

PRIMARY NON-GONOCOCCAL URETHRITIS

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## PRIMARY NON-GONOCOCCAL URETHRITIS.

A study of the aetiology and diagnosis in males based on a series of 118 cases.

That all urethral discharges were not necessarily gonococcal was recognised over two hundred years ago.

1)  
Voltaire in "La Bible Enfin Expliquée, Nombres" refers to gonorrhée and also to a non-contagious discharge. The latter may have been a non-specific urethritis or a urethrorrhoea.

2)  
In 1883, Bochart and Wolfe described pseudo-gonorrhoeal urethritis characterised by the presence of streptococci. They cultivated the organism, and succeeded in reproducing the disease by introducing into a healthy urethra a small quantity of the purulent discharge by means of a contaminated sound. They named the resulting infection "pseudo-blenorrhagia."

In reviewing the literature on primary non-gonococcal urethritis during the last fifty years one is struck not so much by the paucity of the references in genito-urinary textbooks, but by the levity with which this subject is dismissed. From the sociological point of view it is obvious that irreparable damage may be done to marital happiness by describing any case of urethritis as gonococcal until the diagnosis has been definitely established by microscopical or cultural methods. In a case

recently under the writer's observation a man savagely attacked his wife causing her serious injury, because an acute urethritis he had developed, without extra-marital exposure, was at first incorrectly labelled by his doctor as gonorrhoea.

From the psychological aspect in some patients an anxiety neurosis is particularly liable to develop in association with any urethral discharge. It is important, therefore, that the exact aetiology of all meatal exudates be ascertained before the final cure of the condition is made more difficult by psychic trauma.

Although in the large majority of cases of non-specific urethritis the disease is of a mild type and is localised to the genito-urinary tract, occasionally other organs are affected. Kristjansen<sup>3)</sup> records a case of primary non-gonococcal urethritis which developed conjunctivitis and polyarthrititis. Five complement fixation tests for gonorrhoea performed at different stages of the infection were completely negative, as was also the Wassermann test.



PRIMARY AND SECONDARY INFECTIONS.

There are two types of non-gonococcal urethritis, namely, primary and secondary.

Primary non-gonococcal urethritis may be described as a urethritis arising independently of any gonococcal infection.

Synonymous terms are primary non-gonorrhoeal urethritis, primary non-specific urethritis, urethritis simplex, idiopathic urethritis, and pseudo-gonorrhoea. The latter term is chiefly used to describe the more acute cases of primary non-specific urethritis.

Secondary non-gonococcal urethritis is a residual urethritis after the original infecting organism, the gonococcus, has apparently died out. This is a relatively frequent type as in the majority of cases of gonorrhoea, even within a few days of the appearance of the discharge, secondary organisms may be found in the purulent exudate. In 1930 the writer investigated a series of 155 cases of early acute gonorrhoea attending the Venereal Diseases Department of the Royal Infirmary, Edinburgh and cultured secondary organisms from the urethral pus of 130 patients (83.5 per cent). By far the commonest organism found was staphylococcus albus followed by diphtheroids, streptococci, staphylococcus aureus, and bacillus coli in that order of frequency.

In the majority of cases, then, gonorrhoea is a mixed infection from the earliest stages of the



disease. A probable explanation of this phenomenon is that the organisms normally inhabiting the anterior urethra become virulent, and as the disease spreads backwards to the posterior urethra these potential pathogens travel with it.

Frequently secondary organisms gain a firm foothold in the damaged mucous membrane and may result in a continuance of the urethritis for a considerable period after the gonococci have been eliminated.

INCIDENCE.

The general impression is that primary non-gonococcal urethritis is a rare occurrence.

This is a mistaken view, although it is not nearly as common as gonorrhoea.

In view of the extensive range of aetiological agents which may occasion a primary non-specific urethritis, one might reasonably expect this disease or group of diseases to be more frequently met with than gonorrhoea which has only one cause.

4) Kidd in a consecutive series of a hundred cases of urethritis found gonococci in 84 per cent and staphylococci and streptococci in the remaining 16 per cent.

5) Beilin in a hundred consecutive cases of acute urethritis found gonococci in 86, staphylococci in eight, streptococci in two, diplococcus catarrhalis in one, and various unidentified bacteria in three.

In a series of 178 cases of acute urethritis in male patients attending the Venereal Diseases Department of the Royal Infirmary, Edinburgh in 1930 the writer obtained the following results:-

	Number of cases.	Percentage
Gonococci	155	87%
Staphylococci	10)	
Streptococci	5)	
Diphtheroids	2)	23 Non-Gonococcal 13%
Bacillus Coli	2)	
No growth on culture	4)	

The present series of cases was collected from 1361 male new patients attending the Stoke-on-Trent

Municipal clinic during the years 1933 and 1934.

Of this number 726 were suffering from urethritis:-

Gonorrhoea and secondary non-specific urethritis

608 cases.

Primary non-specific urethritis 118 cases.

Urethritis total 726 cases.

That is 16.2 per cent of the total number of cases of urethritis were non-gonorrhoeal - the gonococcus was in no way a causal factor.

The incidence of special forms of infective urethritis - for example tuberculous and syphilitic - will be referred to, when these particular infections are discussed.



PREDISPOSING CAUSES.

These may be briefly summarised as follows:-

1. Phimosis.
2. Hypospadias.
3. Previous urethritis.
4. Ill-health, over-exertion, and exposure to cold.

Eleven patients (nine per cent) of the 118 in this series were phimosed to such an extent that the prepuce could not be retracted over the glans penis. The average frequency with which such an anatomical condition of the prepuce occurs in healthy adult males is difficult to ascertain, but in a large London clinic <sup>6)</sup> for the treatment of venereal diseases only four per cent of all male patients were phimosed. Undoubtedly autoinoculation of the urethra with subpreputial organisms is more likely to occur when the preputial sac remains uncleansed over long periods.

Similarly varying degrees of hypospadias expose a proportionate surface of susceptible mucous membrane and facilitate the entry of pathogenic organisms to the urethra.

Fifty-one patients (43 per cent) gave a history of previous urethritis - forty-four gonococcal and seven non-gonococcal. The average period elapsing between the attacks of urethritis was eight years showing that although 37 per cent of the 118 cases of primary non-gonococcal urethritis had formerly suffered from gonorrhoea this infection had not devitalised the urethral mucosa of any marked extent,

in view of the many years without urethral symptoms. The fact that patients, who have previously attended a V.D. clinic for urethral treatment, are more ready to return for examination on the least sign of meatal discharge must also be taken into account.

Because of the difficulty in chronic infections of differentiating between a primary and a secondary non-specific urethritis, no patient was included in the present series who gave a history of gonorrhoea within twelve months prior to the onset of the disease or in whom subsequent examination revealed a possible gonococcal focus of infection.

Cases of non-gonorrhoeal urethritis may spontaneously arise during convalescence from debilitating illnesses or following exposure to cold. Over-exertion may likewise predispose to a urethral inflammation. The so-called "porter's urethritis"<sup>7)</sup> is common in Africa, but as Castellani points out many of these cases are gonococcal. However it must be remembered that in soldiers and porters doing long marches day after day a mild form of non-specific urethritis is liable to develop.

MODES OF INFECTION.

1. Sexual intercourse.
2. Rectal coitus.
3. Coitus in oram.
4. Meatal organisms.
5. Urethral commensals.
6. Descending infections.
7. Haematogenous.

1. Sexual Intercourse.

Non-gonococcal urethritis may or may not be a venereal disease. Some forms of primary non-specific urethritis are practically always acquired by sexual intercourse, others seldom, and some never.

In the former group lie the urethrités occasioned by the rare intra-urethral lesions of primary syphilis and chancroid, while in the latter group are the urethrites resulting from irritants of the urinary tract such as urethral calculi.

On first considering the question of infection following sexual intercourse, it seems remarkable that a urethritis should subsequently occur; because the majority of pathogenic bacteria entering urethra during coitus must be washed out at the time of ejaculation by the combined secretions of seminal vesicles, prostatic and urethral glands, and also probably by the flow of urine within a few hours.

There is, however, in the roof of the urethra, near the meatus, the lacuna magna and other smaller crypts which open towards the meatus, with the result that organisms finding a nidus there may remain unaffected by the flow of seminal fluid.



It is possible that these lacunae play a highly important part in the mode of transference of infection. They may partly explain the apparent immunity to infection enjoyed by a few individuals, as the location of these crypts is not a constant factor. It is well known that two males may expose themselves to infection from one source within half an hour, and one male may develop no symptoms whatsoever, while the other subsequently develops an acute urethritis, although neither have adopted prophylactic measures.

Undoubtedly many cases of bacterial non-gonorrhoeal urethritis (for example Streptococcal urethritis) are directly spread by sexual relations and hence might come under the classification of venereal diseases. From the statistical point of view, some confusion has arisen in this connection, as the majority of investigators classify all cases of non-gonococcal urethritis, except the rare cases of syphilitic and chancroidal urethritis, as non-venereal. A few clinicians however, refer to cases as non-specific venereal disease where there is a history of recent exposure to venereal infection.

As too much reliance cannot be placed on statements obtained from patients attending V.D. clinics, especially with regard to sexual relations, the figures obtained as non-specific venereal disease tend to be inaccurate. Lees<sup>8)</sup> defines non-specific venereal infection as a large group of genital

diseases including cases of balanitis, urethritis and similar conditions in which there has been an admitted risk of infection followed by symptoms of disease which simulate syphilis, gonorrhoea or chancroid.

Frequently primary non-gonococcal urethritis may result from coitus with a woman suffering from a non-gonococcal urethritis, vaginitis or cervicitis.

Case 1. A potter, aged 27 years, married, complained of a urethral discharge of two days duration. He stated that he had never had any venereal disease. He had, however, since his marriage two years previously, frequently seen a slight discharge from his urethra which lasted for a day or two. He had paid little or no attention to the discharge as it caused him no discomfort. A week previously he had attended a public lecture on venereal diseases and it occurred to him that the cause of his intermittent discharge should be investigated. He denied extra-marital exposure to infection. The last marital intercourse was two days prior to attending the clinic. He had never given himself any treatment and his health in adult life had been good.

On examination there was a very slight mucopurulent urethral discharge unaccompanied by any redness or swelling of the meatal lips. Microscopical examination of the exudate showed a few pus and epithelial cells but no organisms. A

culture was taken and a growth of staphylococcus albus and diphtheroids was obtained.

Using the two-glass test both specimens of urine were clear with a few threads in the first glass.

The anterior urethroscope showed a rather hyperaemic mucous membrane but no lithtritis or lacunitis and no evidence of stricture.

The gonococcal complement fixation test and the Wassermann reaction were negative, and there were no pus cells in specimens obtained after prostatic massage.

In view of the history and findings, no treatment was instituted and the condition cleared up in four days time.

At the patient's request his wife was also examined. She was found to have a chronic non-gonococcal cervicitis with a fairly large cervical erosion.

Her serological tests for gonorrhoea and syphilis were also negative and no gonococci were demonstrated after repeated provocative tests. A culture taken from the cervical canal produced a profuse growth of staphylococcus albus and diphtheroids.

The above case suggests that a urethritis may repeatedly result in a male following intercourse with a female suffering from a chronic cervical infection.

9)  
Kidd quotes three cases of urethritis contracted from women while menstruating.



There seems little doubt that many non-gonococcal urethral infections are acquired directly as the result of sexual intercourse, and may be transferred from one patient to another, and from one sex to another, in a similar fashion to gonorrhoea.

Excluding marital relations 75 of the 118 patients (64 per cent) in this series admitted an exposure to infection within one month of the onset of symptoms.

2. Rectal Coitus.

Because of the enormous number of potentially pathogenic organisms in the rectum a primary non-specific urethritis following sodomy is a highly probable occurrence.

10)  
Kidd quotes two cases and Romanis and  
11)  
Mitchiner refer to a medical student who developed a bacillus coli urethritis, after inserting a thermometer into his rectum and then into his urethra, to compare the difference in temperature. In this case the infection spread beyond the urethra to the bladder and kidneys, and almost resulted in the death of the enquiring student.

12)  
Davies mentions two cases of severe bilateral epididymitis and urethritis due to bacillus proteus. In both patients the infection was obtained per rectum.

Probably coliform bacilli and enterococci are the most frequent organisms found in non-gonococcal urethritis following this mode of infection.

In twenty-three consecutive cases of primary non-specific urethritis the writer isolated streptococci in five (21.3 per cent).

Thereafter the bile resistance, heat resistance, haemolysis and fermentive reactions were studied. The following is a brief summary of the bacteriological methods adopted in order to determine the type of streptococcus.

Bile resistance - 0.2ccs of a 48 hour broth culture was added to 1cc of a 10 per cent solution of sodium taurocholate and subcultured after 24 hours incubation.

Heat resistance - 48 hour broth cultures were subjected to a temperature of 60° centigrade in a water-bath and subcultured at the end of 15 and 60 minutes.

Haemolysis - a) culture on blood agar plates.

b) a 1 per cent solution of washed sheep's cells was added to an equal quantity of bacterial emulsion and incubated in a water bath at 37° centigrade for two hours.

Fermentive reactions - Holman's classification<sup>13)</sup> was used. 24 hour broth cultures were inoculated into Hiss's serum water litmus media and a broth tube was inoculated at the same time as a control of growth or contamination.

These procedures revealed that in all five cases the organism present was streptococcus faecalis (bile resistant, heat resistant, non-haemolytic, fermented lactose, mannite and salicin). Although in every case the mode of infection was not by rectal coitus it seems likely that, owing to the difficulty in obtaining an accurate history, this type of infection is more common than is generally supposed.



3. Coitus in oram.

Owing to the fact that few patients will give a reliable history, our knowledge of this mode of infection is very limited.

Under favourable bacterial conditions it is probable that the organisms commonly inhabiting the mouth and nasopharynx may cause a primary non-specific urethritis.

Streptococcal and catarrhal urethritis are relatively common and Castellani<sup>14)</sup> has described cases of urethritis due to spirochaetes and yeast-like fungi.

The following case is of interest.

Case 2. A schoolboy aged sixteen complained of a urethral discharge of eight days duration, unaccompanied by dysuria or other symptom. He denied exposure to infection but admitted that he frequently "abused himself."

On examination there was a slight muco-purulent meatal exudate, but no other sign of any genital infection.

A stained film of the discharge showed epithelial and pus cells and very many minute Gram-negative bacilli (chiefly extra-cellular, but a few were intra-cellular). No gonococci were seen. On culture a growth of staphylococcus albus was obtained. Further questioning revealed the fact that during the act of masturbation the patient was in the habit of using his pocket handkerchief to collect

the seminal ejaculations.

It seems likely, therefore, that the minute Gram-negative bacilli noted were bacillus influenzae. Serological tests for syphilis and gonorrhoea were negative.

Bidaily irrigations with a 1 in 12,000 solution of mercury oxycyanide cured the urethritis within fourteen days.

Bacteria commonly found in local infections (possibly commensals also) of the nose and throat may give rise to a urethritis if introduced into the urethra under conditions favourable to organismal infection.

Pfeiffer<sup>15)</sup> has described a case of urethritis with a whitish discharge in which no gonococci were found at any time.

The urethral secretion contained a pure culture of bacillus influenzae. The disease was cured by weak sublimate injections for four weeks.

The writer has seen a case of acute pseudo-gonorrhoea in a male due to micrococcus tetragenus. In this case the patient admitted an oral source of infection.

#### 4. Meatal Organisms.

Subpreputial and meatal organisms may spread into urethra especially if associated with phimosis.

Lloyd and Lloyd<sup>16)</sup> found that four per cent of all patients attending their venereal diseases clinic were phimosed.

In this series nine per cent of the 118 cases had a prepuce whose orifice was too small to permit retraction over the glans penis. Such an anatomical condition of the prepuce results in foreign material and organisms collecting subpreputially and eventually a balanitis or a balano-posthitis ensues. In a few cases there may be also an associated urethritis as exemplified in the following case.

Case 3. A miner, aged 21 years, unmarried complained of a discharge and swelling of the penis of nine days duration, and also pain on micturition for two days. There was no history of previous venereal disease and his last exposure to infection was four months prior to the onset of symptoms.

On examination there was intense swelling and redness of the prepuce and some degree of oedema of the body of the penis. The prepuce would not retract. There was a profuse purulent subpreputial discharge.

A stained smear of the purulent exudate revealed many Gram-positive cocci in clusters and in chains, and by dark-ground illumination - after syringing subpreputially with saline - many spirochaetes of the refringens type, but no treponema pallidum. Inguinal glands on both sides felt small and shotty on palpation. A gland puncture was not attempted.

A dorsal slit carried out under eripan anaesthesia exposed a typical acute balano-posthitis.

On resuming the examination the following day it



was evident that there was also a urethral infection. Films of the urethral discharge examined under the microscope were exactly similar to those of the subpreputial exudate. According to the findings of the two-glass urine test the urethritis was confined to the anterior urethra, and was successfully treated by bidaily irrigations with a 1 in 12,000 solution of mercury oxycyanide for one week.

Subsequent bacteriological and serological test gave negative results.

The above case emphasises that where free drainage from a balanitis is obstructed by oedema of the preputial orifice the purulent material and organisms finding their way into the urethra may give rise to a urethritis.

#### 5. Urethral Commensals.

The healthy male urethra harbours many varieties of bacteria, apparently living as commensals until some stimulus interferes with the natural harmony existing between these organisms and the urethral mucosa.

A urethritis due to these organisms may be brought about by a) a lowering of the normal resistance of the mucous membrane; or b) the so-called commensals adopting pathogenic powers.

The development of a bacterial urethritis, subsequent to the ingestion of certain drugs - cantharides for example - unassociated with any infection from without, suggests that these commensals

lying dormant in the urethral crypts and glands are really potential pathogens.

Another example of this phenomenon may be encountered after the too frequent passage of sterile instruments such as bougies, sounds, catheters and dilators. The repeated traumatism leads to congestion and devitalisation of the mucous membrane of the urethra and a bacterial urethritis may ensue.

The subjoined table <sup>17)</sup> gives a synopsis of the findings of a number of workers on the bacteria of the normal male urethra.

Commensals of the Male Urethra.

Authors	Year	Number of cases	Results.
Lustgarten and Mannaberg	1887	8	10 varieties of bacteria.
Steinschneider and Gallewski	1889	13	Gram-positive diplococci.
Rovsing	1891		Staphylococcus Aureus and Streptococci.
Petit and Wassermann	1891		5 forms of micrococci.
Pfeiffer	1891	24	13 varieties of bacteria.
Franz	1896	41	Diplococci.
Savor	1899	93	Diplococci in 9 cases.
Pfeiffer	1904	24	Different bacteria in 23 cases.
Koll	1917		Bacteria in 20% of all cases.

The writer carried out a similar experiment by taking cultures from the urethrae of male patients in whom there was no evidence or history of past or present urethral inflammation. Often cases thus examined no growth was obtained in four and various bacteria were cultured from the remaining six, principally mixed growths of staphylococcus albus and diphtheroids.

6. Descending Infections.

A few cases of bacterial non-gonococcal urethritis arise from pathogenic organisms reaching the urethra in the urinary or seminal stream. The primary lesion may be in the kidney, bladder, prostate, seminal vesicle, vas deferens, epididymis, or testicle. The principal infections in this respect are those associated with the bacillus tuberculosis and bacillus coli, but any infection of the upper urinary tract or generative system may eventually result in a urethritis.

<sup>18)</sup>  
Harkness has described a case of urethritis in this country where the primary disease was found to be bilharzia.

Pyelitis and cystitis due to coliform bacilli are relatively so common that it is remarkable that a urethritis is not more frequently encountered in these cases.

The importance of the prostate gland and seminal vesicles as a primary focus of infection in non-gonorrhoeal urethritis cannot be over emphasised as



the following case illustrates.

Case 4. A collier, aged thirty years, unmarried, was referred to this clinic by his panel doctor as a possible case of gonorrhoea.

He complained of a urethral discharge for three weeks, and a "swollen testicle" of two weeks duration. He suffered no urinary discomfort but had some nocturnal frequency of micturition for five weeks. There was no history of former venereal disease. He admitted an exposure to infection two weeks prior to the onset of symptoms and also one month previously. He stated that his general health was good in other respects.

On examination there was a definite watery mucopurulent urethral discharge which microscopically showed pus cells and epithelial cells but no organisms.

The right epididymis was swollen, slightly tender and adherent to the skin of the scrotum posteriorly. There was also an associated hydrocele which prevented accurate palpation of the scrotal contents. On examination per rectum by palpation there was some enlargement of both prostatic lobes, but no tenderness or irregularity of contour. Both vesicles were definitely palpable and felt nodular to the examining finger. Specimens of urine were clear, with a few threads in both glasses. Microscopical examination of a centrifuged deposit of urine, stained Gram and Ziehl-Neelsen, showed pus cells and

epithelial cells but no organisms.

A urethroscope passed to the region of the bulbous urethra revealed three irregular white spots on the mucous membrane surrounded by an area of hyperaemia. A few days later fluctuation could be detected over the globus minor of the right epididymis and shortly thereafter a small sinus developed. The patient was then transferred for surgical treatment.

The Wassermann, Kahn and gonococcal complement fixation tests were completely negative.

Undoubtedly this was a case of tuberculous infection - although the actual bacillus was not demonstrated - of the genito-urinary tract, involving primarily the seminal vesicles and spreading from there to the epididymis and urethra.

Primary non-gonococcal infections of the prostate gland sometimes give rise to a urethritis and conversely prostatitis is an occasional complication of primary non-specific urethritis. Almost thirty years ago Young<sup>19)</sup> pointed out that a non-gonorrhoeal form of prostatic infection might occur. In a study of 358 cases he found that gonorrhoea was an aetiological factor in 73 per cent cases only.

From a study of the literature and from his own experience Briggs<sup>20)</sup> states that 18 per cent to 20 per cent of all cases of prostatitis are non-venereal in origin and Baker<sup>21)</sup> considers that 15 per cent to 20 per cent of prostatic infections are

are non-gonococcal.

22)  
Bugbee reports four cases of prostatic abscess following influenza in one of which the bacillus influenzae was recovered. Similar infections of the prostate may also give rise to a non-specific urethritis by descending infection.

Malignant growths of the bladder and prostate may spread by continuity to the posterior urethra and cause a urethritis.

7. Haematogenous.

Infection of the urethra may occur through the blood stream. A urethritis has occasionally been observed during the course of certain systemic infections such as measles, smallpox, influenza and typhus fever. It has not been proved that the actual viruses associated with these diseases were the immediate cause of the urethral inflammation or merely toxins excreted in the urine while the febrile process was at its height.

23)  
Bacillus typhoeus has been isolated from a urethral exudate in a case of enteric fever. It is more probable however that the infection was a descending one from the kidney than directly haematogenous to the urethra.

Metastases from malignant growths elsewhere in the body may exceptionally form in the urethra and cause symptoms of urethritis.

In the so-called secondary stage of syphilis lesions may arise in the urethra, similar to mucous



patches found in the mouth, and produce a urethral exudate in which treponema pallidum can be demonstrated. The urethritis is usually of a mild character though Bumstead<sup>24)</sup> and Bassereau<sup>25)</sup> claim to have observed cases with a profuse purulent discharge resulting from the presence of intra-urethral mucous patches. Nunn<sup>26)</sup> has reported ten cases of urethral stricture due to secondary syphilis. In a series of thirty-seven cases of stricture of the urethra Ross<sup>27)</sup> found that syphilis was a contributory factor in 73 per cent. He states that he is convinced that the majority of urethral strictures are the result of syphilis.

Intra-urethral gummata may cause a urethritis. They are usually in the penile portion of the urethra and give rise to difficulty in micturition. When they become ulcerated there is a muco-purulent discharge accompanied by some dysuria. In 1901 Fournier<sup>28)</sup> reported nineteen cases of tertiary syphilis of the urethra.

CLASSIFICATION

A few classifications of primary non-gonococcal urethritis have been proposed based chiefly on clinical findings. The present writer suggests an aetiological and bacteriological classification, on the grounds that, the cure of the condition depends not so much on the type of the discharge, the severity of the urethral inflammation or the method of treatment, as on the discovery and removal of the cause at its source.

		(Chemical (28)
	)Irritative(61)	{Mechanical (9)
	)	{Urinary (15)
	)	{Sexual (9)
Primary Non-Specific Urethritis (118)	)	
	)	{Coccal (41)
	)	{Bacillary (11)
	)Infective (57)	{Protozoal (3)
	)	{Metazoal (0)
	)	{Mycotic (1)
	)	{Ultra-
	)	{ Microscopic(1)

The bracketed figures in the above list represent the approximate number of cases in each group of the present series.

Two types, then, of primary non-gonorrhoeal urethritis may be distinguished A) Irritative and B) Infective (or bacterial). An exact classification of all cases of urethritis into one or other of these two groups is not always possible, however, as organisms may be found in the urethral exudate from cases of irritative urethritis and conversely no organisms may be found in cases where the

primary cause was infective.

The former difficulty is more frequently met with as any non-bacterial irritant of the urethral mucosa may so lower the natural resistance to infection that organisms normally inhabiting the urethra may develop pathogenic properties and result in a urethritis. While in a few cases of infective urethritis (chancroidal, tuberculous etc.,) the causative organisms may be very difficult to detect by ordinary bacteriological methods.



## IRRITATIVE URETHRITIS

The actual irritant may take one of the following forms:-

1. Chemical.
2. Mechanical.
3. Urinary.
4. Sexual.

### 1. Chemical.

The term "chemical urethritis" implies an inflammation of the urethral mucosa resulting from the irritation of chemicals introduced into the urethra through the meatal orifice.

The expression does not refer to those cases of urethritis due to the taking of certain drugs by the mouth.

A chemical urethritis is one of the commonest of all forms of primary non-gonococcal urethritis. In this series of 118 cases twenty-eight (twenty-four per cent) were definitely of this type.

There are two main types of chemical urethritis resulting from a) strong chemicals applied for a short period and b) weak chemicals applied for a long period.

a. A chemical urethritis may arise from the injection or instillation into the urethra of strong antiseptic solutions usually in efforts at prophylaxis. For example, 1 in 100 solution of potassium permanganate, 1 in 400 solution of acriflavine, concentrated solution of Lysol, and undiluted Milton have been used.

One patient rubbed permanganate crystals into the

meatus, leading to acute oedema and inflammation of the terminal portion of the glans penis accompanied by an almost black urethral discharge, acute dysuria and difficulty in urination. Another patient injected an undiluted phenol mouth-wash which produced what was in effect a urethral burn, and resulted in desquamation of the whole mucous membrane. Fortunately subsequent healing was not complicated by stricture formation.

29)  
Pedersen has reported a case of complete sloughing of the anterior urethra caused by lunar caustic inserted into the urethra to abort a gonococcal infection.

As a result of these attempts at prophylaxis there is soon a urethral discharge varying in colour, purulence and time of onset, according to the type and strength of the chemical used. The discharge is frequently accompanied by redness and swelling of the meatal lips and dysuria, and there may be difficulty in micturition if the irritant has been such as to produce intense oedema of the anterior urethral mucosa.

Examination of a stained smear of the discharge under the microscope will show large numbers of leucocytes, very few epithelial cells and usually no organisms.

Occasionally those seeking prophylactic methods insert medicated bougies into the urethra, fortunately with less acute results as the antiseptic is not in

a concentrated form. One patient developed a subacute anterior urethritis from the use of protargol gelatin stylets twice daily for six days.

An important and relatively common form of urethritis especially within recent years is that due to chemicals in contraceptives.

Case 5. A boiler maker, aged twenty-six years, married, complained of an intermittent urethral discharge of five weeks duration, without dysuria or frequency of micturition.

The routine inquiries regarding previous venereal disease, extra-marital exposure to infection and attempts at treatment received negative replies. On examination there was a slight muco-purulent urethral discharge, no meatal redness or swelling, no indurated areas, and no inguinal lymphadenitis. The first specimen of urine was very slightly hazy and the second was clear. No abnormality was discovered on examination per rectum.

A stained smear of the discharge revealed many pus cells and a few epithelial cells but no organisms. The patient was instructed to attend daily, for irrigation with a 1 in 12,000 solution of mercury oxycyanide, but he only received one treatment. When seen a week later he stated that, as the discharge had ceased the day following the irrigation, he considered he was cured.

Four days later the condition recommenced exactly as on previous occasions.



Exhaustive interrogation revealed the fact that for the past six weeks his wife had used quinine pessaries for contraceptive purposes, and on this habit being discontinued the urethritis did not recur.

In this case the inflammatory reaction in the urethra may have been due to the quinine or some irritant in the cocoa-butter medium. It is interesting to note that the patient stated he was not intolerant to quinine by the mouth; but this does not necessarily discount the quinine as an aetiological factor as some drugs may be taken orally with impunity, which on being injected urethrally cause an irritative urethritis.

b. A chemical urethritis may arise from the repeated injection or instillation into the urethra of weak antiseptic solutions over long periods - usually in attempts at treatment. One patient, a chemist's assistant, irrigated bidaily with approximately a 1 in 8000 solution of potassium permanganate for six months before seeking medical advice.

He was astonished to find that his urethral discharge ceased within two weeks without active treatment in any form.

There was no evidence of gonorrhoea either clinical, bacteriological or serological.

In this type of chemical urethritis microscopical examination of stained smears of the urethral

exudate will show many epithelial cells, only a few leucocytes and usually no organisms. As a rule the condition heals quickly when the irritating cause is discontinued.

## 2. Mechanical.

The presence of foreign bodies in the urethra may precipitate a urethritis. Occasionally boys, sexual perverts or lunatics insert into the urinary meatus small articles such as hairpins, lead pellets or slate pencils.

Over dilatation of the urethra with bougies and sounds or the too frequent passage of instruments may cause a urethral inflammation.

The irritation caused by a catheter, which has been left in the urethra for drainage purposes, commonly causes a urethral discharge.

Any urethral obstruction to the free flow of urine including pinhole meatus and stricture may produce a urethritis. Chwalla<sup>30)</sup> describes two cases of primary non-gonococcal urethritis due to small meati.

King<sup>31)</sup> mentions the case of a man who sought surgical advice because of pain in the urethra. The cause was not discovered but the surgeon inserted radon seeds into the urethra for forty-eight hours. This led to a profuse and intractable urethritis. The same authority<sup>32)</sup> describes a similar result from the prolonged and frequent use of diathermy with urethral electrodes.

Case 6. A shop assistant aged twenty-four years, unmarried, complained of a blood-stained urethral discharge for one day and difficulty in urination for two days, accompanied by frequency and urgency of micturition. He denied exposure to infection and stated that he had not suffered from any genital complaint previously. He had given himself no treatment. On examination there was a purulent urethral discharge streaked with blood. The meatal orifice was very small. On palpating the urethra two small indurated areas were felt about one inch from the meatus. These were at first thought to be infected urethral follicles. There was no inguinal lymphadenitis and rectal examination revealed no abnormality.

Microscopical examination of a stained smear of the discharge showed many pus cells, some epithelial cells and blood corpuscles, but no gonococci or other organisms. The urine was hazy and contained blood. The patient was unable to pass more than one or two ounces at a time. Treatment in the form of bidaily irrigation of the anterior urethra with a 1 in 12,000 solution of mercury oxycyanide was instituted along with daily hot hip-baths. A week later the clinical condition was unchanged, but five hard swellings were felt on palpating the penis. These were movable within the penile urethra. They could not be expressed from the meatus owing to the small size of the latter.



Meatotomy was performed and five calculi were removed. Subsequent bacteriological, serological and radiological examinations proved negative, and the urethritis cleared up within a few days.

Calculi found in the anterior urethra may have developed in the urethra itself or may have descended from the upper urinary organs. The former are the results of obstruction to the flow of urine, followed by decomposition and precipitation within the urethra. In the above case the small urinary meatus probably interfered with the free flow of urine and resulted in the formation of concretions from the solid elements of the urine.

Apart from other considerations the mechanical presence of urethral neoplasms, both benign and malignant may provoke a urethritis.

Papillomata and polypi are the most frequent of the benign type, but both are rare.

Intra-urethral papillomata may be associated with condylomata acuminata on the glans penis and prepuce.

Oberlaender<sup>33)</sup> has described "Urethritis papillomatosa". The present writer has seen one case of this type, where the urethroscope revealed large numbers of pale pink, superficial moist and sodden growths throughout almost the whole anterior urethra.

Intra-urethral polypi may be vascular or fibrous; the former being analogous to caruncles commonly found in the female urethra.

Primary malignant neoplasms of the urethra

(carcinoma and sarcoma) are exceedingly rare. Hall<sup>34)</sup> states that the majority are squamous-celled particularly in relation to chronic irritation around strictures. According to Wurmser<sup>35)</sup> urethral epithelioma most commonly occurs between fifty and sixty years of age, and usually follows some previous inflammatory condition of the urethra. The first sign may be a urethral discharge with difficulty in micturition and all the symptoms accompanying stricture. Later there is pain and hæmaturia, and frequently a fistula develops. Mark<sup>36)</sup> has described a case of primary urethral sarcoma. A similar case has been reported by Hall and Frick<sup>37)</sup> - at autopsy a melano-sarcoma was found.

### 3. Urinary.

Varying reactions of the urine may produce a mild inflammation of the urethral mucous membrane.

Hyperacid and hyperalkaline urine may cause a urethritis. A similar condition may occur in association with phosphaturia, oxaluria and glycosuria.

Case 7. A clerk aged forty-six years, married, complained of a urethral discharge of seven days duration, some nocturnal frequency of micturition but no dysuria. He had suffered from gonorrhoea twenty years previously, was treated privately and cured. He admitted extra-marital intercourse with a prostitute three months prior to the onset of symptoms. He had given himself no

treatment.

On examination there was a very slight mucopurulent urethral discharge, redness of the meatal lips and subpreputial surface. There was no inguinal lymphadenitis and per rectum no abnormality was palpable.

Specimens of urine were clear in both the first and second glasses. A stained smear of the meatal exudate showed pus and epithelial cells but no organisms. Urethroscopical examination was negative apart from some generalised hyperaemia of the mucous membrane.

The Wassermann reaction and gonococcal complement fixation tests were negative.

No treatment was given to the urethra, but saline soaks were applied subpreputially.

Fourteen days later there was no improvement in the clinical condition, and the balanitis was more acute with some excoriation of the skin of the preputial orifice. The patient also complained of a carbuncle on the back of his neck. The aetiology of the urethritis and balanitis then became evident as the urine strongly reduced Fehling's solution.

Examination of the urine for sugar may be important in leading to a diagnosis and should never be omitted, in resistant cases of balanitis and urethritis.

The urethral discharge occasionally found in



cases of gout is probably due to the irritation of excess uric acid in the urine.

In a few individuals certain articles of diet may give rise to a urethral inflammation. In rare cases a mild form of urethritis may follow the ingestion of certain vegetables such as asparagus, cress, cucumbers, spinach, strawberries, rhubarb and tomatoes.

Various drugs, for example alcohol, arsenic, cantharides, capsicum, copaiba, cubebs, iodides, juniper and podophyllin may result in a similar condition which rapidly subsides when the cause is removed.

In one case, recently under the writer's observation, a patient had taken nine juniper pills daily for a week. He developed a subacute urethritis which rapidly healed when he ceased taking the drug. In another instance a man and his wife had been taking large numbers of "bile beans" (chiefly extract of podophyllin). Both patients developed a urethritis accompanied by some dysuria for which no other cause could be ascribed. The symptoms subsided immediately they stopped taking the pills.

#### 4. Sexual.

According to the observations of Kidd<sup>38)</sup> irritating vaginal secretions, especially premenstrual, may cause a primary non-specific urethritis.

Pelouze<sup>39)</sup> describes a case of recurrent urethritis of this type. The periodicity of the attacks suggested that they might be related to the menstrual

cycle of the patient's consort.

40)  
McDonagh mentions repeated coitus interruptus as a cause of non-gonococcal urethritis, and frequent masturbation may eventually lead to a chronic inflammation of the urethral mucous membrane.

## INFECTIVE URETHRITIS

Under favourable bacterial conditions the majority of pathogenic organisms gaining access to the male urethra may cause an inflammatory reaction therein. Nearly all the known types of infective non-specific urethritis may be described in association with one of the following groups:-

1. Cocci.
2. Bacilli.
3. Protozoa.
4. Metazoa.
5. Mycetes.
6. Filterable viruses.

1. Associated with Cocci.

The staphylococcus albus is by far the commonest organism found in the urethral exudate in cases of non-gonococcal urethritis.

It is often a commensal in normal male urethra, and therefore may be found in the discharge from cases of undoubted irritative origin. This organism was isolated (occasionally along with other bacteria) in twenty-one of the fifty-seven cases of infective urethritis.

A purely infective staphylococcal urethritis usually runs a mild course with few symptoms or signs apart from a slight muco-purulent urethral discharge and is easily cured by weak antiseptic irrigations.

Staphylococcus aureus may cause a more acute type of primary non-gonococcal urethritis. Two cases of this infection were encountered in the present series.

Nearly all the streptococci found in pseudo-



gonorrhoea are of the faecalis group. In twenty-three consecutive cases of non-specific urethritis the writer isolated streptococci in five and all proved to be enterococci.

Micrococci tetragenous may cause a urethritis as in the case of oral infection previously mentioned.

A urethritis due to the diplococcus catarrhalis is particularly important from the fact that it is liable to be confused with gonorrhoea unless cultures are taken. According to Wolbarst<sup>41)</sup> diplococcus catarrhalis is the commonest cause of urethritis apart from the gonococcus. He states that the symptoms are less severe and the discharge less profuse and more mucoid than in gonorrhoea. McDonagh<sup>42)</sup> also considers that one of the most common urethral infections is that produced by this organism. On the other hand Storer<sup>43)</sup> maintains that the diplococcus catarrhalis is rarely found in the urethra. Ayres<sup>44)</sup> encountered seven cases of this type in one year in his private practice. He states that the general nature of the inflammation closely resembles gonorrhoea but is less acute at the start, symptoms milder, course shorter and complications relatively few. He recognises, however, that an acute urethritis with severe complications may arise from a diplococcus catarrhalis infection. Of the 726 cases of urethritis in males observed by the writer during the two years 1933 and 1934, eight were definitely

proved to be due to the diplococcus catarrhalis group. 608 cases were considered to be gonococcal, but as this diagnosis was made in nearly all cases by microscopical examination alone it is possible that some of these cases were catarrhal.

Case 8. A waiter, aged eighteen years, complained of haematuria, dysuria and nocturnal frequency of two days duration. He gave no previous venereal history and denied exposure to infection.

On examination there was a purulent urethral discharge. A stained smear examined under the microscope showed many pus cells, some epithelial cells and a few extra-cellular Gram-negative diplococci but no intra-cellular organisms.

Culture media were inoculated. On palpation per rectum no abnormality could be detected in the prostate but both seminal vesicles were enlarged, acutely distended and tender.

Using the two-glass test each sample of urine was hazy and contained blood.

Treatment was instituted in the form of hot hip-baths daily and the anterior urethra was irrigated bidaily with a 1 in 12,000 solution of mercury oxycyanide. In addition diathermy with the rectal electrode was given thrice weekly. On culture a pure growth of diplococcus catarrhalis was obtained. A week later the acute symptoms had subsided. There was only a very slight muco-purulent urethral discharge, and the specimens of urine in the first and

second glass were, respectively, very slightly hazy and clear. The seminal vesicles were palpable but not tender. Two weeks later no abnormality could be detected either in the urethra or adnexa. The serological tests for syphilis and gonorrhoea were negative throughout. This case demonstrates that the diplococcus catarrhalis may give rise to an acute urethritis with complications closely resembling gonorrhoea. The acute symptoms were short-lived, and the disease proved much more amenable to treatment than the average gonococcal infection with similar complications.

2. Associated with Bacilli.

Apart from staphylococcus albus and enterococci, the coliform bacillus is the most frequent invader of the male urethra. A bacillus coli urethritis may result from:- a) sexual intercourse, b) sodomy, c) infections of the upper urinary tract, d) idiopathic causes.

The urethral inflammation is often very acute and complications such as vesiculitis and epididymitis are commonly encountered. The writer has observed in this connection that - paradoxically enough - the more acute cases tend to heal up in a relatively short period, while the subacute cases frequently become chronic and are more difficult to cure. This is probably the result of a more rapid development of antibodies in the blood, in the acute urethritis with complications.



Bacillus proteus<sup>45) 46)</sup> may also cause a severe urethritis, and bacillus pyocyaneus<sup>47)</sup> and bacillus typhosus<sup>48)</sup> have been isolated from the urethra in cases of urethritis.

Intra-urethral chancroidal ulceration associated with the bacillus of Ducrey is an important though uncommon cause of a urethral discharge. The most frequent urethral site is in the fossa navicularis by extension from a chancroid near the urinary meatus; but lesions may arise primarily in the anterior urethra without any external signs of the disease apart from the meatal exudate. The latter is frequently purulent and there is always considerable dysuria. Typical suppurating buboes may be found in the inguinal glands.

The bacillus of Ducrey is difficult to find in stained smears of the discharge as there is nearly always a mixed infection and the organism will not grow on ordinary media. The urethroscopic picture is similar to that of chancroids elsewhere on the genitals, namely, a sloughing ulcer with undermined irregular edges.

Even more important is a non-gonococcal urethritis due to the bacillus tuberculosis. In very rare instances, an infection may arise primarily within the urethra, but more commonly is secondary to tuberculosis of the upper genito-urinary tract or other foci in the body. Hogge<sup>49)</sup> states conclusively that no cases of primary urethral

tuberculosis have been recorded, but Walker<sup>50)</sup> considers that direct infection of the male urethra may occur through sexual intercourse. Deville<sup>51)</sup> undertook an investigation of the vaginal discharges in genital tuberculosis amongst women. In four cases out of eight cases examined he was able to demonstrate tubercle bacilli in the discharges. On examining the husbands of these cases he found that all were suffering from tuberculosis epididymitis.

Infection per urethram during coitus is possible but highly improbable. It is certain that infection of the female by the male is more frequent than infection of the male by the female. Tuberculosis of the urethra is relatively uncommon even among patients with definite lesions of the kidney, bladder and seminal vesicles. Ahrens<sup>52)</sup> in a series of 433 cases found it in 18, or about four per cent. Hall and Metz<sup>53)</sup> found it in twelve out of 1,600 patients. As one would expect from the usual source of the infection the posterior urethra is much more frequently affected than the anterior. The lesion can be diagnosed as a rule by urethrocopic examination which may reveal tubercles or tuberculous ulcers.

In the case of tuberculous urethritis previously described urethral tubercles were seen. In stained smears of the urethral discharge bacillus tuberculosis may be confused with bacillus smegmae

unless an acid-alcohol decolourising technique is adopted.

Diphtheroid bacilli apart from their role as urethral commensals may give rise to a mild infective urethritis readily amenable to weak antiseptic irrigations.

54) Luys mentions bacillus diphtheriae as a causative organism. Undoubtedly in susceptible individuals a diphtheritic infection of the genitals may result from sexual intercourse.

55) Wendlberger describes a case of primary non-gonococcal urethritis in a young male where true diphtheria bacilli were associated with staphylococci and diphtheroids. Severe constitutional symptoms may occur, but the infection never spreads further than the anterior urethra. Membrane formation may take place.

56) Pfeiffer's bacillus may also infect the male urethra.

### 3. Associated with Protozoa and allied organisms.

#### Spirochaetes.

Spirochaetes of the refringens type may occasion a urethritis in the male, particularly if associated with balanoposthitis and phimosis.

Treponema pallidum may affect the urethra in three forms, namely, chancre, mucous patch and gumma.

Mucous patches and gummata of the urethra have been discussed previously. Two hundred years ago

57) Astruc described intra-urethral chancres in both men and women, and more than a hundred years



later Ricord<sup>58)</sup> confirmed this fact and suggested that because of the peculiar location of the primary lesion many cases of syphilis remained unrecognised until the later stages of the disease became manifest. Intra-urethral chancres most commonly occur in the fossa navicularis but Keyes<sup>59)</sup> has reported a primary lesion over one inch from the meatus. In uncomplicated cases there is a serous or sero-sanguinous meatal discharge with slight discomfort on urination. An area of induration may be felt on palpating the penis and the inguinal glands may be enlarged and rubbery to the touch.<sup>60)</sup> McDonagh states that lymphadenitis is an early sign, and the patient enters the generalisation stage more rapidly. On the other hand Keyes<sup>61)</sup> considers that lymphatic involvement is late in these cases. In the three cases of intra-urethral chancre in the present series each patient complained primarily of a urethral discharge. The presence of inguinal lymphadenitis suggested that a dark-ground examination should be performed. In all three cases the chancre was situated in the fossa navicularis and was accompanied by an indurated oedema of the terminal portion of the glans penis. There was little or no dysuria but one patient had definite difficulty in micturition and the stream was "forked". This patient had also signs of early secondary syphilis in the nature of a faint roseolar rash. The

diagnosis was confirmed by demonstrating the treponema pallidum in the meatal exudate or by gland puncture. The Wassermann and Kahn reactions were in all cases strongly positive.

The possibility of a mixed infection with the gonococcus must not be forgotten. Oedema of the meatus frequently associated with acute gonorrhoea may result from an intra-meatal chancre. According to Stokes<sup>62)</sup> sixteen per cent of patients with syp syphilis can give no history of previous venereal disease except that of gonorrhoea. In some of these cases the primary lesion must have been intra-urethral.

John Hunter<sup>63)</sup> believed in the unity of gonorrhoea and syphilis because subsequent to inoculating himself on the prepuce and glans penis with gonorrhoeal pus he developed a chancre as well as constitutional syphilis. Unfortunately he overlooked the fact that his gonorrhoeal patient had also an intra-urethral syphilitic lesion.

Primary syphilis of this location in males is considered to be very rare but Fournier<sup>64)</sup> in a review of 414 cases of primary lesions found that seventeen (four per cent) were in the urethra. The present writer diagnosed it in three (1.7 per cent) out of 169 consecutive cases of early syphilis in males.

Amoeba.

65) A urethritis due to *Entamoeba histolytica* has occasionally been described during the course of amoebic dysentery.

Ciliata.

66) Castellani describes a case of urethritis in a Singalese man in Ceylon in which he found a balantidium-like ciliate. He states that he had previously observed a similar organism in the vaginal secretion of several native women.

Flagellata.

In recent years considerable attention has been paid to the frequent occurrence of trichomonas in the female vagina.

67) Koelsch and Tsutsulopulos in an examination of 150 women found this flagellate in more than 49 per cent. 68) Neumann and Meyer state that trichomonas vaginalis normally inhabits the vagina in 30 per cent to 40 per cent of women.

They occur in the form of flagellated pear-shaped cells about the size of leucocytes and are best seen by dark-ground illumination.

69) Grimm and Wahlin 70) have described cases of urethritis in the male due to these protozoa; but as in the female it has not been finally proved that these organisms were entirely responsible for the condition.

If trichomonas vaginalis are considered to be pathogenic organisms, it is remarkable that a urethritis



in the male due to these flagellates is relatively uncommon, especially in view of the frequency with which they are found in the vagina. ~~vagina.~~ The most satisfactory explanation is that of Davies <sup>71)</sup> who suggests that these commensals become pathogenic in the presence of other organisms favourable to their growth.

#### Sporozoa.

A non-gonococcal urethritis may occur in association with plasmodium infections. A case of urethritis accompanying every attack of malaria in a male patient has been reported by Moscato. <sup>72)</sup> It is doubtful if the actual parasite was the true causative agent of the urethral inflammation.

#### 4. Associated with Metazoa.

<sup>73)</sup> Harkness has described a case of non-gonococcal urethritis in a male due to bilharzia. <sup>74)</sup> Hawe points out that this disease may closely simulate gonorrhoea. Occasionally a urethral discharge is the only sign with associated pyuria and dysuria. The urethritis is almost always due to schistosoma haematobium - the sister parasite schistosoma mansoni is only occasionally met with.

Myiasis rarely results in pseudo-gonorrhoea. Certain flies may deposit their eggs upon the skin of the genitals; the larvae burrow into the tissues and may reach the urethra.

<sup>75)</sup> Harkness mentions a case in which fly larvae were passed in the urine and Castellani <sup>76)</sup> confirms

the fact that larvae of flies occasionally set up a urethral inflammation. The screw worm, *chrysomya macellaria*, found chiefly in the West Indies is probably the most frequent invader.

5. Associated with Mycetes

Numerous fungi may cause intra-urethral lesions. The following table indicates four families and the genera associated with primary non-specific urethritis.

Family	Genera
Hypomycetidae	(Discomyces (Odium
Perisporacidae	(Aspergillus (Pencilium
Saccharomycetidae	(Endomyces (Saccharomyces (Cryptococcus (Monilia
Gymnoascidae	(Microsporon.

Scudder and Belding<sup>77)</sup> have described a case of chronic urethritis of six months duration in a young male. Urethral cultures showed numerous pin-point colonies of a pleomorphic chain organism subsequently shown to be of the claudothrix and streptothrix group.

Castellani<sup>78)</sup> classifies mycotic urethritis clinically according to the colour of the discharge into three subgroups:-

a. Urethritis with a white or yellow discharge which is usually associated with yeast - like fungi

of the genera monilia, cryptococcus or saccharomyces;  
b. urethritis with a brownish-black or greenish-black discharge mostly due to the presence of cladosporium, aspergillus or pencillium; and  
c. urethritis associated with red pigment producing yeast-like fungi.

He states that all the fungi found in non-gonorrhoeal urethritis in the male have also been found in vaginitis and vulvo-vaginitis, so that transmission of these infections by sexual intercourse is not improbable.

Case 9. A bus conductor, aged thirty years, unmarried, while receiving his third course of treatment for primary syphilis, developed a localised rash involving the skin of the upper inner aspect of the thighs, scrotum, and penis. A slight muco-purulent urethral discharge was also evident, but he complained of no dysuria or nocturnal frequency of micturition. His only symptom was slight itching around the meatus and in the groins. He denied recent exposure to infection. The rash was non-inflammatory, sharply demarcated, and consisted of a collection of reddish-brown patches with some degree of desquamation. The condition was diagnosed as erythrasma, and microsporon minutissimum was demonstrated microscopically in a cover glass preparation in potash using the oil-immersion lens. The same organism was found in a similar preparation of the urethral discharge. The





urine was very slightly hazy in the first glass and clear in the second. Rectal palpation revealed no abnormality.

Serological tests for syphilis and gonorrhoea were negative. The urethritis proved resistant to treatment with a 1 in 12,000 solution of mercury oxycyanide but rapidly cleared up when a 1 in 5,000 solution of acriflavine was substituted.

This case demonstrates that a mycotic urethritis may result from a fungus disease of the skin - the infection probably spreading to the urethra by continuity.

6. Associated with Filterable Viruses.

Intra-urethral herpes is a painful recurrent condition, usually accompanied by herpes genitalis on the glans penis and prepuce.

There is always considerable dysuria due to the passage of urine over an acutely inflamed surface. On examination through the urethroscope the picture is that of small, tender, inflamed papules becoming vesicular, later rupturing and eventually coalescing to form a superficial ulcer. The latter if infected by secondary organisms may simulate an intra-urethral chancroid, but the herpetic ulcer is more superficial the base more inflamed, the edges not undermined and the bacillus of Ducrey is absent.

A urethritis has been described during the course of measles <sup>79)</sup> and mumps. <sup>80) 81)</sup> Urethritis accompanying any of the exanthemata may be due to:-

- a. a generalised inflammation of the mucous membranes;
- b. the excretion of toxic products in the highly concentrated urine; or
- c. the causative virus infecting the urethral mucosa.

A combination of the first two factors is probably the true explanation in the majority of cases.

A urethritis occurs in lymphogranuloma inguinale when the primary lesion is intra-urethral. In this situation it is a very infectious condition, but unless a urethroscope is used climatic bubo is not suspected until lymphadenitis is evident. Gibson describes a case of climatic bubo with a slight urethral discharge containing some leucocytes and no organisms.

82)83)

84)

DIAGNOSTIC TECHNIQUE.

The technique employed in this series of 118 cases was as follows:-

1. A detailed history was first taken with particular reference to the duration of symptoms and previous venereal infections. Recent exposures of infection and the patient's habits as regards prophylaxis, self-treatment, alcohol, medicines, diet, etc., were noted.

Urinary symptoms such as dysuria, nocturnal frequency or urgency were inquired into.

2. An examination was then made of the genitals, noting the type and condition of the prepuce, any abnormality of the position or size of the meatal orifice, and the presence and character of any urethral discharge.

The penis was then palpated in order to detect any indurated areas or peri-urethral infiltrates.

The inguinal lymph glands, spermatic cords, epididymes and testicles were examined, and the skin of the scrotum, thighs, abdomen, buttocks and anal region carefully scrutinized. The buccal mucous membrane, tongue, palate and fauces were examined with an illuminated spatula.

3. A film of the meatal discharge was then made and stained by Jensen's modification of Gram's method and examined under the oil-immersion objective.

4. In the majority of cases cultures were taken in order to identify, if possible, any infecting



organism, and to assist in eliminating the gonococcus as a possible aetiological agent.

Having carefully cleansed the glans penis and meatal lips with sterile gauze soaked in spirit, the culture media - serum agar slopes and trypsin broth tubes - were inoculated with a platinum loopful of the urethral discharge.

After incubation for forty-eight hours subcultures were made from the trypsin broth onto plates of MacConkey's medium and serum agar.

In the examination of the serum agar slopes for colonies of gonococci the oxidase reaction was of considerable assistance.

This test was carried out by adding a few drops of a one per cent solution of dimethyl - para - phenylene - diamine hydrochloride to the slope. After half-an-hour any colonies of gonococci appeared jet black in contrast to the whitish growths of other organisms, with the exception of diplococcus catarrhalis and diplococcus flavus types which also gave a positive oxidase reaction.

5. The urine was passed into two glasses and a note taken of the presence of haze or threads in either glass.

6. The condition of the prostate gland and seminal vesicles was then ascertained by rectal examination.

7. Where the urethritis was not acute, as determined by clear urine samples in the two

glass test, a urethroscope was passed and a note made of the condition of the urethral mucosa, any evidence of littritis, the presence of stricture or other abnormality.

8. A sample of venous blood was taken for the Wassermann and Kahn reactions, and the gonococcal complement fixation test.

These tests were also repeated before the patient was finally discharged as cured.

DIAGNOSIS.

No case was included in this series of primary non-gonococcal urethritis where there was a history of gonorrhoea within the preceding twelve months, or where subsequent examination revealed a chronic prostatitis or other focus of infection of doubtful aetiology.

On microscopical examination of a stained smear of the urethral discharge, the absence of pus cells rules out all question of urethritis. A urethral exudate in which epithelial cells only are present is never associated with acute inflammation of the urethral mucous membrane.

The number of leucocytes per field gives some indication of the degree of inflammatory reaction. In very mild cases of non-specific urethritis occasioned for example by hyperalkaline or hyperacid reactions of the urine, sexual excesses or various articles of diet, there may be only two or three pus cells per field (using the 1/12 inch oil immersion objective and number 6 eyepiece). In severe cases resulting from streptococcal or bacillus coli infections the whole field is occupied by pus cells with an occasional epithelial cell; while in cases of chemical urethritis resulting from the use of weak antiseptic instillations or irrigations over a long period, epithelial cells predominate.

Though the diagnosis of acute gonorrhoea by



microscopical examination may be a relatively simple matter, the reverse is the case with pseudo-gonorrhoea.

Even after prolonged search of many films, one may be reluctant to come to a diagnosis of non-specific urethritis even when other bacteria are present in stained films. Harrison<sup>85)</sup> states that if pus is examined, in acute cases of urethritis before treatment is applied, the absence of gonococci with the presence of large numbers of other organisms will justify a diagnosis of non-gonococcal urethritis. In our opinion the presence of large numbers of other organisms merely increases the difficulty of finding the gonococcus in cases of untreated urethritis, but does not exclude that organism as an aetiological factor. In addition Gram-negative diplococci morphologically resembling the gonococcus may be found in cases of urethritis which are non-gonococcal.

Of these diplococci - *D. Catarrhalis*, *D. Flavus* types and the meningococcus - the former is a relatively common invader of the urethra, while the latter is an exceedingly rare cause of urethritis.

<sup>86)</sup> Storer referring to urethritis states that metastatic meningitic infection of the genitals is not an uncommon complication of cerebro-spinal fever. This statement, however, is not substantiated in other recent textbooks.

A typical smear from a case of urethritis due to

the diplococcus catarrhalis group (D. Catarrhalis and D. Flavus types) reveals Gram-negative diplococci arranged in pairs and clusters, but pus cells crowded with cocci, as in acute gonorrhoea, are exceptional. One must remember, however, that in the very early stages of a gonococcal urethritis the gonococci are more extra-cellular. In all doubtful cases, particularly of medico-legal importance, culture on a suitable medium such as Thomson's serum agar should be carried out.

The diplococcus catarrhalis group will grow on ordinary agar at room temperature, while the gonococcus requires a blood or serum enriched medium and a temperature in the vicinity of 37 degrees centigrade.

The final differentiation depends principally on the fermentive reactions shown in the subjoined table.  
87)

Fermentive reactions of Gram-negative diplococci.

Diplococcus	Glucose	Lactose	Saccharose	Maltose
D. Catarrhalis	-	-	-	-
D. Flavus types	<u>1</u>	<u>1</u>	<u>1</u>	<u>1</u>
D. Pharyngis siccus	<u>1</u>	-	<u>1</u>	<u>1</u>
D. Crassus	<u>1</u>	<u>1</u>	<u>1</u>	<u>1</u>
Meningococcus	<u>1</u>	-	-	<u>1</u>
Gonococcus	<u>1</u>	-	-	-

(1 = acid      1 = variation of reaction among  
different types)

D. Pharyngis siccus and D. Crassus have not been described in the literature on non-gonorrhoeal urethritis.

Regarding the gonococcal complement fixation test<sup>88)</sup> Price states that a strongly positive or even a positive reaction is definite evidence that the patient is suffering from gonorrhoea. On the other hand Dörffel<sup>89)</sup> quotes a number of cases in which a positive reaction persisted for several years although there was no evidence of persisting gonococcal infection. In the writer's experience a positive reaction means either active or recently active gonorrhoea.

In exceptional cases cross fixation, in infections with organisms other than the gonococcus, such as diplococcus catarrhalis, diplococcus flavus types (especially type 2) and the meningococcus, may give rise to a false positive result.

Price<sup>90)</sup> shows that this difficulty can be avoided by testing the serum against separate antigens of these organisms.

He quotes the case of a female child with a diplococcus catarrhalis rhinitis. Her blood serum tested by the complement fixation reaction recorded a negative result with a gonococcal antigen and a strongly positive result with a catarrhalis antigen.

In all the eight cases of diplococcus catarrhalis urethritis in the present series the complement fixation test was completely negative.

A misleading positive reading may also be obtained



in cases of non-gonococcal urethritis where large doses of gonococcal vaccine have been administered, For this reason all forms of vaccino-therapy should be withheld until a definite diagnosis has been reached. The present writer has found that the administration of a single provocative dose of gonococcal vaccine (500 million organisms non-detoxicated polyvalent vaccine) does not affect the gonococcal complement fixation test in cases of non-gonococcal urethritis, provided the sample of blood serum to be tested is taken within seven days of the provocative injection.

In early acute gonorrhoea the complement fixation test usually becomes positive about the third week after the commencement of symptoms if no treatment has been given.

From the clinical standpoint Price<sup>91)</sup> has noticed that a negative reaction changes to a positive when the gonococcal infection spreads to the posterior urethra or when there is a "closed" focus of infection.

It is, therefore, insufficient to rely on a negative complement fixation test for the diagnosis of non-gonococcal urethritis, as a negative reaction may also be obtained in male gonorrhoea:-

- a. in early acute infections of less than three weeks duration;
- b. where the infection is limited to the anterior

urethra; and

c. where there is an "open" focus of infection.

In all the cases of non-specific urethritis in this series the gonococcal complement fixation test was completely negative throughout the disease.

The above observations lead to the conclusion that:-

1. with two rare exceptions (cross-fixation and vaccino-therapy) the gonococcal complement fixation test is always negative in non-gonococcal urethritis; and

2. a urethritis with a negative complement fixation reaction does not necessarily exclude gonorrhoea, but is fairly strong evidence against it.

DIFFERENTIAL DIAGNOSIS.

In a consideration of the conditions which may simulate a primary non-gonococcal urethritis the following must be distinguished:-

1. Gonococcal urethritis.
2. Secondary non-gonococcal urethritis.
3. Urethrorrhoea<sup>1</sup>/<sub>2</sub>
4. Prostatorrhoea.
5. Spermatorrhoea.
6. Acute balanitis with phimosis.

1. Gonococcal Urethritis.

Microscopically there is nothing characteristic to distinguish a gonococcal from a non-gonococcal urethritis. The discharge in either disease may be mucoid or purulent, green or bloody, scanty or profuse. As has been shown, the fact that Gram-negative diplococci other than the gonococcus may be found in the male urethra presents the chief difficulty in diagnosis by microscopical examination of the urethral discharge.

In the large majority of cases a correct diagnosis of gonorrhoea can be reached by finding typical intra-cellular Gram-negative diplococci. Gonococci may be found extra-cellularly but as Harrison <sup>92)</sup> points out, "it is well to be very cautious about extra-cellular Gram-negative diplococci although they may look like two opposed coffee beans and be Gram-negative. Sometimes staphylococci may appear rather like gonococci having failed to retain the stain."

A positive complement fixation test points to a



gonococcal infection with the rare exceptions mentioned above.

2. Secondary non-gonococcal urethritis.

This condition differs from primary non-specific urethritis only in the history of recent gonorrhoea, and probably a positive gonococcal complement fixation reaction although a negative reaction does not exclude it. Chronic littritis and chronic prostatitis frequently accompany this condition, but these complications may be also found in the primary variety.

Recent observations <sup>93)</sup> on the morphology and cultural characteristics of the gonococcus suggests that typical Gram-negative organisms may, by cultural methods, be transferred into Gram-positive ones.

Wychmann and Schlunk <sup>94)</sup> referring to the clinical behaviour of the Gram-positive gonococcus state that the change in staining is associated with a diminution in virulence.

It is suggested that, possibly many Gram-positive streptococcal and staphylococcal - like organisms which are commonly reported as being found in smears in the later stages of gonorrhoea, may in reality be evolutionary forms of the gonococcus.

3. Urethrorrhoea

This term is applied to a clear sticky meatal exudate, which results from hyper-activity of the urethral glands, or which may appear following

sexual excitement without gratification.

Microscopical examination shows epithelial cells, but no leucocytes.

4. Prostatorrhoea.

This name is given to a thin opalescent meatal exudate consisting of prostatic secretion, and occurring during defaecation or after urination. The discharge is alkaline and contains corpora amylacea.

5. Spermatorrhoea.

This consists in the escape of seminal fluid from the urinary meatus without erection or desire. It may occur at anytime, but occasionally appears after defaecation particularly in association with constipation.

A stained film of the meatal exudate examined microscopically will show spermatozoa, but no pus or epithelial cells.

6. Acute Balanitis with Phimosis.

In this type of case it is frequently difficult to determine whether the subpreputial discharge results from a balanitis, a urethritis or both.

Repeated syringing subpreputially with saline will wash away a considerable amount of the balanitic discharge and subsequent examination of the urine will determine whether there is an acute urethritis present or not. By far the best procedure to adopt, however, is to perform a dorsal slit in all such cases and thoroughly examine the whole prepuce, the

glans penis and the urinary meatus.



CONCLUSIONS.

1. Primary non-gonococcal urethritis is a relatively common condition. Approximately one in every seven cases of urethritis is non-specific.
2. There are two types of primary non-specific urethritis - irritative and infective - occurring with almost equal frequency.
3. In this district, where self-applied prophylactic measures are rife, chemical urethritis is the most frequent type encountered. In history-taking it is insufficient to ask "Have you given yourself any treatment?" Direct inquiry must also be made regarding the possible injection or instillation of antiseptic solutions into the urethra; as many patients do not consider that this form of prophylaxis is treatment. Some contraceptives may give rise to a urethral inflammation in susceptible individuals.
4. Sexual intercourse is the commonest mode of transference of the disease in cases of infective urethritis.
5. In resistant cases of non-gonococcal urethritis, especially if accompanied by balanitis, the urine should be examined for sugar.

6. Under conditions favourable to bacteria normally inhabiting the male urethra, a non-specific bacterial urethritis may arise without the introduction of organisms into the urethra from without.
7. Staphylococcus albus is by far the commonest organism found in the urethral discharge of these cases.
8. Diplococcus catarrhalis may cause an acute urethritis with complications closely resembling acute gonorrhoea.  
Differentiating features are:-
  - a) On microscopical examination of stained smears the Gram-negative diplococci are more extracellular than in gonorrhoea;
  - b) diplococcus catarrhalis can be cultured at room temperature on ordinary media;
  - c) the gonococcal complement fixation test is negative; and
  - d) the disease responds more rapidly to routine methods of treatment.
9. Almost all the streptococci, found in the urethral discharge from cases of urethritis in the male, are of the faecalis type.
10. In order that intra-urethral chancres shall not be overlooked, the following details should be attended to in every case of urethritis whether gonococcal or non-gonococcal:-

- a) the penis and inguinal regions should be palpated with the gloved hand;
  - b) the skin of the thighs, abdomen, back and anus should be thoroughly inspected. The buccal mucous membrane and tongue should be examined in a good light;
  - c) where a lymphadenitis exists a dark-ground examination should be performed on the urethral discharge or on serum obtained by gland puncture;
  - d) all patients admitting a risk of venereal disease should be kept under observation for a period of not less than four months from the date of the last exposure to infection; and
  - e) a specimen of the blood for serological tests should be taken at the first visit of the patient and also shortly prior to the final attendance.
11. If a urethritis is present leucocytes can always be found in the meatal exudate.
12. Under suitable conditions for infecting the urethra, almost any pathogenic organism may cause a primary non-gonococcal urethritis.
13. The diagnosis of non-specific urethritis depends principally on the elimination of the gonococcus as an aetiological factor.
- This can only be done if:-



- a) repeated Gram-stained smears show no typical intracellular Gram-negative diplococci;
- b) no colonies of gonococci are grown on culture under favourable conditions; and
- c) the gonococcal complement fixation test is negative throughout the course of the disease.

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