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## ACUTE PYELONEPHRITIS DUE TO BACILLUS COLI.

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## INTRODUCTION.

INFECTIONS of the urinary organs with *B. coli* have only comparatively recently attracted general recognition and attention. It is important to be on the look-out for infection of the urinary tract with *Bacillus coli*, because it may give rise to grave constitutional symptoms without any prominent local manifestations; this is particularly so in children (*vide* p. 9), but it may also occur in adults. The urine is nearly always acid, and this may account for the omission of a more thorough investigation of the urine, and especially of a microscopical examination for pus.

*The Mode of Infection* of the urinary tract by *B. coli* has given rise to much interesting discussion. The *Bacillus coli* may gain a footing in the urinary tract in three ways:—

(1) Ascending infection, or the upward extension of the micro-organism from the urethra to the bladder, ureters, and pelves of the kidney. This method of infection occurs in females, especially in early life, and has been explained by the shortness of the female urethra and by its liability to be infected from the adjacent anus by fæcal discharges, and by thread worms. An ascending infection with *B. coli* appears to be rare in boys, but an undoubted example of this is its occurrence after circumcision (Morse). In adults there may be definite clinical evidence that the infection ascended from the bladder to the kidneys, namely, the onset with symptoms of urethritis or cystitis. Ascending infection has been disputed on the ground that the bladder and vesical orifices of the ureters may be healthy in cases in which there is pyelitis. Against this it has been urged that organisms may pass up mucous channels by means of ascending currents without any concomitant inflammatory changes (Bond). Ascending



infection has been advocated by many writers (Barnard, Dudgeon, Bond, and Box), and is probably the most frequent path of infection.

(2) Descending infection or infection due to the excretion of organisms from the blood into the tubules of the kidney. From experimental observations it is probable that the kidney tissue must be damaged before micro-organisms can pass through it (Sherrington), but this may be done by their toxins and by minute emboli, or may be the result of some existing disease of the kidney, such as a calculus, new growth, or nephroptosis. In some cases the isolation of organisms from the blood has been obtained, and thus favours the view that hæmatogenous infection may occur. Albarran (1889) and Macaigne (1896) early recognised hæmic infection of the kidney with *B. coli*, and described an ordinary parenchymatous nephritis and multiple miliary abscesses due to this cause. It is assumed that the organisms usually gain entrance into the blood stream through some damaged area of the mucous membrane of the bowel. Thus, it may follow gastro-enteritis, diarrhœa, or constipation. It has also been suggested that cracks about the anus may be the point of entrance for *B. coli* into the blood stream (Ritchie, Thomson).

(3) Trans-parietal infection or the passage of micro-organisms from the colon to the kidney, probably by means of the lymphatics. In order that this may occur the mucous membrane of the colon must be damaged so as to allow bacteria to penetrate freely into the wall of the bowel and so reach the lymphatics and pericolic tissues. There is reason to believe that *B. coli* may pass from the colon to the urinary bladder; and it is also logical to assume that the bacteria may pass from the colon to the pelvis of the adjacent kidney.

In one case which I often saw the history of a previous case of appendicitis one year before might have suggested that infection passed direct from an abnormally situated vermiform appendix to the pelvis of the right kidney; but in this case there were several relapses, and the left kidney was nearly always subsequently attacked, so it was more probable that the infection was not trans-parietal. If the signs of infection are confined to one kidney a local trans-parietal infection would appear to be a reasonable explanation. If an inflamed appendix



became adherent to the pelvis or ureter of the right kidney the latter might readily become infected.

It is unnecessary to argue that any one of these three modes of infection is the only one that occurs; probably each method is responsible for certain cases.

It seems reasonable to believe that in cases of descending hæmatogenous infection casts would be found in the urine, as the infection travels down the renal tubules; whereas in cases of ascending infection there would not be the same likelihood of finding casts in the urine. The presence or absence of casts would therefore appear to be a means of deciding in any given case whether or not the infection is hæmatogenous.

#### ÆTIOLOGY.

*Sex.*—It is most common in women, especially in connection with pregnancy; but it also occurs in males. In Morse's 50 cases in infants, 20 were males and 30 females. Out of 11 cases which have come under my personal observation 7 were males and 4 females.

*Age.*—It may occur at any age; my oldest case was in a man aged 77. In pregnant women Ward found the greatest incidence between 23 and 25 years of age. It is fairly common in young children.

*Pregnancy.*—Pregnancy is a disposing factor. The uterus may compress the ureters, especially the right ureter, and so favour infection. Further, toxæmia in pregnancy reduces the bactericidal power of tissues, and so may render the pelvis of the kidney more liable to infection. Constipation in pregnancy may favour the passage of colon bacilli into the circulation or their passage directly through the intervening tissues and lymphatics to the kidney. Pyelitis in pregnant women may be due to micro-organisms other than *B. coli*, but this organism is the most frequent cause. Out of 56 cases of pyelitis in pregnancy 44, or 78·57 per cent., were due to the colon bacillus (Ward). The period of pregnancy at which most cases occur is the fifth month (Ward). Pregnancy may light up an acute attack in a patient who has a chronic infection of the urinary tract with *B. coli*. In a case recorded by Routh there had been symptoms for 16 years pointing to chronic infection of the urinary tract.

*Chill.*—Chill appears to be an antecedent in some cases,



but it must be borne in mind that the initial chilliness due to the infection may be regarded as the cause rather than the first symptom of the affection.

*Food Poisoning.*—Food poisoning appears in some instances to have been the cause of colon infection of the pelves of the kidneys. It must, however, be remembered that the initial severe gastro-intestinal symptoms thought to be due to food poisoning may in reality have been the first evidence of acute colon infection of the kidneys. Previous illness, such as influenza, infantile scurvy (Thomson), has been thought to favour infection by lowering the patient's resistance.

*Site of the Infective Process.*—The symptoms may indicate that the affection is cystitis, prostatitis, pyelitis, pyelonephritis, or nephritis. But it may be difficult in a given case to decide that the infection is sharply confined to one of these regions. It may begin in the bladder and extend up to the pelvis of one or both kidneys, and in some instances the progress of this ascending infection can be quite clearly determined. Infection of the bladder is much commoner than pyelitis.

*Kidney Affected.*—The right kidney is much more often affected than the left. In 65, or 93 per cent., out of 70 cases collected by Legueu the right kidney was involved; this has been explained by greater liability to compression of the right ureter, at a point about an inch from the bladder, against the brim of the pelvis by the gravid uterus which inclined more towards the right side (Cumston, quoted by French). In order to explain the greater frequency of the affection of the right kidney in males and non-pregnant females it may be argued that the right kidney is more liable to be injured or to be floating, and so is a place of diminished resistance.

#### MORBID ANATOMY.

There are obviously varying grades of severity. In the most severe there are multiple abscesses, in the milder forms there is no suppuration. The condition of the kidney has been noted in cases treated by nephrotomy or by nephrectomy. In less severe cases the kidney is enlarged, sometimes to double its normal size; there is intense congestion and dilatation of the subcapsular veins; subcapsular hæmorrhages have been described. Catarrhal changes, œdematous swelling, and con-



gestion of the mucous membrane of the pelvis of the kidney with submucous hæmorrhages are seen.

Microscopically, the kidney shows cloudy swelling and a varying amount of small-celled infiltration. In more severe cases the kidney shows multiple foci of suppuration—pyelonephritis. In one case of this kind Barnard removed the kidney. In one of French's cases the kidney was exposed by operation and seen to be studded with multiple abscesses. As the patient's condition contra-indicated nephrectomy it was left; the patient recovered.

The inflammation may be confined to the pelvis of the kidney, or may implicate the ureter. The symptoms will vary accordingly; if the ureter is blocked swelling of the kidney and pain will result.

The only fatal case under my care was in a man aged 46, who died after an illness of three weeks resembling enteric fever in some respects, but not giving a Widal's reaction. His urine contained pus and a coliform bacillus. The kidneys weighed 10 oz. each and were soft and enlarged, and externally showed multiple discrete small areas, sometimes in clusters, in aspect resembling pyæmic abscesses. On section there were larger white areas, the colour of anæmic infarcts. In addition to those in the cortex there were some in the pyramids which were not unlike caseous tubercle; they were as large as a sixpenny piece and presented a most remarkable and unusual appearance. Microscopically these areas were commencing abscesses.

Primary and secondary forms of infection of the kidney and its pelvis with *B. coli* should be recognised. In secondary cases there is some existing disease such as calculus, whilst in primary cases no such cause for an acute infection with *B. coli* is forthcoming. Cases of secondary colon infection are prone to be extremely chronic.

#### SYMPTOMS.

The clinical features of colon infection of the urinary tract vary considerably. There may be bacilluria with few or no symptoms; in some instances the onset is very acute and the constitutional disturbance great, and in other cases again the course is very chronic, and a relapsing form may be



recognised. Just as pyorrhœa alveolaris may be the cause of grave symptoms, or may appear to be comparatively harmless, so is it to a less marked degree with colon infections of the urinary tract.

In cases of acute pyelitis the symptoms vary in different cases, and, though too rigid divisions must not be made, may be roughly divided into the following groups:—

- I. Local symptoms pointing to infection of the pelvis of the kidney, pain in the renal region, not infrequently a palpable tumour, and occasionally hæmaturia.
- II. General constitutional symptoms suggesting influenza, typhoid fever, infective endocarditis in adults. This type without any striking local symptoms is specially seen in children.
- III. Acute abdominal symptoms, vomiting, constipation, distension.

I. *Cases with Local Symptoms.*—There is severe pain in the back usually confined at first to one side, and more commonly the right, which is tender and rigid. The kidney is often distinctly palpable; this enlargement, which is probably largely due to distension of the pelvis caused by obstruction of the upper end of the ureter, may disappear very rapidly. The pain and enlargement of the kidney may subside and reappear on the opposite side, each attack lasting a few days. In recurrent attacks the sequence of events may be the same; thus in one case, with several relapses, the right kidney was first affected, and when this subsided the left followed suit. The pain may run down the ureter and imitate that of renal calculus. In one case the patient—a doctor—passed thick flakes, which accounted for the severe pain. For this reason it may occur in paroxysms. There may be increased frequency of micturition, pain on passing urine, and pain in the penis pointing to the presence of concomitant cystitis. The repeated calls to pass urine may greatly interfere with sleep.

II. *Cases characterised by Constitutional Symptoms, the Local Manifestations being latent.*—In this group there is the sudden onset of acute illness suggesting influenza or pneumonia. The patient usually feels extremely ill, may have severe headache, rigors, and a rapid onset of high fever. After suddenly shooting up, the temperature may remain high for some days and then suddenly fall; more often it is irregular



and may then suggest suppuration, infective endocarditis, or malaria. In rare cases herpes labialis has been noted (Herringham). In children there is usually an absence of symptoms pointing to the urinary organs. There are fever, malaise, loss of appetite, vomiting, and intestinal disturbance. John Thomson lays stress on the significance of rigors, for, unlike any other disease (except malaria) in children, it frequently causes rigors; in children, as a rule, the place of a rigor is taken by a convulsion. Delirium, squint (Thomson), and head retraction (Morse) have been noted in some cases, so that, as in other infective conditions, meningism may appear. Restlessness and distress have also been described as prominent features in children by Thomson.

III. *Cases with Acute Abdominal Symptoms.*—This group is characterised by abdominal pain, nausea, vomiting, most obstinate constipation, and abdominal distension. There is complete loss of appetite and a furred tongue. The clinical picture is therefore that of the "acute abdomen." Some of the cases I have seen were so like appendicitis or acute intestinal obstruction that a surgeon was on the point of being called in. It is most important that the urine should be examined in all cases of the "acute abdomen" type, for the presence of pus in acid urine should at once make the medical attendant revise a diagnosis of probable acute appendicitis. It seems highly likely that some cases in which a healthy, or practically healthy, vermiform appendix has been removed may in reality have been examples of acute infection of the kidney and its pelvis with *B. coli*.

After this brief consideration of the different groups of symptoms due to infection of the kidney and renal pelvis by *B. coli*, the clinical manifestations common to all cases may be mentioned. The onset is usually acute with a high temperature, which may shoot up to 104° or 105° F. in a few hours. There is often a rigor and the patient usually feels extremely ill. There is usually severe headache, and the patient may be extremely depressed, and even show some evidence of mental perturbation; afterwards his memory of what took place may be very vague. In acute attacks the pulse has been stated to be very rapid (Wright); in a case reported by Herringham the pulse rate was 168 during a rigor; but in the cases I have seen it has been remarkable how little



the pulse was quickened. There is a leucocytosis. Wright gives the average as 18,000–24,000, but in one of Morse's cases it was as high as 51,700. Anæmia develops rapidly and has been thought to be due to a specific hæmolysin (Durante, quoted by Morse). The blood is nearly always sterile. Dudgeon found that the agglutination reaction was of little or no value in the diagnosis of this disease.

The temperature may, after suddenly shooting up, remain persistently high for two or three days and then suddenly fall; but more often it is irregular, and may suggest supuration, malaria, or infective endocarditis. Some cases appear to be afebrile.

The urine is nearly always acid. It is paler than its specific gravity would suggest (Briscoe). In some cases it may be clear, or nearly so, and yet on cultivation show colon bacilli. Occasionally the odour is very foul, but usually there is nothing specially noticeable in this respect. It contains pus and commonly is turbid; the turbidity is due to the admixture with pus cells, epithelium, and bacilli. The turbidity is diminished, but not removed, by filtering; the pus and epithelial cells are removed, but the bacilli pass through (Thursfield). The amount of pus varies both in different cases and in the same individual. Large quantities may be passed almost suddenly, as if there was an abscess opening into the renal pelvis, or more probably as if the opening of the ureter into the renal pelvis had been temporarily blocked. Flakes, strings, or small masses of pus may be seen floating in the urine. Bladder, ureteral, and renal cell may be found microscopically. In one case the large epithelial cells of the kidney pelvis closely simulated gregarines. In rather rare cases renal casts are present, but generally they are absent; as already suggested, the presence of casts may be correlated with a descending or hæmic infection of the kidney. Albumin in small quantities—usually less than 0·1 per cent.—is present, and is generally in proportion to the amount of pus. In some instances there is blood. I have seen a very large quantity of blood in the urine; in this case the urine became clear and free from blood very rapidly, *i.e.*, in 24 hours. Twenty-four hours later blood appeared again; possibly the ureter had been temporarily blocked.



The acidity of the urine is a striking feature ; it is associated with the power of the colon bacillus to multiply in acid urine, and with the fact that the colon bacillus does not decompose urea into ammonia. As the acidity is inimical to the growth of other organisms, a pure culture of *B. coli* is often obtained. In infants the condition may be first suspected from the presence of a yellow stain on the napkins (Morse). Pus and bacilli may remain in the urine for some weeks after fever and symptoms have subsided ; chronic forms of infection are met with, in some of which there are no symptoms, whilst in others there is fever, obscure ill-health, or acute attacks are superimposed.

Crystals are seldom found in the urine, but when present in centrifuged specimens usually have bacilli grouped around them, which may retain the fuchsin in films stained for tubercle bacilli and so appear acid-fast (Dudgeon). In the urine of women and children the starch used for dusting the pudenda must not be mistaken for crystals, which it somewhat resembles. This starch does not present the concentric rings of the ordinary starch figured in text-books. In women catheter specimens of urine must be obtained. Similar symptoms may result from infection of the urinary tract with other micro-organisms, such as coliform bacilli, *B. proteus*, streptococci, and staphylococci.

The opsonic index is usually low ; vaccines usually lead to a gradual rise, which may reach such a considerable figure as 5, 6, 7, or 8 (Dudgeon).

#### RELAPSES.

A special and very troublesome feature about these cases is the liability to relapse. Relapses may occur time after time and without any obvious reason, such as exposure to cold or over-exercise. The relapses may come after a considerable interval of convalescence ; in one case a severe relapse occurred after 25 days of normal temperature. Relapses, like the original acute attack, may come on with the greatest suddenness. In another case, seen in consultation in December, 1909, the disease had persisted on and off from September, 1908. Routh's case, in which there was reason to believe that the disease had existed for 16 years, has



already been mentioned. Thursfield has pointed out that the condition of periodic pyelitis in children manifested by attacks of vomiting, headache, malaise, and painful micturition, closely resembles the condition of cyclical vomiting, which has been thought to be due to acidosis, and therefore treated by alkalis. It is, therefore, important to examine the urine carefully in every case of periodic or cyclical vomiting in children; fortunately alkalis do good in both.

Complications and sequelæ are fortunately rare. In one case, seen in consultation, of long-standing coli bacilluria in a woman with a renal calculus, there had been recurrent attacks of phlebitis, in one of which severe pulmonary embolism occurred.

Wright refers to a case in which one kidney had been excised for colon infection, with transient aphasia regarded as uræmic.

It is possible that repeated attacks of pyelitis in early life may eventually lead to the production of hydro- or pyonephrosis for which no obvious cause is forthcoming (Box, Thursfield). Thomson (quoted by Herringham) states that if treatment with alkalis is neglected extension of inflammation from the pelvis to the substance may occur with the production of multiple abscesses.

#### DIAGNOSIS.

This depends on the isolation of *B. coli* from the urine and from the absence of evidence of any further lesion such as stone. Before the bacteriological diagnosis is made the following symptoms should suggest a diagnosis of infection of the urinary tract with *B. coli*:—Pus in an acid urine with some albuminuria; pain and palpable enlargement of one kidney; fever.

As already mentioned, Thomson insists on the diagnostic importance in children of rigors.

#### PROGNOSIS.

This must be considered under heads:—(a) As to life; the outlook is extremely good. In 50 cases in children Morse only had 1 death. (b) As to duration; an acute case may become chronic and so last for weeks or months or even years; 3 or 4 months is not a long time. Relapses are very prone



to occur, and, as already mentioned, may appear very suddenly and without any satisfactory cause.

#### TREATMENT.

The question whether the urine should be made alkaline has led to some difference of opinion. "Theoretically," as Morse says, "alkalis should do harm rather than good, because the colon bacillus grows more luxuriantly in alkaline or neutral than in acid media. Moreover, there is more opportunity for a concurrent infection with other bacteria if the urine is alkaline." Some therefore have thought it advisable to give acid phosphate of sodium to keep the urine acid; this I have done in some cases, sometimes apparently with good results, in others without any benefit. In one case in which it was carried out there were a number of most troublesome relapses. It has been suggested that as the growth of the bacterium is probably inhibited by a different reaction from that to which it is accustomed the urine if acid should be made alkaline, and if alkaline, acid (Brown). The general experience, however, is that the proper treatment is to make the urine neutral with alkalis; with this object citrate of potassium or bicarbonate of sodium should be given with plenty of water; in this way mild cases may be cured without any further treatment.

As the pyuria and bacilluria may persist, though the symptoms are in abeyance, while the patient's urine is kept alkaline, and as relapses may occur when the alkaline treatment is interrupted (Thomson), it appears that the alkaline treatment either inhibits the virulency of the colon bacilli or maintains the resistance of the body at a sufficiently high standard.

If the urine is ammoniacal it has been thought advisable to remedy this by giving acid phosphate of sodium or benzoates, and then to give alkalis.

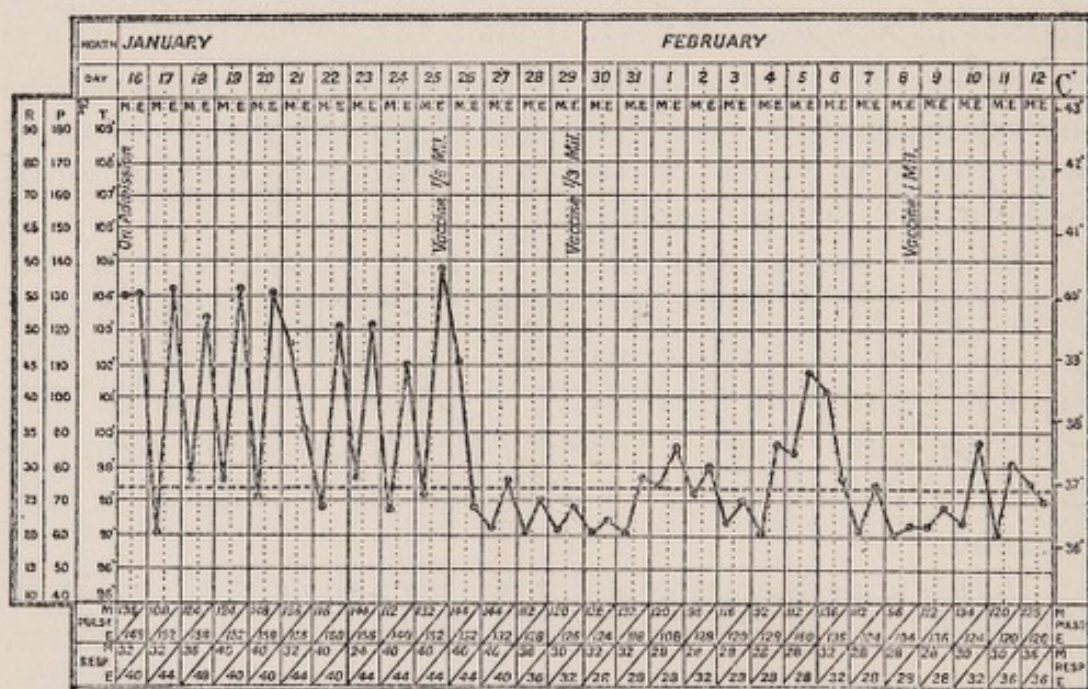
Urinary antiseptics, such as urotropin, helmitol, and salol, have been given a very extended trial. Unfortunately urotropin, which is so successful in urinary affections due to the allied *Bacillus typhosus*, appears to be of comparatively little use in the case of coli-bacilluria. It may be combined with alkalis, and it seems right to give it, especially as it does no



harm.

Benefit has been noted after the addition of salicylate of sodium to potassium citrate in a case of pyelitis due to *B. coli* in a child (Ritchie).

*Vaccines.*—Vaccines made from *B. coli* isolated from the patient's urine have been largely given, but opinion is not unanimous in their favour. Morse was disappointed with their effect in children; Herringham speaks with considerable reserve as to their effect in adults, and Dudgeon finds that they occasionally do good in chronic cases, make the patient feel better, and raise the opsonic index, but do not influence the bacilluria. I have on the whole seen good effects from their administration. Increasing doses of dead colon bacilli are given at intervals of three to seven days, according to the opsonic index and the temperature. The doses given have varied very greatly. In a child aged 2 years the administration of a vaccine of  $\frac{1}{8}$  of a million bacilli was immediately followed by a fall of temperature (*vide* chart).



Temperature chart of a child with infection of the urinary tract with *B. coli*.

There was a sudden fall of temperature after the administration of a vaccine.

In one of French's cases injections of 500,000,000 dead colon bacilli were given at intervals of a fortnight.



A polyvalent *anticolon serum* has been recommended and employed with success by Dudgeon, but others have not found it successful. In one case, which had persisted for some months, I gave it at the same time as a vaccine, and alkaline treatment; this course was followed by cure.

Surgical treatment is unnecessary except (1) in the most severe cases in which there is suppuration spreading into the kidney substance; (2) in chronic cases in which a pyonephrosis has developed; (3) in secondary cases in which there is a calculus in the kidney.

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