was liable to become acid again and if this occurred there was sometimes a return of the fever and of the acute symptoms. Large doses of alkalies sometimes caused diarrhoea, and this necessarily lessened the effect of the alkali on the urine.

Among 60 cases alkalies were administered at the onset of the disease in 51 or 85%. Of these 35 were acute cases with fever, severe constitional symptoms and much pus in the urine; 16 were subacute with little or no fever and a considerable quantity of pus in the urine.

ACUTE CASES.

In 10 of the 35 acute cases after the administration of the alkali, the temperature fell, the general condition of the child improved, the pus in the urine diminished and soon disappeared and the child made a good recovery. (See Charts 2 and 7) pages 12 and 30)

In 9 of these cases the fever and the acute symptoms subsided, but the pus in the urine did not diminish, and, in order to effect a complete cure, on e of the other forms of treatment, either urotropin or a vaccine, had to be adopted. (See Charts 8 and 9) pages 30 and 31)

In 16 cases the alkali had no effect in reducing the temperature, in relieving the acute symptoms or in diminishing the amount of pus in the urine. (See Chart 10) page 31)

SUBACUTE CASES.

In 16 subacute cases complete recovery took place in 8 with treatment with alkalies alone, (see Chart 11), (page 32) but in the other 8 cases although the general condition of the child improved, the pus in the urine did not diminish till an antogenous vaccine had been given (See Chart 12) page 32)

In those cases therefore in which alkalies were given at the onset of the disease good results were obtained in 68.6% of the cases, but in 31.4% the alkalies proved unsuccessful.

Antiseptics.

Urinary antiseptics, such as urotropin and helmitol, act directly on the bacilli by the liberation of formaldehyde in acid urine.

Urotropin was given at the beginning of the infection in 7 cases, 5 of which were acute and 2 subacute. In none of the acute cases did urotropin seem to have any effect during the febrile period. In one of the subacute cases, however, urotropin proved successful, but in the other it was of no avail. (See Charts 13 and 14) page 33).

In 6 cases urotropin was given after a period of unsuccessful treatment with alkalies, and in 2 of these the urine cleared while the drug was being administered (see Chart 15), (page 34) but in 4 it produced no change. Thus in only 3 out of 13 cases (23%) did urotropin prove successful.

Intravenous injections of proflavine were tried in the following 3 cases but without any benefit.

The preparation used was a .2% solution of proflavine. The first case was that of a boy 10 years of age.

Case 10. There was a history of incontinence of urine and pain on micturition since he was 2 years old. He had been circumcised, but this had not improved the condition. He had been troubled with constipation for a year before admission to hospital. The urine contained numerous pus cells and coliform bacilli. He was treated with helmitol for 4 weeks without any improvement in the condition. An antogenous vaccine was then given in increasing doses for other 4 weeks, but the pus continued abundant in the urine. An intravenous injection of 100 cc. of .2% solution of proflavine was then given, and this was followed by three other injections at intervals of 4 days. After the injections the child's skin and conjunctivae were coloured a deep orange and the urine also was strongly yellow in colour. During the height of the action of the drug the amount of pus in the urine became less, and the bacilli became large, arranged in chains and less motile, but the improvement did not continue, in a few days the pus became as abundant as before and the small actively motile bacilli reappeared. No further injections of proflavine were given. The vaccine treatment was continued.

At this time an X ray photograph of kidneys and bladder was taken but it showed no evidence of stone. Six weeks later the child complained of severe pain on micturition, and there was tenderness over the bladder. Another X ray photograph was taken and this showed the presence of a stone in the bladder. After removal of the stone the pus gradually disappeared from the urine.

The second case in which proflavine was given was one of acute pyelonephritis in an infant aged 14 months. (See Chart 15) page 34)

Case 11. There was a history of occasional vomiting and wasting of about 1 year's duration. On admission the child was much emaciated, and there was a pemphigoid eruption on head and hands. The urine contained pus and coliform bacilli and streptococci. The temperature was 100.6. Urotropin was given at first for 5 days, but without any effect. Then sod. bicarb. was given and in 5 days the temperature fell to normal but the pus did not diminish. 15 cc. of .2% solution of proflavine was then injected into the longitudinal sinus. Three days later 10 cc. were injected into the longitudinal sinus. After these injections the pus diminished slightly for 24 hours and the bacilli became less motile, but the improvement did not last. The reaction of the urine, when these two injections were given, was alkaline. The alkali was stopped and 3 days later the urine became acid. When it had been acid for 3 days 10cc. of solution of proflavine was injected with the longitudinal sinus on three consecutive days. The amount of pus in the urine varied a little from day to day but after the last injection of proflavine it was more abundant than before. The fever returned/

returned, the child was very irritable and there was rigidity of the legs. Sod. bicarb. was started again, and an antogenous vaccine was given. This seemed to have some effect in reducing the amount of pus, but in spite of all treatment the child died. Post mortem multiple abscesses were found in both kidneys.

The third case in which proflavine was given was an extremely chronic case of cystitis in a boy of 5 years of age.

Case 12. There was a history of frequent and painful micturition for 3½ years. The child looked healthy and well nourished. The urine was alkaline, contained scanty pus cells and very numerous bacilli of a long type. The temperature varied between 97.6 and 99.2 for a few days and then remained normal. Three days after admission sod. bicarb., 120 grains daily, was given. The following day an intravenous injection of 75 cc. of .2% solution of proflavine was given. The next day the amount of pus in the urine showed no change but the bacilli were of long filamentous forms. Four days later 200 cc. of .2% solution of proflavine was introduced into the bladder. This had no effect in reducing pus or organisms. Three further injections of 75 cc. solution proflavine were given intravenously without any permanent improvement taking place. The alkali was continued and an antogenous vaccine was given for 2 months but the condition remained the same as on admission. Urotropin was then given for 6 weeks, when pus and organisms seemed to diminish very slightly, and the child was dismissed.

VACCINE THERAPY.

Antogenous vaccines were prepared from cultures obtained from catheterized specimens of the patients' urine. The vaccine was injected subcutaneously in increasing doses every 4 days. The first dose was usually 5,000,000 or 10,000,000 bacilli. In some cases there was a slight rise of temperature or a little sickness after an injection but generally there was no reaction.

Vaccines were given at the onset of the disease in 2 cases only, but they did not relieve the acute symptoms and alkalies had to be administered instead.

In 27 cases in this series vaccines were given after varying periods/

periods of treatment with alkalies or urotropin and in all these cases good results were obtained. In some of the cases the amount of pus began to diminish after 2 or 3 injections (See Charts 8 and 12 (pages 30 and 32), but in others many injections were required before the urine finally became free from pus and organisms. (See Charts 16 and 17) (pp 34 and 35)

In 8 acute cases in which alkalies had been given without relieving the acute symptoms vaccines were tried, but they were unsuccessful. All these cases proved fatal and post mortem abscess formation was found in one or both kidneys. (See Charts 3 and 5, and Cases 5 and 8). (pages 13 and 21)

Alkalies were generally continued along with the vaccine treatment, and this combination was undoubtedly the most successful. In some of the very prolonged chronic cases in which the pus and organisms were long in disappearing from the urine urotropin with a vaccine proved useful.

Of the cases treated with antogenous vaccines good results were obtained in 73%.

CONCLUSIONS.

Pyogenic infection of the urinary tract occurs with comparative frequency in infants.

The Bacillus Coli is the most common exciting cause of the infection, though occasionally there is a mixed infection.

The chief predisposing cause is some disturbance of the intestinal canal, such as gastro-enteritis or ileo colitis.

Children under 2 years of age are especially susceptable to the infection.

Under 6 months girls and boys are almost equally affected. Girls 58%, boys 42%.

Over 6 months girls are much more susceptible than boys. Girls 78%, boys 22%.

The diagnosis depends on the detection of pus and organisms in the urine.

The prognosis is favourable in children over 2 years, but is grave in infants as they are very liable to develope an acute suppurative pyelonephritis.

The administration of alkalies during the acute stage of the infection gives the best results.

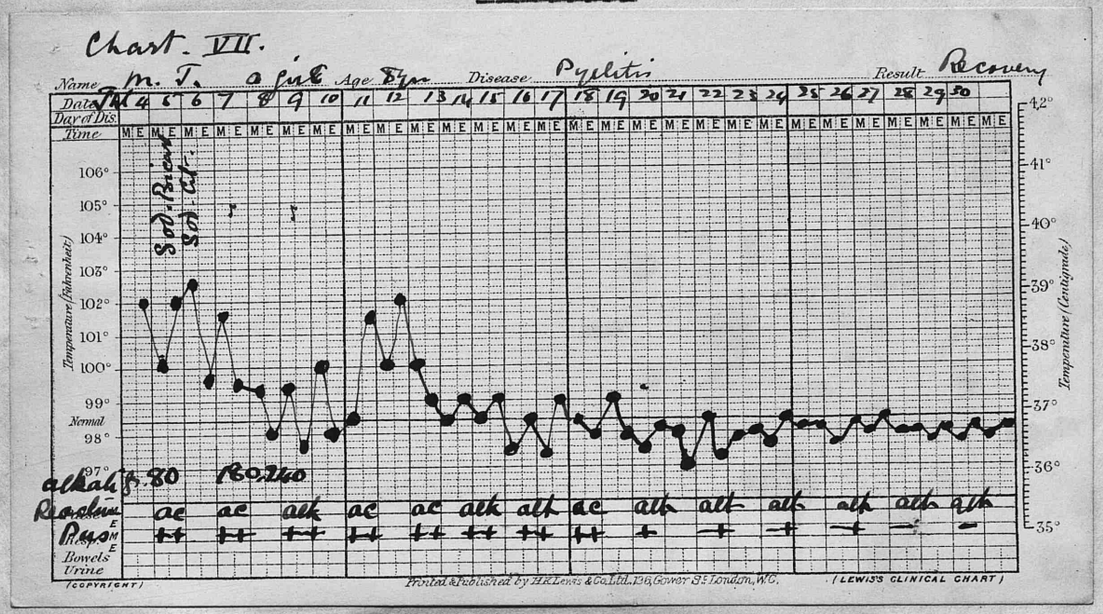
Urotropin is not successful in the acute period, but may prove useful in chronic cases.

Proflavine was not found of any benefit in the few cases studied.

Vaccines are not successful during the acute stage, but give good results when used later.

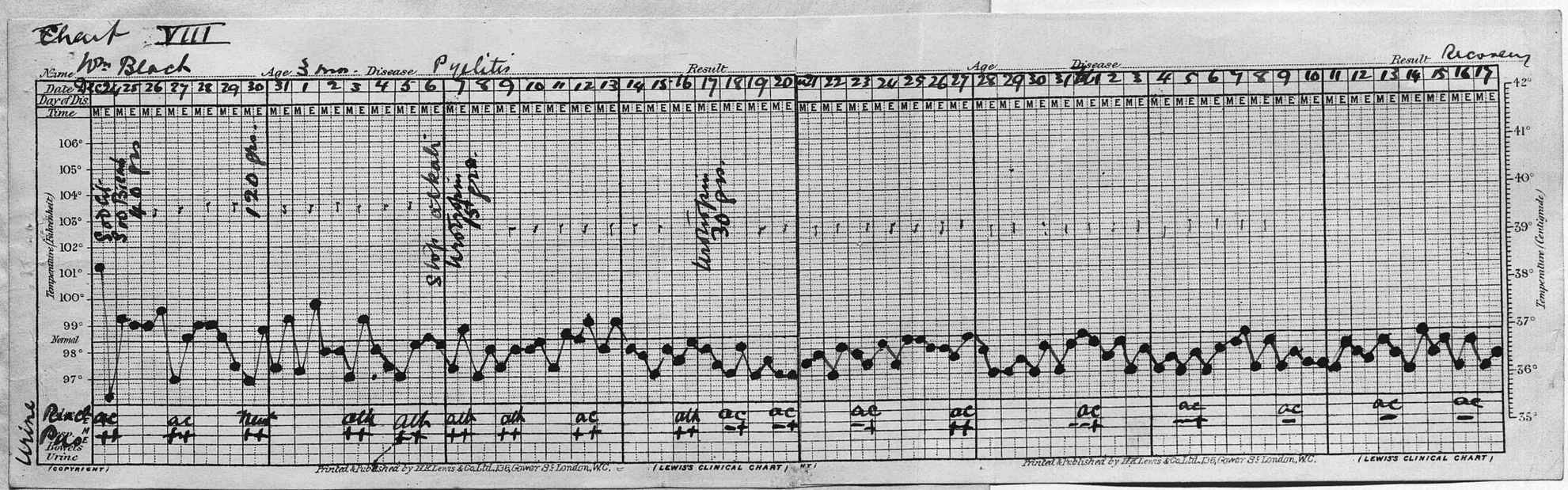
The most useful combination, in my hands, has been that of alkalies and antogenous vaccines.

CHART 7.



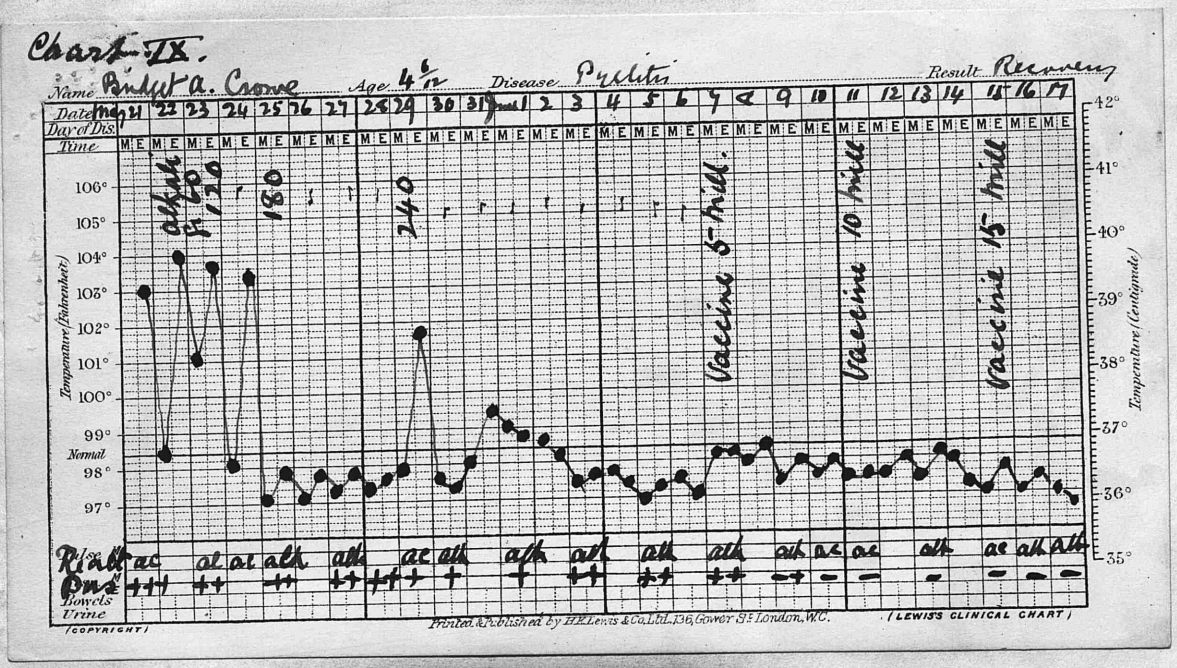
Acute case treated with alkalies. Recovery.

CHART 8.



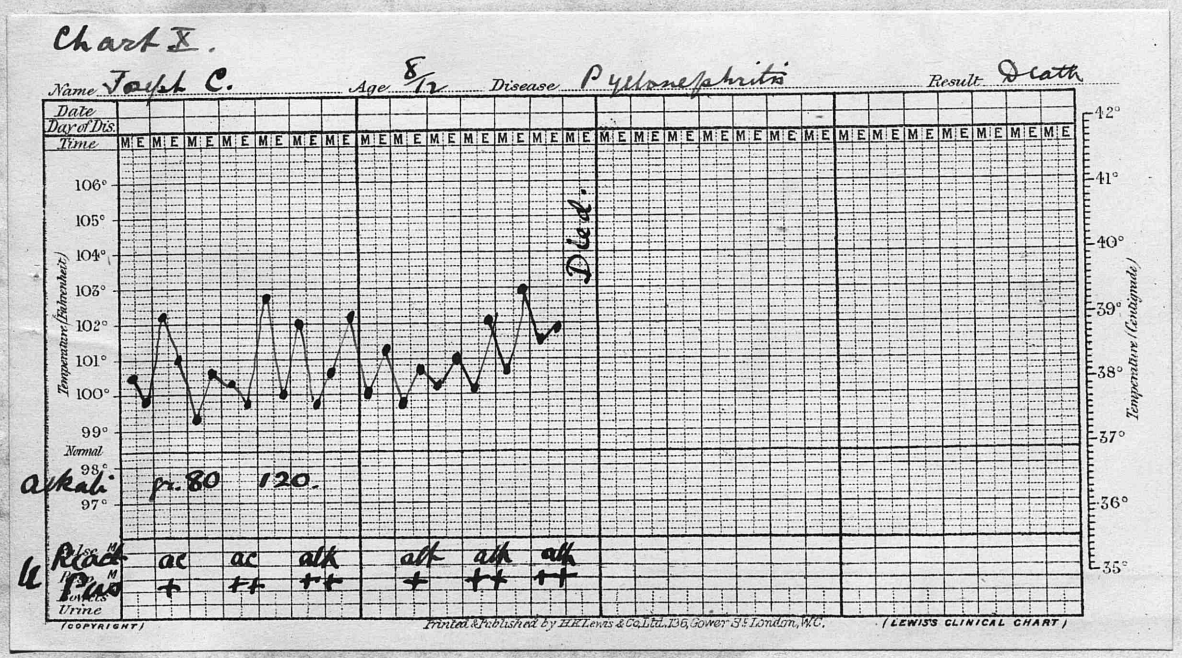
Alkalies did not diminish the amount of pus; after urotropin was given urine soon cleared.

CHART 9.



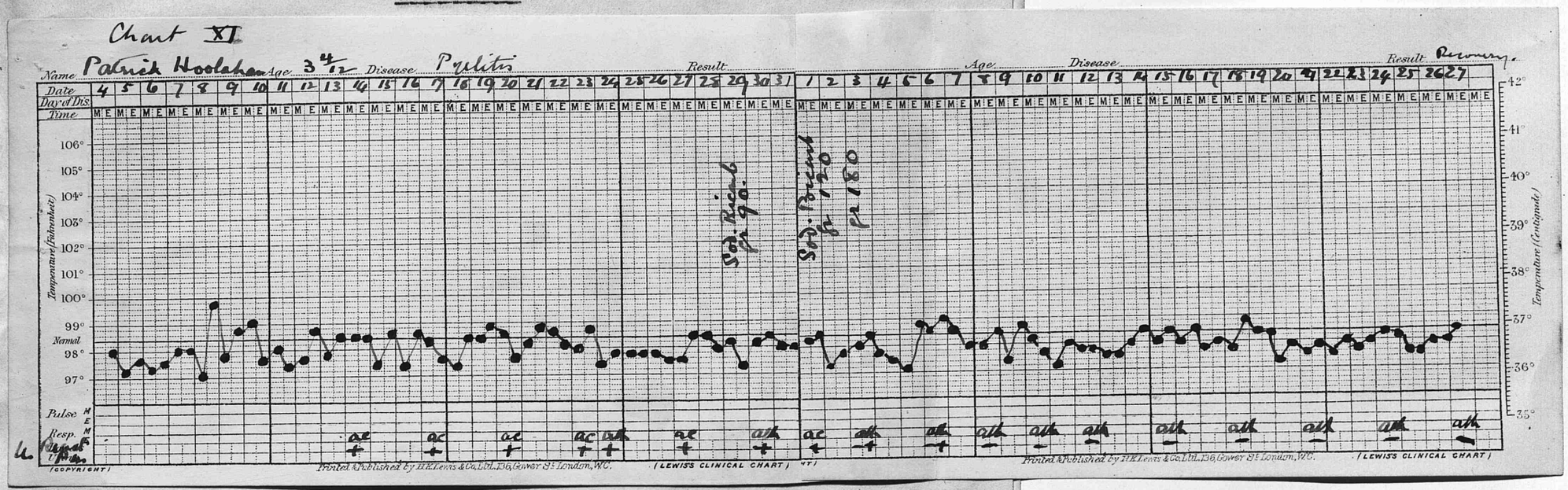
Acute case treated with alkali at the beginning. The amount of pus did not diminish with alkali treatment but diminished after the first injection of vaccine. Recovery.

CHART 10.



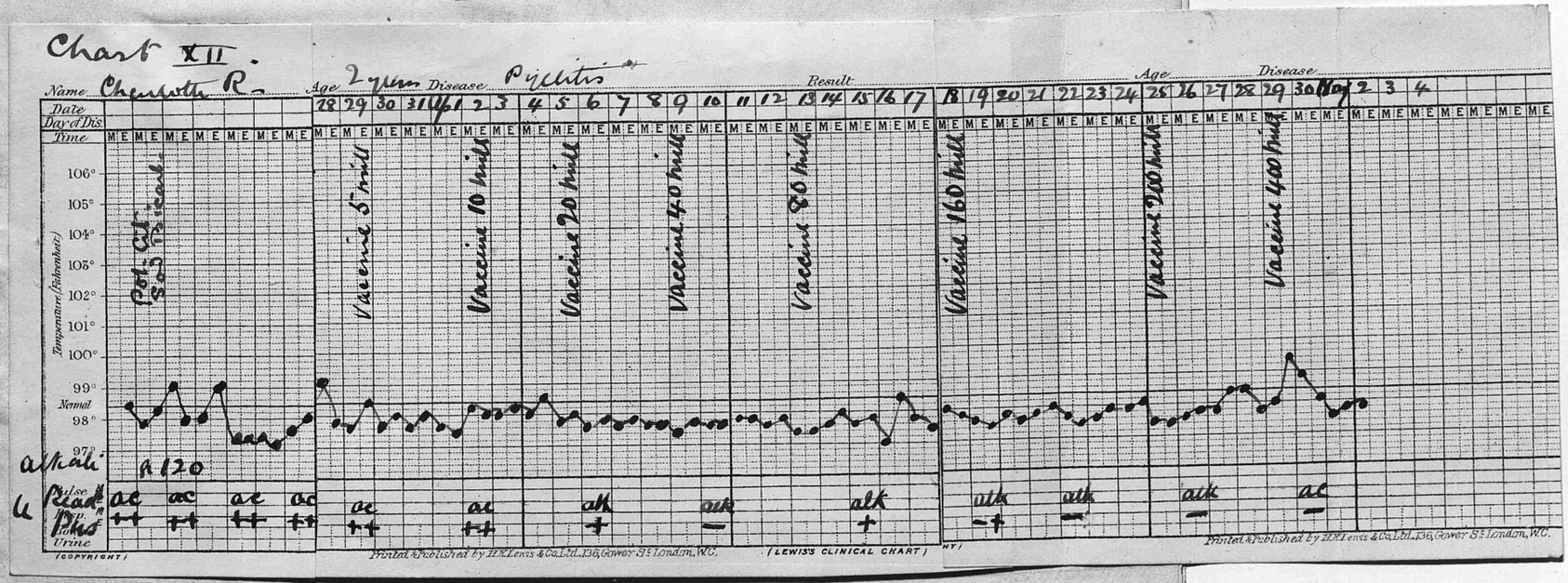
Acute fatal case in which alkali was unsuccessful in spite of urine becomming alkaline in 3 days.

CHART 11.



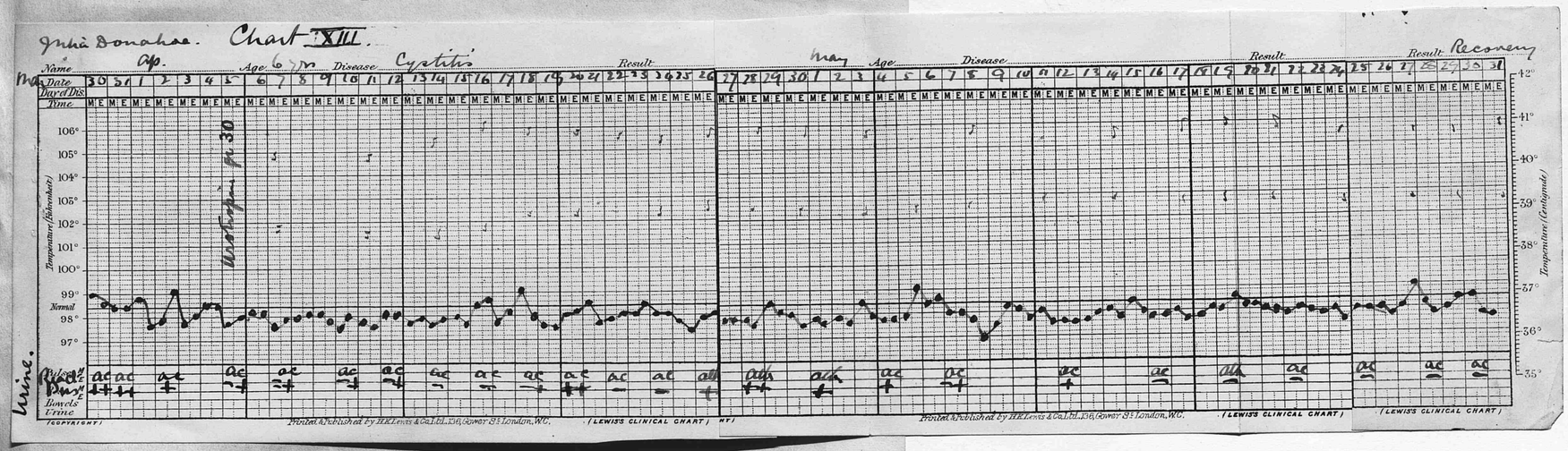
Subacute case which recovered rapidly when alkali was given.

CHART 12.



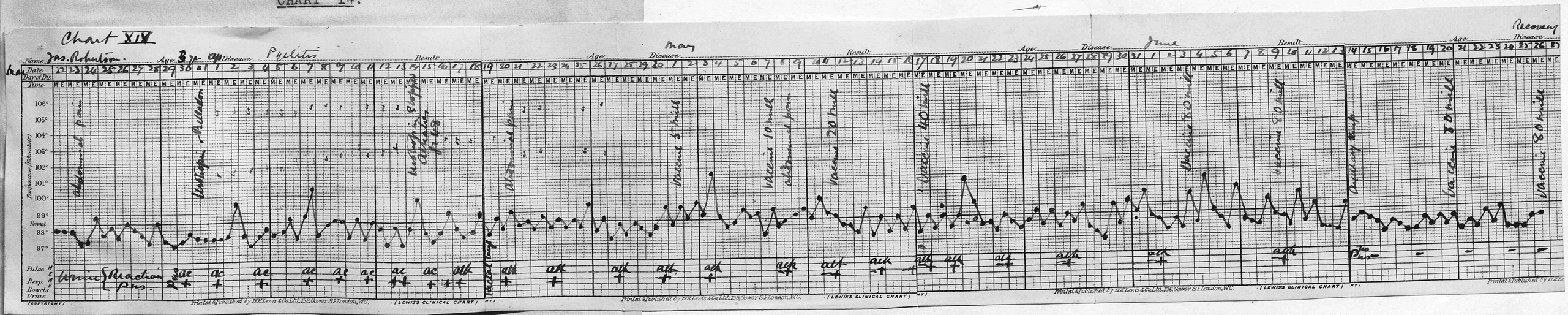
Subacute case treated with alkali at the beginning. Pus diminished after 2 injections of vaccine.

CHART 13.



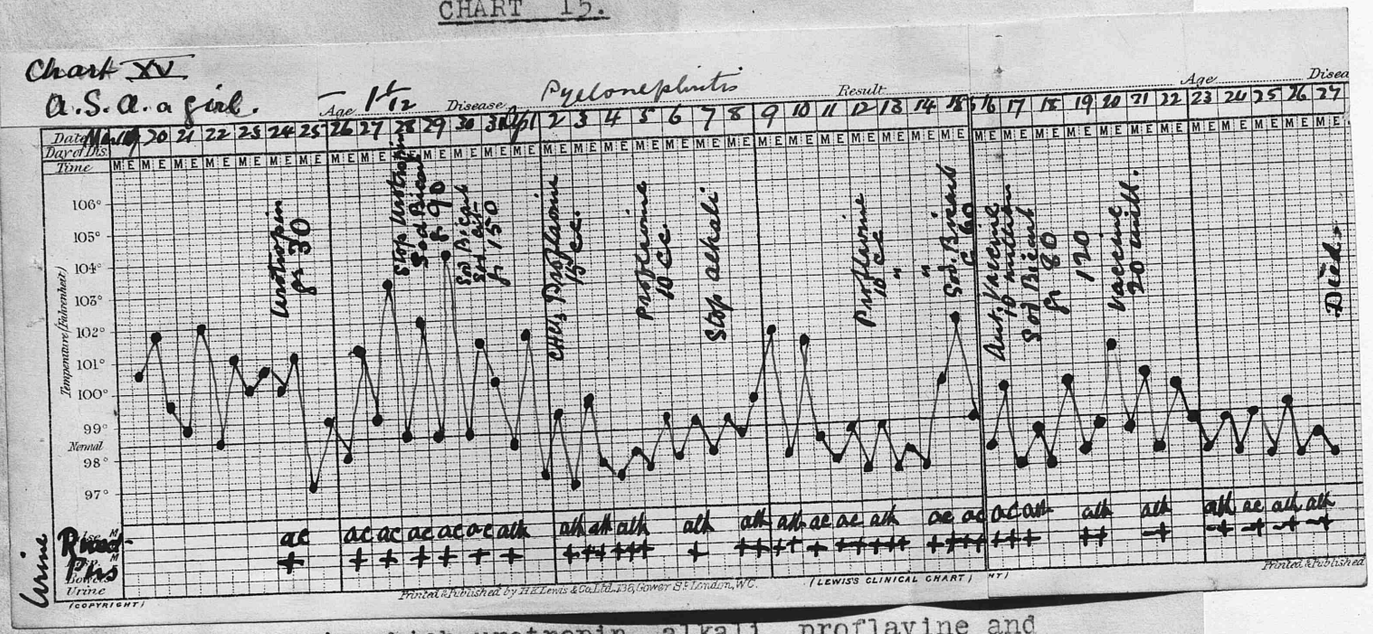
Subacute case which made a good recovery under urotropin alone.

CHART 14.



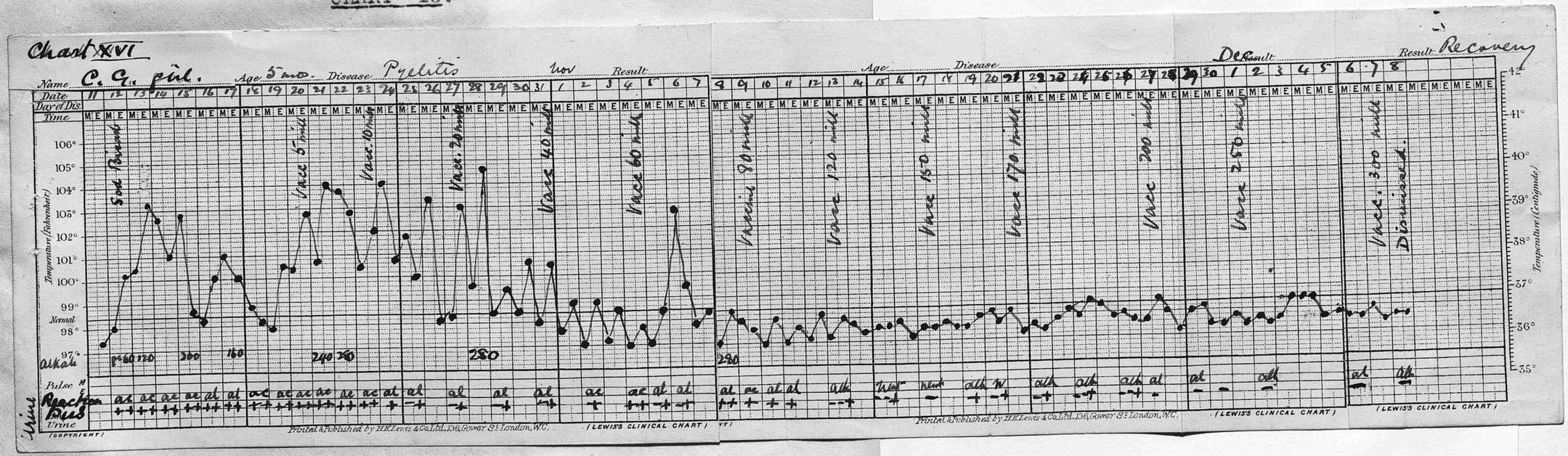
Subacute case in which urotropin and alkali had not any effect, but which recovered after a vaccine was given.

CHART 15.



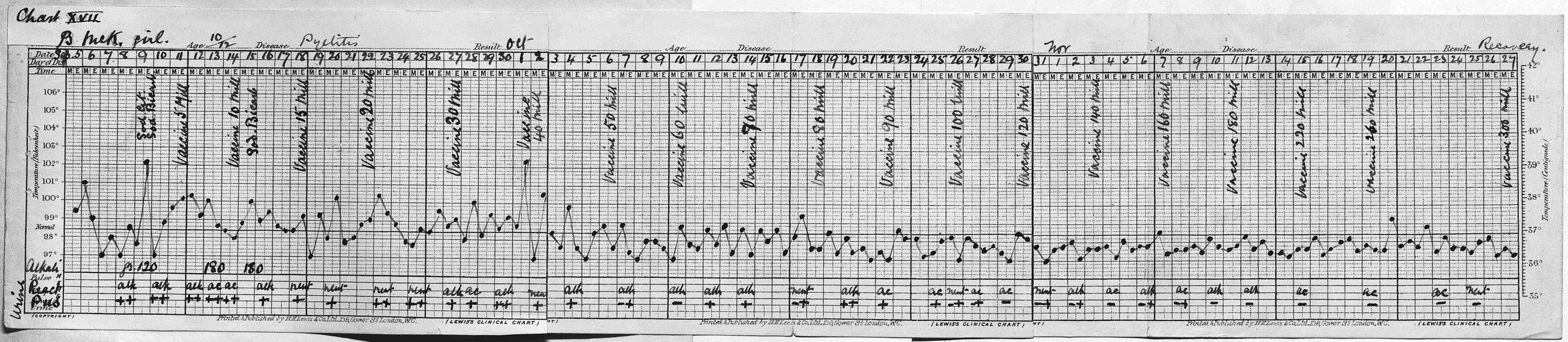
An acute case in which urotropin, alkali, proflavine and vaccine were given without any benefit. Post mortem multiple abscesses were found in both kidneys.

CHART 16.



An acute case treated with alkali and vaccine. 9 injections of vaccine were given before the urine was free from pus.

CHART 17.



A prolonged case treated with alkalies and vaccine. Pus diminished after 6 injections of vaccine, but did not disappear until after 15 injections had been given.

SIGNS.

++ = abundant pus.
+ = considerable.
−+ = little.
− = none.

TABLE 5.

SUMMARY OF CLINICAL SYMPTOMS.

Number.	Name.	Sex.	Age.	Date.	Previous diarrhoea.	Vomiting.	Chronic constipation.	Blood in motions.	Oedema.	Dysuria. Frequent micturition.	Abdominal pain.	Nervous Symptoms.	Other predisposing or accompanying conditions.	Result.
1	J.M.	F	3/52	19. 9.19	+	+								Died.
2	D.H.	M	5/52	23. 6.19									Wasting	Died.
3	J.F.	M	6/52	30. 7.18		+								Died.
4	H.M'L.	M	7/52	16. 6.17	+	+						Convulsions.	Marasmus.	Died.
5	W.B.	M	3/12	6.11.14	+									Recovered.
6	E.R.	F	4/12	11.10.19	+									Recovered.
7	D.S.	F	4/12	22. 5.19			+							Improved.
8	M.R.	F	5/12	6.11.17			+							Died.
9	D.H.	F	5/12	10. 9.14										Improved.
10	R.N.	M	5/12	17. 8.18					+				B. Pneumonia.	Died.
11	C.G.	F	6/12	11.10.17	+	+								Recovered.
12	I.C.	F	6/12	7.12.14										Died.
13	J.C.	M	6/12	18. 1.16								Convulsions Nuchal rigidity.		Recovered.
14	E.S.	F	6/12	17. 4.16		+						Twitching		Recovered.
15	M.G.	F	6/12	11. 7.19	+									Died.
16	M.R.	F	7/12	20.11.16						+		Convulsions	Tetany.	Died.
17	J.C.	F	7/12	3.12.19								Nuchal rigidity.		Died.
18	R.S.	F	7/12	15. 1.20		+						Nuchal rigidity stiffness of limbs.		Died.
19	N.M.	M	7/12	20. 2.20									Congenital stricture urethra& hydronephrosis.	Died.
20	S.K.	F	7/12	6. 3.16	+	+							Congenital hydronephrosis.	Died.

TABLE 5 CONTINUED.

Number.	Name.	Sex.	Age.	Date.	Previous diarrhoea.	Vomiting.	Chronic constipation.	Blood in motions.	Oedema.	Dysuria. Frequent Micturition.	Abdominal pain.	Nervous Symptoms.	Other predisposing or accompanying conditions.	Result.
21	J.L.	M	7/12	11.11.14	+	+								Recovered.
22	D.H.	M	7/12	31. 7.15	+	+	+						Wasting.	Improved.
23	F.M.	M	7/12	5. 3.15	+		+						Wasting.	Died.
24	M.L.	F	7/12	12. 8.17	+	+								Died.
25	J.C.	M	8/12	8. 5.20										Died.
26	M.D.	F	8/12	25. 8.19	+									Died.
27	D.C.	M	8/12	21.11.18									Wasting.	Improved.
28	A.S.	F	8/12	17. 8.19	+	+						Convulsions		Died.
29	J.C.	F	9/12	20. 4.16	+	+		+					Scurvy.	Recovered.
30	B.M'L	F	10/12	5. 9.17	+	+		+						Recovered.
31	N.H.	F	10/12	1. 2.16	+	+						Convulsions Nuchal rigidity.	Meningitis.	Died.
32	M.K.	F	10/12	20. 8.19	+	+						Nuchal rigidity.		Died.
33	B.G.	F	1	20. 8.19	+	+								Recovered.
34	N.C.	M	1	5. 9.19	+	+							Congenital cystic kidney.	Died.
35	A.R.	F	1	15. 6.17								Convulsions.	Tetany. Wasting.	Died.
36	M.F.	F	1 1/12	14.12.17										Died.
37	E.S.	F	1 2/12	13. 6.16		+								Improved.
38	E.D.	F	1 4/12	21. 6.15										Recovered.
39	R.W.	F	1 4/12	27. 9.19	+									Recovered.
40	A.S.	F	1 4/12	19. 3.18		+								Died.
41	E.A.	F	1 8/12	19. 5.18					+					Died.
42	S.T.	F	1 9/12	23.12.14										Recovered.
43	M.H.	F	1 10/12	22.11.15	+			+	+				B. pneumonia.	Died.
44	C.R.	F	2	21. 3.16							+			Recovered.
45	A.M'L	F	2	18.10.17					+				Anaemia.	Recovered.
46	J.M.	F	2 1/12	13. 8.19									Marasmus.	Died.
47	J.R.	M	3	22. 3.15						+	+			Recovered.

TABLE 5 CONTINUED.

Number.	Name.	Sex.	Age.	Date.	Previous diarrhoea.	Vomiting.	Chronic constipation.	Blood in motions.	Oedema.	Dysuria. Frequent micturition.	Abdominal pain.	Nervous symptoms.	Other predisposing or accompanying conditions.	Result.
48	P.H.	M	3,4/12	4. 5.18					+				Prolapsus ani	Recovered.
49	N.M'D	F	4	22. 8.16						+				Recovered.
50	B.C.	F	4,6/12	21. 5.17						+				Recovered.
51	W.M'C	M	5	4. 12.17						+				Improved.
52	C.M'C	F	6	29. 9.17						+	+		Vesical calculus.	Recovered.
53	B.S.	F	6	20. 3.15	+									Improved.
54	J.D.	F	6	20. 3.16						+	+			Recovered.
55	M.M'G	F	7	3. 7.16										Improved.
56	M.J.	F	8	4. 7.17						+	+			Recovered.
57	N.S.	F	8,6/12	11. 4.16										Improved.
58	J.R.	F	10	23. 3.16						+				Recovered.
59	R.H.	F	11,6/12	29.12.15		+	+			+				Improved.
60	J.T.	M	11,9/12	19. 9.17			+			+			Vesical calculus.	Recovered.

Table arranged according to age of children, showing prevalence of gastro-intestinal disturbances and nervous symptoms in children under 2 years, and the more frequent occurrence of dysuria, frequent micturition and abdominal pain in children over 2 years.

REFERENCES.

1. Box C.R. "Infections of the Urinary Tract by Bacillus Coli in Infants and Children."
Brit. Med. Jour. Oct. 15, 1912.

2. Thiele and Embleton. "The Path of Spread in Bacterial Infections".
Proc. Roy. Soc. Med., 1913.

3. Findlay, L. "The Intestine in Health and Catarrh as a Pathway of Infection to the Tubercle Bacillus."
Amer. Jour. Dis. of Child. May 1914. Vol.7.

4. Kidd, F. "Common Infections of the Kidneys."
1920.

5. Thomson, J. "On acute Pyelitis due to Bacillus Coli, as it occurs in Infancy".
Quart. Jour. Med. April 1910.
"Infection of the Urinary Tract in Children by the Colon Bacillus."
XVIIth Int. Cong. Med. London. 1913.

6. Rowntree and Geraghty. J. Phar. and Exp. Therap.
Vol. 1, 1910.

Other Books and Papers Consulted.

Fowler, J.S. "Diseases of the Genito-Urinary System."
Dis. of Child. March 1915.

Gorter, E. Leiden. "On Vaccine Treatment of the Infection of the Urinary Tract due to the Colon Bacillus."
XVIIth Int. Cong. Med. London. 1913.

Hanzlik and Collins. "Hexamethylenamin: the Liberation of Formaldehyde and the Antiseptic Efficiency under Different Chemical & Biological Conditions."
Arch. Int. Med. Nov. 1913, Vol, 12.

Holt, Emmet. "Diseases of the Uro-Genital System."
Dis. of Child. 1917.

Pardoe, J. Brit. Med. Jour. Oct. 15, 1915.

Ross, Athole. "The Bacteriology of the Urine in Children, more especially with Reference to acute Summer Diarrhoea."
XVIIthe Int. Cong. Med. London 1913.

Still, G.F. "Pyelitis in Infancy and Childhood."
Common Disorders and Diseases of Childhood.
1913.

Waller, H.K. "The Incidence of the Colon Group of Organisms in the Urine of Children suffering from Severe Enteritis."
XVIIth Int. Cong. Med. London 1913.

Wideroe, S. "Pyelocystitis in Infancy."
Brit. Med. Jour. Dec. 1, 1913.