A Clinical Lecture

ON

THE TREATMENT OF URINARY SEPSIS.

GIVEN AT THE ROYAL VICTORIA INFIRMARY,
NEWCASTLE-UPON-TYNE,

BY

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(With Special Plate.)

ACUTE inflammation of the urinary tract is anything but a rare disease; too often the response to treatment is disappointing, whereupon the sequel of the acute stage, chronic urinary sepsis, becomes one of the common ailments met with in general practice. The treatment of the chronic stage is not an easy problem, and often little is done to assist such patients.

A typical history given by a patient tells of an attempt made by the doctor to treat the usual symptoms of frequency of micturition and dysuria; that much medicine had been swallowed, and perhaps the bladder had been washed out, or a vaccine had been employed; that no permanent good had accrued, and the sorely disappointed patient had gone to another doctor, who carried out an exactly similar programme to his predecessor.

The condition attacks either sex, and at any age, though it predominates in females. It usually affects both kidneys. In my experience the great majority of cases of urinary sepsis are "descending" infections. The function of the kidneys is to eliminate waste products, including any bacteria, which may be present in the blood stream.

That a kidney is able to eliminate micro-organisms without any damage being done to that kidney is an established fact. Probably the alternative usually happens, when the extruded pyogenic bacteria gain a footing in some situation in the urinary tract—for example, in the solid part of the kidney (causing pyelonephritis); in the mucous membrane of the renal pelvis (causing pyelitis); in the mucous membrane of the ureter (causing ureteritis); in the mucous membrane of the bladder (causing cystitis); or, rarely, in the mucous membrane of the urethra (causing urethritis).

If bacteria are circulating in the blood stream, and have damaged the patient's filtering apparatus, it is the medical man's duty first to endeavour to discover the focus of entry of the bacteria, and secondly to ascertain the extent of the damage which has already been done. The commonest foci of sepsis are found either in the teeth or the tonsils, but the focus may be in the ear, the air sinuses, or, in the case of females, it may be in the uterus, associated or not with pregnancy.

I will relate some clinical examples of acute and chronic urinary sepsis, with the treatment employed in each case.

ACUTE URINARY SEPSIS.

During the acute stage of the condition it is not always possible to treat the causative focus, because the doctor must concentrate upon giving the patient relief by treating the symptoms. The urine is invariably hyperacid, and the acute symptoms will persist until its reaction is less acid, or even alkaline. This can best be effected by giving 30 grains of potassium citrate every two or three hours, and by auto-irrigation of the urinary tract—that is, by making the patient drink. The best diuretic is Contrexéville water, up to two bottles a day, though barley water or plain water are also good. Care, however, must be taken that the urine reaction is not kept alkaline by undue continuation with the potassium citrate. The hyperacid septic urine pouring down the ureters infects, and later digests, a fan-shaped area of mucous membrane on the bladder base in front of each ureteric orifice, forming an area of ulceration; later, if highly alkaline urine is continually pouring over these ulcers, the phosphates are deposited upon them, and the terribly distressing condition of "alkaline phos-

phate cystitis" develops. Where the patient is of ordinary intelligence this can be avoided by giving him or her a book of litmus paper with instructions to diminish the alkaline mixture dose when the litmus paper indicates that the urine has become neutral. If it can be managed, the urine in all stages of the treatment of urinary sepsis should be kept faintly acid.

Some urinary antiseptic should be given, either salol, 5 grains three times a day, when the urine reaction is alkaline, or hexamine, 10 grains three times a day, when the reaction is acid. The application of linseed meal poultices every six hours to an affected loin seldom fails to relieve acute renal pain.

If an obvious septic focus—for example, a dental focus—can be easily dealt with, the acute stage can often be cut short by dealing with it forthwith. A saline purge should also be given. The diet should consist of milk, eggs, and fish; meat, and irritants to the urinary tract such as coffee, condiments, pickles, etc., should be avoided.

It is far from easy to demonstrate the causative organism of acute urinary sepsis. Probably staphylococci or streptococci are the commonest bacteria, but unless a bacteriological examination is made in the early stages of the illness the chance of recognition of the actual organism is gone, for the ubiquitous *Bacillus coli communis* is quickly on the scene when the other bacteria disappear or are masked. This is the reason why the treatment of urinary sepsis by vaccines is so terribly disappointing, for only the secondary infection, not the primary infection, is found, the original organism still being at work, though bacteriologically it is masked by the *B. coli communis*.

Clinical Examples.

A typical history of a case of acute urinary sepsis which yielded to treatment is as follows:

CASE I.

A woman, aged 28, was taken suddenly ill with shivering and acute pain which radiated to both groins, accompanied by strangury, with blood and pus in the urine. I saw her four weeks later, by which time she had recovered from the acute stage, but she still had frequency of micturition, acute pain after micturition, and a heavy deposit of pus in the urine.

A routine examination showed marked follicular tonsillitis, though the patient denied having had any "sore throat."

Cystoscopy showed a fan-shaped area of ulceration in front of the ureteric orifices, the apex of the fan being at each orifice. The case was referred to a laryngologist, who removed two highly offensive tonsils. Within one month not only had the patient's symptoms disappeared, but the bladder ulceration had healed, and all pus cells had disappeared from the urine.

I now give a history of two typical cases of alkaline phosphatic cystitis. The first of these was one of mild degree easily cured, while in the other the condition was very advanced.

CASE II.

A married woman, aged 25, gave a typical history of cystitis extending over two years. Her doctor's letter on her condition on admission to the Royal Victoria Infirmary, Newcastle-upon-Tyne, in September, 1924, is worth quoting:

"This patient appears to have suffered from cystitis ever since her confinement of three years ago.

"She complains to me of pain during and after micturition, and of passing blood, slime, and gravel. She brought a piece of fairly hard material which she said she had passed per urethram. It was apparently phosphatic. Effervescence took place on the addition of pure nitric acid. She said she passed several pieces, which sometimes stuck in the urethra and took a lot of dislodging with the finger. The size of the pieces was that of a pea or split pea. Gravel was also passed in quantity. On examining the urine I found it was alkaline and contained much mucus and a fairly large piece of bladder mucous membrane, but little pus. Since putting her on to hexamine and daily wash-outs with boracic lotion she has improved considerably, but still passes an occasional piece of phosphate debris. This morning, when the catheter was passed on her, I could not feel a stone, but rather think she must have one or more."

Cystoscopy showed phosphates encrusted upon ulcers on the base of the bladder. These were scraped away under vision, by cystoscopy, by a "spoon" introduced through the urethra. The urine was kept acid, and the patient was completely well six weeks later, by which time all pus cells had disappeared from the urine.

CASE III.

A spinster, aged 24, came in August, 1924, to the Royal Victoria Infirmary, Newcastle-upon-Tyne, complaining of passing urine every few minutes night and day; she brought with her a large pill-box

full of pieces of phosphate grit (some of them large) which she was accustomed to pass daily. Two years previously she had had a typical acute attack of urinary sepsis, and on close questioning I found she had been taking some medicine, and the same medicine, for the whole of the two years. Doubtless this medicine contained potassium citrate. She had dental sepsis; the urine was alkaline, and contained blood and pus; no abnormal shadows were seen on a radiogram of the urinary tract.

The dental sepsis was first attended to. As the bladder capacity was under one ounce, cystoscopy under a general anaesthetic was necessary. The surface of the bladder was found to be studded with ulcers, upon each of which were encrusted patches of phosphatic deposit—that is, she had the condition of alkaline phosphatic cystitis. The deposits proved too extensive to scrape away through the urethra, so this was effected through a suprapubic approach.

Life is now tolerable for her, for her bladder capacity is 5 ounces, she can work, and she is only disturbed once at night to micturate. Her urine is acid, but still contains pus. Cystoscopy shows a small ulcer on the right lateral wall of the bladder; this is not covered by phosphates. The bladder is being irrigated twice weekly, and she is having hexamine with acid phosphate of soda. I have every hope that the ulcer will eventually heal and that she will be completely cured.

There is a valuable lesson to be learnt from these two cases, and it is that the potassium citrate treatment was overdone; had this drug been confined to the acute stage only, the phosphates would almost certainly never have been deposited on the ulcers formed in the acute stage, after the hyperacid urine had digested the bladder mucous membrane. Immediately the acute stage was over care should have been taken to keep the urine faintly acid.

CHRONIC URINARY SEPSIS.

The successful treatment of a case of chronic urinary sepsis depends upon a correct appreciation of the location and extent of the inflammation, and such a diagnosis cannot be made without routine cystoscopy and pyelography.

Cystoscopy will indicate the condition of the bladder; ureteral catheterization will enable the urine collected from each kidney to be examined for pus cells; while pyelography will prove whether the sepsis is merely pyelitis or pyelonephritis, or whether extensive destruction of the solid part of the kidney has taken place. I invariably make a double pyelography, and in no single instance have I seen any ill effects from both kidneys being "pyelogrammed" at the same time.

For the benefit of those who are not familiar with the making of a pyelogram I may say that a ureteral catheter is passed, under vision, by means of the cystoscope up the ureter into the pelvis of the kidney. The ureters are insensitive to the passage of the ureteral catheter; therefore the only discomfort of catheterization of the ureters is the introduction of the cystoscope into the bladder. A solution opaque to x rays (I employ sodium iodide solution) is injected with a syringe through the hollow ureteral catheter into the pelvis of the kidney, and the patient is x-rayed. A pyelogram should only be taken in a patient who is fully conscious; it is a dangerous proceeding to distend the renal pelvis of an unconscious person. The radiogram shows up the hollow part of the kidney, and an interpretation can be made by an estimation of the shape and size of the renal pelvis and calyces.

It is essential to watch the reaction of the patient's urine, for it should be kept just faintly acid. I use sufficient doses of potassium citrate to reduce the acidity, or, alternatively, use acid phosphate of soda to keep the reaction acid. In addition, salol 5 grains must be given thrice a day if the urine is alkaline, and alternatively hexamine, 8 grains thrice a day, when the urine is acid; of the two I prefer the hexamine, largely because of the constipating effect of salol.

A routine general examination of the patient should be undertaken to find a possible focus of sepsis. The diet should be light, red meat being taken only seldom. Urinary tract irritants such as coffee, condiments, pickles, etc., should be avoided. Care should be taken to avoid constipation. Diuresis is an important factor in treatment, and Contrexéville water is a valuable help.

Example of Chronic Pyelitis.

A married woman, aged 38, had had for three years periodic attacks of left-sided renal pain associated with frequency of micturition, haematuria, and some pain after micturition. In the acute stage there was a continuous temperature of 100°, and she

was confined to bed. Bacteriologically a pure culture of *B. coli communis* was obtained, and prolonged vaccine treatment had proved useless. Her teeth showed evidence of pyorrhoea.

A routine radiogram of the urinary tract showed normal shadows; the urine contained pus and some blood; cystoscopy showed ulceration of the left ureteric orifice, with a slight degree of basal cystitis; pyelography of both kidneys showed that the solid portion of the kidney remained unaffected. Urine collected from the left kidney contained pus; urine from the right kidney was normal.

A diagnosis of left-sided pyelitis was made and the dental sepsis attended to. The patient's condition improved, but progress was slow, so the left renal pelvis was irrigated with a 1 in 10,000 solution of silver nitrate through a ureteral catheter every three weeks on six occasions. No anaesthetic was used, for apart from the discomfort of passing the cystoscope the treatment was painless. The patient carried on her ordinary life the day following each treatment.

Now, three months later, the patient is cured of her symptoms, and no pus cells can be found on microscopic examination of her urine. The silver nitrate effected a cure by destroying the organisms in the mucous membrane of the pelvis.

Example of Chronic Pyelonephritis.

A married woman, aged 55, had for two years complained of ill health, associated with attacks of increased frequency of micturition, together with smarting pain during the act. She had occasionally "a mild backache," but the vesical symptoms predominated.

The urine contained pus, and bacteriologically *B. coli communis* in pure culture was found. An autogenous vaccine failed to improve matters.

Cystoscopy showed a mild degree of cystitis, while pyelography showed certain changes in the renal calyces, which were conclusive evidence of a chronic pyelonephritis. The urine collected from each kidney contained pus cells.

The renal pelvis were irrigated on four occasions with a 1 in 10,000 solution of silver nitrate; she has remained quite well and free from all abnormal symptoms and signs for the last three months, and a permanent cure seems assured. No anaesthetic was ever necessary, and the patient was up and about on the following morning after each treatment.

Fortunately for the patient the infection must have been in the apices of the pyramids, and probably it had not penetrated deeply into the solid tissue.

Example of Infected Hydronephrosis.

In March, 1924, three months after a confinement, a married woman, aged 25, had an acute attack of right renal colic, with the typical severe pain, vomiting, and strangury. She got over the acute stage, but she never recovered her health, and was frequently ailing. She had an indefinite ache in the right flank; there was neither frequency nor haematuria, but she had lost weight, and the urine contained pus. Bacteriologically, *B. coli communis* was repeatedly found in pure culture; prolonged treatment by vaccines failed to give any relief.

Cystoscopy showed a basal cystitis, being much worse on the right half of the base of the bladder. Pyelography (see Fig. 1) showed the right kidney to be disorganized; the shadows were normal on the left side. The urine from the right kidney contained pus; that collected from the left kidney was free from pus cells. The phenolsulphonaphthalein excretion from the left kidney was 5 per cent. (a normal amount).

Right nephrectomy was performed; the removed kidney contained infected urine, but there was no actual pyonephrosis.

The photograph of the specimen (Fig. 2) shows that the kidney was disorganized and incapable of recovery. It is possible that if early treatment of the kidney had been undertaken in this case the condition might never have progressed beyond the stage of pyelonephritis, although clinically there was never any indication of a very serious condition. The pyelonephritis was the initial stage of the infected hydronephrosis.

The patient has made an uneventful recovery; six months later she is fat and well and the urine is normal, the microscope now failing to detect any pus cells, showing that the basal cystitis has healed.

Example of Pyonephrosis.

A spinster, aged 22, for six years had had increased frequency of micturition with pain during and after the act. Two years ago she began to have pain in the back, but more particularly in the right flank. Six months before admission she had haematuria. She had tenderness in the right flank, the urine contained albumin, blood, and pus, but x rays disclosed nothing abnormal in the urinary tract.

Cystoscopy showed a general cystitis, also that a thick column of pus was extruded from the right ureteric orifice, this giving the appearance of toothpaste being squeezed out of a metal tube. The urine from the left kidney was free from pus and the renal function tests showed it to be functionally good. A pyelogram was not made. The right kidney was removed by operation and she did well.

The removed kidney (Fig. 3) showed the last stage of sepsis, being disorganized; it is possible that by treatment in the early stage it might have been saved. I was unable to find the primary focus of the sepsis.

S. GILBERT SCOTT: METHOD OF DEALING
WITH A SWALLOWED OBJECT.
(See p. 133.)

FIG. 1.

FIG. 2.

R. J. WILLAN: TREATMENT OF URINARY SEPSIS.

FIG. 1.—Pyelogram showing normal left side with right hydronephrosis (see Fig. 2).

FIG. 2.—Infected hydronephrosis removed by operation (see Fig. 1).

FIG. 3.—Kidney completely disorganized by old-standing sepsis.

Primary or "Residual" Cystitis.

By this is meant an inflammation of the urinary tract entirely confined to the bladder; either it is a primary cystitis, or it is secondary to pyelitis, pyelonephritis, etc., which has been cured. Cystoscopy shows the cystitis, while the urine obtained from each kidney (by means of a ureteral catheter) is free from pus. If the bladder is constantly reinfected by septic urine, then the source of the sepsis in the kidney must be attacked before local treatment to the bladder is of any use.

Primary or residual cystitis, with or without ulceration, can be cured, or at any rate the distressing symptoms can be abated, by treatment with antiseptic emulsions. The details of the treatment are as follows.

Twice weekly a catheter is passed and the bladder distended under the usual strict aseptic precautions with either solution 1 or solution 2. The iodoform emulsion (No. 2) is too irritating to use too often. Solution 1 is used three times to one of solution 2—that is, solution 1 is used on the 3rd, 6th, 10th, 17th, 20th, and 24th days of a month, while solution 2 is used on the 13th and 27th days of a month. The solution is allowed to remain in the bladder for thirty minutes, when it is micturated. I carry out the treatment for eight weeks, or longer if a cure has not then been obtained. The composition of the solutions is as follows.

Silver-Iodide Emulsion, or Solution 1.

Potassium iodide ... 21.66 grams in 150 c.cm. water.
Silver nitrate ... 21.66 grams in 150 c.cm. water.

These solutions are mixed with 150 c.cm. of mucilage of Irish moss.

Iodoform Emulsion, or Solution 2.

Iodoform ... 45 grams.
Glycerin ... 315 grams.
Aq. dest. ... 90 c.cm.

The emulsions are made up for me by Messrs. Brady and Martin, Newcastle-upon-Tyne.

Examples of Primary or Residual Cystitis.

CASE A.

A married woman, aged 48, had had for twenty years periodic attacks of cystitis, obviously exacerbations of a chronic cystitis. She had had three severe ones during the previous twelve months. There was increased frequency of micturition day and night accompanied by pain; she took very little fluid as "she was afraid to." The urine contained albumin and pus cells.

Medicines, vaccines, and the ordinary bladder irrigations had all failed to cure her.

Cystoscopy showed acute ulcerative cystitis in a contracted bladder; the pyelograms were normal, and urine collected from each kidney was free from pus cells.

The view taken was that the trouble was now entirely in the bladder, and that if the ulcers could be induced to heal she would be cured. She was treated by the emulsions and she quickly responded to treatment.

CASE B.

A married woman, aged 75, had for some years been troubled with severe attacks of urinary stranguy accompanied by pain and haematuria. So acute was the pain that she was frequently reduced to tears, and life was a misery to herself and her relations. Treatment was of no avail and nothing could be done to relieve her distress, even morphine having no beneficial effect.

Cystoscopy showed general ulcerative cystitis; the ureters were not catheterized, as the bladder distension occasioned distress to the patient.

Although a diagnosis of primary or residual cystitis was not definitely established, treatment by the emulsions was recommended and carried on for three months; by the end of that time the pain, stranguy, and haematuria had disappeared. Her urine contained pus cells, therefore she was not cured, but the relief of her symptoms restored her interest and pleasure in life. Her degree of relief can be gauged by a recently received letter, where she states:

"I thought I would like you to know how grateful I feel for all you did for me. I've had no pain for four months—before that, I had it pretty badly for over four years. Of course, I know it will probably return at my age, but it is something to be free for a time, and I feel most grateful."

"Please do not think it necessary to answer this note. I just thought I would like you to know how thankful I feel."

INOPERABLE SARCOMATA TREATED WITH RADIUM.

BY

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(With Special Plate.)

THE object of this paper is to give the clinical data of a series of thirty cases of sarcomata treated at the London Radium Institute. All the growths recorded were inoperable, and only those cases in which a histological investigation had been made are included. There might be added many cases of sarcomata diagnosed clinically, by x rays or by the subsequent progress of the disease, and such cases might prove of considerable interest to the less critical. It has been difficult to get information about many patients treated before the "follow-up" scheme was introduced at the Radium Institute.

The treatment of all forms of sarcomata is best carried out by the use of gamma radiation. Certain known clinical facts are as follows:

1. Many sarcomata will disappear under the effect of gamma radiation, the malignant cells being destroyed by doses which do not harm the surrounding tissues.
2. Some sarcomata are more susceptible to the rays than others. In the case of lymphosarcomata too great an importance should not be attached to the rapid disappearance of the primary growth, and the patient should be kept under observation for some considerable time so that the appearance of any metastases may be promptly dealt with.
3. The same type of tumour in different parts of the body does not always react in the same way.
4. Radium rays have only a local effect. Separate metastases may be treated, but widely disseminated recurrences when present will eventually gain the upper hand.
5. There comes a time when tumours which have previously reacted well will no longer respond to radiation, even when there is no evidence of metastases.
6. Relief of symptoms and prolongation of life are seen in most cases, and some patients remain in good health for long periods, the growth becoming shrunken and fibrosed.

TREATMENT.

Comparatively little can be said of the "dosage" owing to the varied situations and extent of the growths, but the treatment must be vigorous. Both needles and surface applicators are employed and a large quantity of radium should be used. Speaking in general terms, it is best to give a maximum dose at the first exposure; if it be necessary to repeat the treatment the strength of the subsequent exposure must be diminished.

Surface applicators are rectangular, square, or circular, with superficial areas ranging from 1 to 30 sq. cm. The applicators used in these cases are of two strengths, containing either 1.25 or 2.50 mg. of radium element per square centimetre. They are disposed in such fashion as to obtain a cross-fire of focal radiation in all parts of the growth. All external applicators should be screened with 2 mm. of lead or its equivalent, and covered with rubber. These are applied over a thick layer of wool. The needles used contain 1, 2.5, 5, 7.5, 10, or 25 mg. of radium element, their lengths varying from 1.2 to 4 cm. and the wall of the needle varying from 0.3 to 0.5 mm. of platinum or 1 mm. of silver. Recently needles with a wall of 0.4 mm. of Monel metal have also been used.

The action of large doses is to produce progressive degeneration. It has been suggested that with very small doses it is possible there may be stimulation of certain types of growth, but there is no certain evidence on this point. The time factor has been much discussed of late. At the Radium Institute the principle underlying the treatment is to give a large dose for a comparatively short time—seldom longer than forty-eight hours. It seems, however, quite possible that weaker doses for a longer time would give equally good results. There are many obvious difficulties in keeping needles in some situations for perhaps a week; a very common and serious complication is that of sepsis. Tissues subjected to radium rays are very susceptible to attack by bacteria, and every aseptic precaution should be taken when introducing needles into any tumours.

Case 1.—A woman, aged 62. On May 21st, 1913, a swelling of the right clavicle was explored and found to be an inoperable sarcoma. When seen at the Radium Institute on June 6th there