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CHRONIC URINARY INFECTION

WITH *B. COLI COMMUNIS*.*

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OF all the diseases of the urinary tract that the practitioner has to diagnose and treat, chronic infections are the most common, and the *Bacillus coli* is the infecting agent in the majority of cases. It is a subject therefore which will interest all of you and in which many of you have acquired the special knowledge that comes of long familiarity.

The *Bacillus coli* reaches the urinary tract by two paths.

There may be an infection from without, frequently spontaneous in women where the motile bacillus can ascend the short urethra, but often introduced by means of the catheter or other instrument, or by operation upon the bladder or urethra. That is the ascending form of infection.

The second path of infection is the blood stream, hæmatogenous infection. Here the *Bacillus coli* arrives at the kidney in the blood stream and passes through the renal tubules to infect the renal pelvis and bladder. I will discuss only hæmatogenous infection, for the discussion of ascending infection would lead us into cognate subjects for which we do not have time in this lecture.

RELATION OF DISORDER OF THE BOWEL TO INFECTION OF THE URINARY TRACT.

The source of the *Bacillus coli* in hæmatogenous infection of the urinary tract is the bowel, and it is all important for the purpose of treatment to study the method of escape of the bacteria from the bowel. The *Bacillus coli* is indigenous in the bowel, where it becomes established at an early period of life. In the healthy bowel there are certain barriers against escape into the lymphatic stream or blood stream.

1. *Intact Intestinal Epithelium*.—It has been shown that the mucus covering the intestinal mucosa has bactericidal properties, and, moreover, it forms a mechanical covering for the epithelium which acts as a protection against the action of bacteria. The epithelium itself exercises a selective action in regard to the bowel contents,

passing some of the material through into the lymph channels and rejecting the rest.

2. *Masses of Lymphoid Tissue in the Intestinal Wall*.—In the wall of the small intestine there are Peyer's patches and the solitary glands, which have an important influence in checking bacterial escape from the bowel. A striking illustration of this is obtained in typhoid fever. The appendix is another mass of lymphoid tissue which is of importance in preventing the spread of bacteria, and it lies at the part of the bowel where the bacteria are most abundant and where the passage of the bowel contents is longest delayed. Appendicitis develops when this barrier has been overcome by bacteria.

3. The chain of lymph glands along the ileocolic vessels are the final barrier against invasion of the blood stream by intestinal bacteria. The importance of this barrier in infants and children is shown by the reaction to the tubercle bacillus in the disease known as *tabes mesenterica*.

CAUSES OF THE ESCAPE OF BACTERIA.

The predisposing or exciting causes which promote the escape of bacteria from the intestine are numerous.

1. *Mistakes in Treatment*.—Among the causes that are unsuspected or overlooked are mistakes in treatment. Excessive purgation denudes the mucous membrane of its protective covering of mucus and damages the epithelium. Overdistension of the large bowel in Plombières treatment is another exciting cause for the escape of bacteria into the blood stream. It is no uncommon experience to see a patient return from a spa, where very energetic methods of bowel lavage have been used, with a bacilluria, where previously the urine had been sterile.

Mottram and Kingsbury have shown that prolonged exposure of the bowel to the action of radium or X rays so impairs its resisting power that bacteria escape into the blood stream. It is a common experience in investigating urinary infections to note a rise of temperature after the patient has been examined by the X rays. This, I believe, is due to disturbance of the bowel by the X rays.

The almost universal practice of removing the normal appendix when the abdomen has been opened for exploration or for some operation on another organ is, I believe, a mistake, for in so doing one of the protective barriers against the escape of bacteria into the blood stream is destroyed.

2. *Diseases of the Bowel*.—Chronic intestinal stasis or inflammation of the mucous membrane or of the accessory organs is a familiar source of the escape of bacteria into the blood stream. Thus we have as predisposing causes of bacilluria, chronic

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constipation, colitis, old-standing dysentery, diverticulitis, piles, appendicitis, and cholecystitis.

3. *Operations on the Bowel and the Female Pelvic Organs.*—No more striking example of cause and effect is met with than bacilluria immediately following an operation on the bowel or pelvic organs where the urine was previously sterile.

The after result of a brilliantly performed and successful excision of the rectum may be marred by the development of *Bacillus coli* infection of the urinary tract.

In order to demonstrate the close relation of the bowel and operations on the female pelvic organs to urinary infections, I have taken 100 consecutive cases of *Bacillus coli* infection of the urinary tract. In 61 cases there is some disorder of the bowel as follows:—

Severe constipation	22
Typhoid fever	3
Colitis	8
Appendicitis	10
Pile or fistula operation	11
Abdominal operations	7

There was disorder or had been an operation in female pelvic organs in 19 of the 100 cases.

CLINICAL FEATURES OF CHRONIC URINARY INFECTION.

To enumerate the symptoms of chronic urinary infection would give a very confused picture of the forms in which these infections are observed. I shall therefore describe a few of the common types which illustrate the outstanding clinical features of these cases.

The following types will be considered: (1) chronic cystitis; (2) recurrent cystitis and pyelitis; (3) bacilluria with toxæmia.

Chronic Cystitis.

Chronic cystitis persisting in spite of long and careful treatment is one of the most troublesome conditions with which the practitioner has to deal.

The symptoms are few, but they become painfully familiar. There is frequent micturition. The intervals are evenly spaced throughout the day and night. The bladder must be emptied in one hour or two hours and occasionally under the influence of various irritants at the shorter intervals of a quarter to half an hour. Periods of active incontinence may be a feature of the case.

There is pain at the neck of the bladder and along the urethra. The pain is usually described as burning or scalding. It is sometimes very distressing, and in women may be so localised as to give rise to the belief that a single ulcer in the urethra is the cause of all the trouble. I have searched the urethra in such cases many times, but have never found an ulcer present. These patients are very sensitive to changes in weather. They are comfortable on a dry warm day, they are miserable when the weather is damp and cold. Sudden changes in temperature upset them. They are better in an inland climate than by the sea. Some are only comfortable when recumbent and warm in bed. When they are

interested in some subject and their attention is distracted from the bladder they may hold the water for a longer time. Certain articles of diet such as alcohol, curries, peppery dishes, acid fruits (currants, raspberries, strawberries, gooseberries) increase the symptoms. From time to time there is a rise of temperature with backache and aching muscles that may be diagnosed as influenza.

Causes of Persistence of Cystitis.—(1) In some cases the only condition present is inflammation of the bladder mucous membrane, and the persistence of the cystitis is due to a virulent strain of bacteria and the weak resistance of the patient. This, however, is rare, and there is usually some other reason why the inflammation should continue.

(2) There is frequently a local cause of persistence such as obstruction by a stricture of the urethra or by an enlarged prostate. A growth in the bladder, a stone or diverticulum are conditions in which cystitis develops spontaneously and persists in spite of treatment. Gradual development of cystitis without any cause such as the passage of a catheter occurring in an old man and becoming chronic, is very frequently due to malignant growth and may be unaccompanied by hæmorrhage. Spontaneous cystitis developing quietly and becoming chronic in young people is frequently due to urinary tubercle. Most cases of infection with the *Bacillus coli* commence acutely in an attack of so-called "influenza."

(3) The chief focus of infection may be in the prostate and seminal vesicles, and from this source bacteria continually reinfect the bladder.

(4) Pyelitis is a common cause of persistence of cystitis. In chronic pyelitis the bacteria in the bladder are constantly renewed by the infected urine passing down, and this is unaffected by local treatment of the bladder. In order to ascertain what proportion of cases of chronic urinary infection with the *Bacillus coli* had pyelitis in addition to cystitis, I took the records of 100 consecutive cases where the ureters had been catheterised. In 42 the bladder was infected and both kidney urines sterile, and in 58 there was infection of the kidney urine (one side 30, both sides 28). Pyelitis is frequently present without any local symptoms pointing to renal infection, and in such cases it is only discovered by ureteral catheterisation.

Recurrent Cystitis and Pyelitis.

The initial acute attack of urinary infection has settled down and the patient returns to work. After a few weeks or months there is a second attack and subsequent attacks follow.

There are two classes of case included under this type.

(a) There is persistent infection of the urinary tract with recurrent exacerbation. Between the attacks there is often a slight irritability of the bladder and the urine is cloudy and contains the *Bacillus coli*. The patient after a few attacks knows when the attack is threatening. There is lassitude, mental irritability, loss of appetite and headache and the patient is over-sensitive to changes of

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temperature. If there is a tendency to constipation this becomes more severe, or there may be an attack of diarrhoea, or not infrequently flatulent disturbances of the bowel.

(b) In other cases there is recurrent pyelocystitis with a sterile urine between the attacks. Here there may be a focus of infection connected with the urinary tract but temporarily shut off, and from this the urine became infected from time to time. This is found in the male subject in the prostate or seminal vesicles, but in the female there are no such accessory organs in which the infection can be temporarily buried, and I do not consider that any such pocket can form in the kidney. In these cases and in the male where the prostate and vesicles are not the nidus of infection the recurrent pyelocystitis is due to reinfection from the bowel, usually hæmatogenous, but occasionally ascending in the female.

Bacilluria without Local Symptoms, but with Toxæmia.

The urine in bacilluria has well-known characteristics. It is cloudy without flakes and there is no deposit on standing. There is a peculiar stale-fish odour, and in swinging the glass a peculiar shimmering appears like drifting mist or smoke.

This condition is due to the development of the bacteria in the urine as a culture medium with no reaction of the mucous membrane of the urinary tract. It frequently occurs alone, but may be present with other forms of urinary infection. It is usually a very persistent type, although occasionally it may be transient and appear and disappear suddenly.

Toxæmia is not confined to this type of urinary infection, but it is frequently present with it. The toxæmia may be acute and give rise to sudden attacks of high fever without other symptoms.

These cases were at one time classed with others under the term "febricula," in more modern times they not infrequently receive the title of "influenza." Occurring in children, they may be accompanied by nerve symptoms such as squinting, vomiting, and convulsions, and the diagnosis may be obscure until the urine is examined.

In chronic toxæmia there may be a doubt whether the toxin is absorbed from the bowel or from the urinary tract. These patients are never well. They have a sallow, muddy complexion. They wake in the morning with a headache and are lacking in energy. In the afternoon they may feel better. There is aching of the muscles and joints. Night sweats are frequent, but the skin is otherwise dry and harsh. Fibrositis is common and affects the lumbar and neck muscles and the ligaments of the sacrum. Stiffness of the joints is a constant complaint, and in old-standing cases osteo-arthritis is common.

EXAMINATION OF THE PATIENT.

In acute infections of the urinary tract instrumental interference should be avoided. In the

chronic cases that we are discussing, success in treatment depends on accurate localisation of the chief focus of infection and the discovery of the cause of persistence or recurrence. For this purpose all the modern methods of diagnosis may be required.

1. *Symptoms and Examination.*—The symptoms may assist in localising the chief focus of infection. Thus in pyelitis there is pain in the loin either in the anterior or the posterior renal area, and there is tenderness on palpation of the kidney. In pyelitis or pyonephrosis the kidney will be enlarged. In prostatitis and seminal vesiculitis, rectal examination will show enlargement and tenderness of these organs. It must be remembered, however, that pyelitis may be present without any pain in the loin or tenderness on palpation, and that a focus of inflammation may exist in the prostate or vesicles which cannot be detected by rectal palpation. Too much reliance is usually placed on the presence or absence of symptoms for the localisation of chronic urinary infection, and it is not sufficiently realised how much these chronic infections depend on what may be termed "quiescent disease."

2. *Urine.*—In chronic infections of the urinary tract it is necessary to exclude tubercle. There are some cases of chronic cystitis apparently due to the *Bacillus coli* or to a coccal infection that are old-standing cases of urinary tuberculosis with a secondary infection. Examination of the urine may show tube casts, renal epithelium, or epithelium from the renal pelvis or bladder. The value of a report on the urine as a means of localisation of urinary infection is, however, much overrated at the present day. A report that shows there are no casts, renal epithelium, or epithelium from the renal pelvis does not exclude pyelitis, and the presence of bladder epithelium does not localise the inflammation to the bladder.

3. *A Specimen of the Secretion of the Prostate and Vesicles should be Obtained where the Focus of Infection is likely to Reside in these Organs.*—The bladder and urethra are thoroughly washed with boracic lotion by Janet's method and the bladder is then filled with sterile fluid. The patient is placed in the knee-elbow position with a sterile glass funnel and bottles below the penis and the prostate and vesicles thoroughly massaged. The patient then passes the fluid from the bladder into the bottle and this is examined for pus and bacteria.

4. *Cystoscopy.*—By cystoscopy the cause of the persistence of the inflammation may be discovered in the bladder. There may be a growth, a stone, or the orifice of a diverticulum may be seen. The prostate may project into the bladder causing obstruction, and residual urine may be present. The bladder may be healthy and the orifices of the ureters may show evidence of inflammation of the upper urinary tract by thickening or puffiness of the lips or a halo of inflammation surrounding the orifice, or the orifice may be rigid and open. The efflux may be seen to be cloudy and contain flakes, or a thick purulent efflux may be observed.

5. *Ureteral Catheterisation*.—Catheterisation of the ureter is the most accurate method of diagnosis, and without this method of examination the diagnosis and treatment of chronic urinary infection is mere guesswork. A specimen of urine is obtained from each kidney and is examined for bacteria. In passing the catheter up the ureter the presence or absence of obstruction due to stone or stricture of the ureter is noted. The capacity of the renal pelvis is ascertained by drawing off its contents with a small syringe. Important information is thus obtained as to the presence or absence of dilatation of the pelvis.

6. *Radiography*.—A calculus may lie wedged in a calyx or in the pelvis without causing pain, and if present will be the cause of persistence of the infection.

7. *Pyelography*.—By injecting a fluid opaque to the X rays into the renal pelvis an accurate picture of the outline of the renal pelvis is seen and the presence or absence of dilatation is already demonstrated. This method is useful in trying to ascertain the cause of persistence of chronic pyelitis.

8. *Examination of the Bowel*.—In all cases of urinary infection this is important. Such conditions as chronic stasis, piles, colitis, appendicitis, cholecystitis are causes of urinary infection, and the urinary tract may be constantly or intermittently reinfected from this source.

TREATMENT OF CHRONIC URINARY INFECTION.

This consists in—

1. Medicinal treatment: (a) urinary antiseptics; (b) alkalis; (c) diuretics; (d) soothing drugs.
2. Vaccine.
3. Local treatment: (a) bladder washing; (b) renal lavage.
4. Operation.
5. Treatment of the bowel.

Urinary Antiseptics.—Salol and boracic acid have a moderate antiseptic action. The chief urinary antiseptics belong to the formaldehyde group.

Hexamine or urotropin is a combination of ammonia and formaldehyde. The combination is maintained in an alkaline medium, but broken up in an acid medium. It has no antiseptic action unless the combination is broken up and formaldehyde set free. Hexamine is absorbed as such and is excreted by the kidneys. In contact with the acid urine the combination is dissociated and formaldehyde set free. It is important not to prescribe hexamine with an alkali as the alkali will reduce the acidity of the urine and thus interfere with the antiseptic action of the drug.

The relief of symptoms that is often claimed as a result of prescribing a combination of hexamine and an alkali is due to the action of the alkali or to the fact that the urine has been so acid that the alkali has not been sufficiently powerful to prevent the splitting of the hexamine. If the alkali has any action on the reaction of the urine it will

maintain the hexamine in combination and thus render it useless as an antiseptic.

It is often desirable to increase the acidity of the urine or necessary to render an alkaline urine acid for the purpose of splitting the hexamine, and for this purpose acidifying drugs, such as sodium acid phosphate, sodium or ammonium benzoate, and the mineral acids, are used. These acids should not be prescribed in the same mixture as the hexamine, as the dissociation of the hexamine will take place in the bottle and the medicine will contain free formaldehyde, which is irritating to the gastric mucous membrane and will cause indigestion.

The action of hexamine as a urinary antiseptic depends upon a number of factors, chief of which are: (1) the amount excreted; (2) the acidity of the urine; (3) dilution by artificial or pathological diuresis; (4) time during which the drug is in contact with acid urine; (5) amount of mucus in the urine.

Space does not permit of a full discussion of all these factors. The time during which hexamine is in contact with the acid urine is one of the most important. The longer a germicide acts on bacteria the greater will be its killing power. The liberation of formaldehyde from hexamine is slow and gradual and time is required for the process. This time factor interferes with the utility of the drug in a number of cases. Thus hexamine is of comparatively low value in infection of the kidney and renal pelvis. In disease, where there is frequent micturition and polyuria, and in cases where the bladder is continuously drained by catheter or by a temporary or permanent fistula, the period of contact of the hexamine and the acid is too short for a free liberation of formaldehyde. Thus after prostatectomy or operations on the bladder, hexamine is practically worthless until the bladder wound is closed.

A further handicap in the administration of hexamine is the intolerance of the inflamed bladder to highly acid urine. This is more important in the acute than in chronic infection, and in the former the distress caused by a highly acid urine may be so great that the administration of urinary antiseptics must be abandoned and the urine rendered neutral by alkalis and soothed with sandalwood oil.

In chronic urinary infection the prolonged administration of urinary antiseptics is often disappointing, and in bacilluria they appear to have little effect. I prefer to give short courses of urinary antiseptics and frequently prescribe large doses. This has led me to use alternating courses of urinary antiseptics and alkalis. Hexamine is prescribed in doses of 30 or 40 gr. in 24 hours for two or three weeks and then stopped, and an alkali prescribed with sandalwood oil and diuretics.

Recently a combination of hexamine and resorcinol has been introduced under the name of hexyl resorcinol and this drug is on trial at present. The number of cases in which I have used the drug is limited, but in some, very pronounced improvement

has been noted where other urinary antiseptics had proved of little value.

A note of warning should, I think, be sounded in regard to the administration of this drug where nephritis is present. In a case where chronic urinary infection and parenchymatous nephritis were present the symptoms of the latter were very seriously increased by the administration of hexylresorcinol. I would suggest, therefore, that this drug be given with the greatest caution where nephritis is present. These urinary antiseptics act only in an acid medium and there are many cases where this cannot be obtained. There is urgent need, therefore, for a urinary antiseptic which will act in an alkaline medium. Methylene-blue has long had a reputation as a urinary antiseptic, but its action is somewhat ill-defined. It is a useful drug, especially in coccal infection, and acts in an alkaline urine.

Recently the intravenous administration of antiseptic drugs has been advocated. Acute and chronic infections of the urinary tract have been treated by intravenous infusion of urotropin. In acute cases $\frac{1}{4}$ gr. has been injected daily, and in chronic cases the same dose with intervals of two or three days; 10 or 12 injections were used on an average. Larger doses have also been employed. The method appears attractive at first sight, but in certain cases serious symptoms have arisen. It is not necessary as a routine method, for there is rarely any delay in absorption of the drug from the intestinal tract, and it must be reserved for rare cases where absorption is retarded.

Intravenous injections of mercurochrome or of methyl-violet have recently been used in America. Some success has been claimed for this treatment, but the action appears to be very uncertain. In the few cases in which I have felt justified in using this method neither of the drugs has had any influence on the course of the disease.

Vaccine Treatment.

In chronic urinary infections vaccine treatment is very frequently disappointing in its results. In a few cases improvement follows the use of vaccines, but there are many cases where vaccine therapy appears to be worthless. Which cases are likely to benefit by vaccine treatment we have not been able to define.

I cannot believe that all patients are equally suitable for vaccine treatment, or that the somewhat rigid scheme of dosage that appears to be wellnigh universal can be the best method for its administration. The cases in which I have seen the best results are those in which the vaccine was administered during the decline of the infection, when the temperature had fallen and the symptoms abated but the urine was still infected.

In very chronic cases and in the type we know as bacilluria, vaccine therapy has in my experience done no good at all. I have tried the method of infusion of blood from an immunised healthy

individual (immuno-transfusion) but so far with disappointing results. The fact that a chronic urinary infection of many years' standing may suddenly clear up after an acute exacerbation and show no tendency to recur leads me to suppose that vaccine therapy, if properly handled, might give better results than it does at the present time.

Two important methods of local treatment are washing the bladder and the renal pelvis. Time does not permit of a discussion of the former, but I will say a few words about renal lavage.

Lavage of the Renal Pelvis.

When proof has been obtained that the focus of infection lies in the renal pelvis lavage is a very valuable method of treatment.

Great care should be exercised in the selection of cases. Lavage of the renal pelvis is contra-indicated when there is infection of the prostate and vesicles, when there is incurable infection of the lower urinary tract such as that complicating malignant growth of the bladder, and when there is obstruction in the lower urinary tract. In acute infections this method should be avoided. The only exception to this is the pyelitis of pregnancy when good results sometimes follow the passing of a ureteral catheter and careful lavage. It is not necessary and may be harmful to use the method in young children. Renal lavage is most useful in cases of recurrent attacks and in cases of chronic cystitis secondary to pyelitis.

In many cases the infection is cured. In other cases the urine from the renal pelvis is much improved but is still infected. The distressing bladder symptoms may have entirely disappeared, but they will probably recur at a future date.

Persistence of infection in spite of renal lavage may be due to the use of too weak antiseptic, too long intervals between treatment, dilatation of the renal pelvis, or stress in the renal pelvis. Recurrence of the infection of the renal pelvis after the urine has been found sterile is due to reinfection from the bowel.

Operation.

Space does not allow of the discussion of the indication for operation in chronic urinary infections. Such operation may involve the drainage or removal of the kidney, drainage of the bladder, excision of the seminal vesicles and prostate, and emptying the uterus in pregnancy.

Treatment of the Bowel.

The bowel is the chief source of the bacteria causing urinary infection, and the infection may be repeated time after time. It is therefore necessary in all urinary infections to examine and treat the bowel. The treatment will consist in the administration of bowel antiseptics, in the treatment of atony of the bowel wall, and the causes of constipation; and the operative treatment of piles, chronic appendicitis, and cholecystitis will also arise for discussion.